The association between an increased body mass index (BMI) and Chiari malformation Type I (CM-I) is not clear. There are several individual reports of obese individuals with CM-I, which have led some authors to speculate that an elevated BMI may be a causative factor for CM-I.4,18 The authors of 2 recent case series found that patients with CM-I frequently had a BMI in the obese range, and they postulated that an elevated BMI may play a pathophysiological role in CM-I, syrinx formation, or CM-I symptoms.4,9

CM-I is defined on imaging by determining the inferior extent of the cerebellar tonsils with respect to the foramen magnum; a measurement of ≥ 5 mm is generally considered consistent with an imaging diagnosis of this condition.1,8,12,20,26 To our knowledge, there has never been an analysis of the role of BMI in cerebellar tonsil position or CM-I in any study that included individuals who were not selected for CM-I evaluation. The true relationship between CM-I and elevated BMI, if any, is therefore unclear. Our objective was to determine the relationships, if any, among BMI, tonsil position, and CM-I.

Impact of body mass index on cerebellar tonsil position in healthy subjects and patients with Chiari malformation

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OBJECT It is unclear if there is a relationship between Chiari malformation Type I (CM-I) and body mass index (BMI). The aim of this study was to identify the relationship between BMI and cerebellar tonsil position in a random sample of people.

METHODS Cerebellar tonsil position in 2400 subjects from a cohort of patients undergoing MRI was measured. Three hundred patients were randomly selected from each of 8 age groups (from 0 to 80 years). A subject was then excluded if he or she had a posterior fossa mass or previous posterior fossa decompression or if height and weight information within 1 year of MRI was not recorded in the electronic medical record.

RESULTS There were 1310 subjects (54.6%) with BMI records from within 1 year of the measured scan. Of these subjects, 534 (40.8%) were male and 776 (59.2%) were female. The average BMI of the group was 26.4 kg/m², and the average tonsil position was 0.87 mm above the level of the foramen magnum. There were 46 subjects (3.5%) with a tonsil position ≥ 5 mm below the level of the foramen magnum. In the group as a whole, there was no correlation (R² = 0.004) between BMI and cerebellar tonsil position.

CONCLUSIONS In this examination of 1310 subjects undergoing MRI for any reason, there was no relationship between BMI and the level of the cerebellar tonsils or the diagnosis of CM-I on imaging.

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KEY WORDS body mass index; Chiari malformation; obesity; syrinx; diagnostic and operative techniques

ABBREVIATIONS BMI = body mass index; CM-I = Chiari malformation Type I; ICP = intracranial pressure; SD = standard deviation.

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DISCLOSURE The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
Methods

After approval by the University of Michigan Institutional Review Board, we performed a search of our imaging database, which contains data on 62,533 consecutive patients who underwent brain or cervical spine MRI for any reason over an 11-year interval at our institution. From this cohort, 300 patients from each of 8 age cohorts (0–10, 11–20, 21–30, 31–40, 41–50, 51–60, 61–70, and >71 years) were selected randomly. Ages were determined at the time of MRI. The subjects were chosen from the database by matching the last 2 digits of their randomly assigned record numbers to randomly generated 2-digit numbers. Randomization was completed when the target cohort size was achieved.

Our initial analysis of tonsil position in these patients was reported previously.26 The current analysis of the role of BMI in tonsil position was carried out in this cohort. Patients were excluded from the initial cohort of 2400 randomly selected patients if there was imaging evidence of any significant posterior fossa comorbidity that would influence tonsil position. Excluded patients included those with a posterior fossa tumor (n = 26), a posterior fossa arachnoid cyst (n = 45), previous posterior fossa surgery other than CM decompression (n = 23), previous CM decompression (n = 17), a significant mass effect from a primarily supratentorial process (including untreated hydrocephalus) (n = 17), volume loss from previous stroke (n = 9), or a developmental abnormality (including CM Type II) (n = 14). MRI scans of 2551 patients were reviewed to assemble 8 groups of 300 patients each (2400 total patients) for the initial analysis.26 Furthermore, to be included in this subsequent analysis of the role of BMI and tonsil position, each patient must have had a height and weight measurement within 1 year of the measured scan; 1090 were excluded because of insufficient height (n = 104 patients), weight (n = 5), or height and weight (n = 981) data points.

The MRI scans of each of the selected patients were then reviewed, and tonsil position measurements were recorded as detailed in our previous report.26 For purposes of this analysis, tonsils that extended caudally to the basion-opisthion line were assigned positive values, and tonsils that ended rostrally to the basion-opisthion line were assigned negative values; tonsils that ended at the basion-opisthion line were assigned a value of 0. CM-I was defined on imaging as a cerebellar tonsil position ≥ 5 mm below the basion-opisthion line.1,8,12,20,26 Measurements were recorded to the nearest millimeter. Two tonsil measurements were taken for each patient, one in the midsagittal plane and one in the parasagittal plane that corresponded to the lowest tonsil position on the left or right side. Each image was measured, and the measurement was agreed upon by 2 investigators, one of whom was a board-certified pediatric neurosurgeon.

SAS 9.2 statistical software (SAS Institute) was used to generate reports and figures based on the data. Mean differences were evaluated for statistical significance using t-test analysis. Simple descriptive statistics were generated using the means procedure.

Results

Of the subjects who met all the inclusion criteria, 534 (40.8%) were male and 776 (59.2%) were female. The mean BMI was 26.4 kg/m². Of the 1310 included subjects, there were 963 adults (≥18 years) with an average BMI of 28.5 kg/m² (SD 6.9 kg/m²) and 347 children with a mean BMI of 20.4 kg/m² (SD 6.4 kg/m²) (Fig. 1). There were 46 subjects (3.5%) with a tonsil position ≥ 5 mm below the level of the foramen magnum. The mean BMI for all subjects with a tonsil position ≥ 5 mm below the foramen magnum was 25.75 kg/m² (SD 9.8 kg/m²) compared with 26.4 kg/m² (SD 7.5 kg/m²) for those with tonsils above the 5-mm line (p = 0.57) (Fig. 2). In our group, a BMI of at least 41.6 kg/m² was >2 SDs from the mean. The percentages of subjects at ≥2 SDs above the mean did not differ (p = 0.98) between the CM-I group (n = 2 [4.3%]) and the non–CM-I group (n = 54 [4.3%]). In the group as a whole, there was no correlation (R² = 0.004) between BMI and tonsil position (Fig. 3). When children and adults were considered separately, we still found no effect. The pediatric (R² = 0.0003) and adult (R² = 0.0005) groups both showed no correlation between BMI and tonsil position.

Excluded were 104 patients—86 adults and 18 children—because their heights were not recorded within 1 year of the scan. Adult subjects excluded for this reason had a mean weight of 78.5 kg (SD 20.8 kg), and the adults included in the study had a mean weight of 80.4 kg (SD 20.6 kg). The weights of the included and excluded adults did not differ significantly (p = 0.41). Children excluded for this reason had a mean weight of 49.6 kg (SD 27.2 kg), and the children included in the study had a mean weight of 40.9 kg (SD 28.6 kg). The weights of the included and excluded children did not differ significantly (p = 0.21). In the excluded subjects, the mean tonsil position was 1.2 mm above the level of the foramen magnum (SD 3.2 mm). In the subjects included in the analysis, the mean tonsil position was 0.9 mm above the level of the foramen magnum (SD 3.5 mm).

Most of the patients with a tonsil position at least 5 mm below the foramen magnum had no syrinx (41 of 46 [89.1%]). Those patients with CM-I but no syrinx had a mean tonsil position 7.7 mm (SD 3.1 mm) below the foramen magnum and a mean BMI of 26.3 kg/m² (SD 9.6 kg/m²). The mean BMI in the subjects with CM-I and no syrinx who were ≤18 years of age was 19.6 kg/m² (SD 5.2 kg/m²), and for adults with CM-I and no syrinx who were >18 years of age, the mean BMI was 31.1 kg/m² (SD 9.1 kg/m²). Five of the 46 patients with CM-I also had a spinal syrinx. The mean BMI for patients with a syrinx was 21.2 kg/m². Of the 5 patients with a syrinx, 4 (80%) were ≤18 years old, and each had a BMI of ≤20 kg/m². Patients with a syrinx had a mean tonsil position 14.2 mm (SD 4.1 mm) below the foramen magnum, which is significantly lower than the position in those without a syrinx (7.7 mm [SD 3.1 mm]; p = 0.0001).

Of the 46 patients with CM-I, 7 (15.2%) were considered possibly symptomatic by the treating physician and 6 (13.0%) underwent surgical decompression. Five patients had CM-I surgery at our institution, and 1 decompression was performed at another hospital. The mean tonsil position in symptomatic patients was 13.6 mm (SD 3.7 mm).
below the foramen magnum, and for those with asymptomatic CM-I, it was 7.5 mm (SD 3.0 mm). Seventeen patients had a history of headaches recorded in the medical record, and most of these patients (15 of 17 [88.2%]) had a neurological evaluation. In most cases, the headaches were long-lasting and lacked significant tussive characteristics. Three patients had headaches with a tussive component; 2 of them had a BMI in the normal range, and 1 was obese. The mean BMI for all the patients with CM-I with a recorded headache history was 27.6 kg/m², and the mean BMI for the 3 patients with tussive headaches was 26.3 kg/m². Of the patients with any report of tussive headache, 1 patient had only tussive-type headaches, and 1 patient presented with long-lasting holocranial headaches with a relatively minor tussive component; the patient with the holocranial headaches had a normal BMI (20.2 kg/m²) and underwent surgical treatment because of an associated syrinx and scoliosis. Two patients had typical tussive-type headaches that were associated with the CM-I and underwent CM-I decompression surgery. Both of these patients were adults at the time of diagnosis. One of these patients had a normal BMI (17.4 kg/m²), and the other had a BMI in the obese range (41.3 kg/m²). The mean tonsil position below the foramen magnum was 16.3 mm for the patients with tussive headaches and 6.2 mm for those with headaches without a significant tussive component.

Discussion

Some authors have suggested that CM-I or its symptomatic presentation may be associated with an elevated BMI. We analyzed cerebellar tonsil positions and BMIs in a large series of patients of all ages who underwent MRI for any reason to explore the relationship between low tonsil position or CM-I and BMI. We found no relationship between tonsil position and BMI. The mean tonsil position with respect to the foramen magnum can be expected to vary according to the ages of the population but is not affected by BMI. We also found no convincing evidence that an elevated BMI is associated with syrinx in those with CM-I.

The authors of 2 recent case series found that the mean BMI of patients who underwent CM-I decompression was above the normal range. Batzdorf et al. found that the mean BMI for 177 adult patients who underwent CM-I decompression at their institution was 26.4 kg/m². Similarly, Arnautovic et al. reported on 60 adults who underwent CM-I decompression, and they found a mean BMI of 30.4 kg/m². In both reports, these authors focused on the patients who underwent CM-I decompression and did not provide a control group. In our population, the mean BMI for all patients regardless of tonsil position was 28.5 kg/m², not substantially different than the BMI for those patients with CM-I.

The basis of the putative relationship between an elevated BMI and CM-I rests on theories of the relationship between CM-I and elevations in intracranial pressure (ICP). There is robust evidence for an association between obesity and idiopathic intracranial hypertension (pseudotumor cerebri). Just as obesity has been linked to

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Fig. 1. Line graph illustrating the mean tonsil locations in patients grouped according to BMI.

Fig. 2. Line graph indicating the mean BMIs (with SD) of patients with a low or normal cerebellar tonsil position (p = 0.57).
elevated ICP, at least in some cases, there have also been several reports that have linked elevated ICP with CM-I. It is probable that symptoms of CM and the formation of spinal syrinxes are the result of crowding at the foramen magnum, which results in abnormal cerebrospinal fluid flow at the cranio cervical junction. Theoretically, elevations in ICP may exacerbate this condition and lead to an increased risk of syrinx. Because an elevated BMI may be associated with increased ICP in certain cases, some authors have speculated that an elevated BMI may contribute to syrinx formation. In a series reported by Arnautovic et al., the length of the syrinx was slightly shorter in 7 individuals with a normal BMI (BMI 18.5–24.9 kg/m²) than that in 5 overweight individuals (BMI 25–29.9 kg/m²). In that study, however, the syrinx length was actually shortest in 14 obese individuals (BMI ≥ 30 kg/m²), which casts doubt on any real causative relationship. Similarly, the authors found no correlation between syrinx width and BMI and no difference in BMIs between those with and those without a syrinx. Arnautovic et al. also reported on a single case of syrinx improvement after weight loss. Because spontaneous syrinx improvement has been reported, it is difficult to draw any conclusions from individual case reports.

There are several limitations to our analysis. Selection bias must be considered in any interpretation of these results. All patients in this analysis were selected from a population of those who were undergoing imaging. The method for measuring the tonsil position in this group cannot be expected to exactly match that of the population as a whole. The detection of tonsil position must be considered when comparing analyses of the prevalence of CM. In our previous studies of the prevalence of CM-I in children who were undergoing imaging, we found different prevalences of CM according to the methods used in our searches. Direct examination of the MR images with measurement of tonsil positions resulted in an increased rate of patients with a tonsil position ≥ 5 mm below the foramen magnum over that from analyses that we performed by searching the text of radiology records. We acknowledge that this study could be improved with a

FIG. 3. Scatterplot showing the relationship between tonsil position and BMI.
larger sample size. A power analysis was performed, and our sample could detect a 0.3-mm difference between the groups with adequate (0.8) power. Although a larger sample size would have allowed us to detect smaller differences between the groups, we believe that our sample size was powered adequately to detect any clinically significant effects.

There is much to dislike about the current definition of CM-I. First, as noted by several other groups, CM-I does not meet the usual definition of a malformation. Furthermore, on the basis of recent information, the imaging diagnosis of this condition, once a straightforward matter of measuring the tonsils below the foramen magnum, is also a fair subject for debate. In this analysis, the diagnosis of CM-I via imaging was made in the usual way by determining the cerebellar tonsil position to be ≥ 5 mm below the foramen magnum. It is likely that patients with CM-I have a reduced posterior fossa volume, which results in crowding at the foramen magnum. Although cerebellar tonsil position is a convenient marker for crowding at the foramen magnum, the correlation is not exact. In some cases, patients with < 5 mm of descent can have a clinical presentation of Chiari syndrome and even syringomyelia caused by crowding at the foramen magnum. Nevertheless, to make our analysis clear and consistent with other analyses in the literature, we followed the usual custom of considering those with tonsils that are ≥ 5 mm below the foramen magnum as a separate group.

Conclusions
For most patients, cerebellar tonsil position is not influenced by BMI.

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Conception and design: Maher. Acquisition of data: Smith, Strahle, Kazarian. Analysis and interpretation of data: all authors. Drafting the article: Maher, Smith, Strahle. Critically revising the article: Maher, Garton, Muraszko, Smith, Strahle. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Maher. Study supervision: Maher.

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5 THINGS I BELIEVE ABOUT CHIARI MANAGEMENT

1. I always open the dura when there is a syrinx.
2. I almost never place a syrinx shunt.
3. I do not think that FM CSF flow is clinically useful.
4. I almost always recommend CM decompression if there is a large cervical syrinx, even in asymptomatic cases.
5. I almost never restrict sports participation for CM patients that are not selected for surgery.

5 THINGS I BELIEVE ABOUT CHIARI EPIDEMIOLOGY

1. There is no consensus about how to define CM.
2. Symptomatic CM is rare BUT asymptomatic CM on imaging is very common.
3. Symptoms and syringes are more likely with increasingly lower tonsil position.
4. The 5mm rule for tonsil position is a seriously flawed criterion.
5. The natural history for asymptomatic or minimally symptomatic individuals is good in most cases.

CHIARI EPIDEMIOLOGY:

1. PREVALENCE
2. NATURAL HISTORY

HOW DO WE DEFINE DISEASE?
**SYMPTOMATIC CM**

- 741,815 patients under age 20 in Kaiser Northern California
- 5,248 underwent MRI (0.71%)
- 32 symptomatic children with CM on imaging
- 2 year period prevalence = 0.7/10,000

**SYMPTOMATIC CM IS RELATIVELY RARE**

**SYMPTOMATIC CM IS RELATIVELY RARE**

**CLINICAL OR IMAGING CRITERIA?**

**THE "5MM RULE"**

- Chiari 0
- "Asymptomatic Chiari I"
- It is, at best, a marker for more important but harder to measure pathoanatomical features.

**THE "5MM RULE"**

- So why do we still use it?
  - Historical reasons
  - Easy
  - Somewhat objective - at least more than "crowding"
WHY 5MM?

Asymptomatic / incidental CM is very common

Does age matter?

Tonsil position distribution by decade of life

Tonsil position is a typical morphometric measurement

Mikulis et al., Radiology 1992

Smith et al., JNS

Sun et al., Spine

JNS 2013
MORPHOMETRIC MEASUREMENTS TO DEFINE SPECIES

WHAT IS THE CLINICAL RELEVANCE OF TONSIL POSITION?

TONSIL POSITION IS A RISK FACTOR FOR CM SYMPTOMS

TONSIL POSITION IS A RISK FACTOR FOR SYRINX

SYRINX ASSOCIATION

ARE CHIARI-ASSOCIATED SYRINGES DIFFERENT?
SYRINGE LOCATION

SYRINGE WIDTH

PREVALENCE - CONCLUSIONS

5mm should not be considered a cut-point with definite pathological implications

5mm is the low end of the normal distribution that may be associated with symptoms in some individuals

The lower the tonsil position, the more likely to be symptomatic and to be associated with syrinx

AGE MATTERS

NATURAL HISTORY

- Novegno et al:
  - 22 patients over 6 years
  - 6 had new CM sx
  - 3 had CM decompression

- Benglis et al:
  - 124 patients over 9 years
  - 14 had CM sx
  - 7 patients had syrinx
  - 5 patients worsened and surgery was recommended

- Strahl et al:
  - 148 patients over 5 years
  - 16 had CM decompression
  - 7 had NEW syrinx
1. There is no consensus about how to define CM.

2. Symptomatic CM is rare BUT asymptomatic CM on imaging is very common.

3. Symptoms and syringes are more likely with increasingly lower tonsil position.

4. The 5mm rule for tonsil position is a seriously flawed criterion.

5. The natural history for asymptomatic or minimally symptomatic individuals is good in most cases.
Natural history of Chiari malformation Type I following decision for conservative treatment

Clinical article

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Object. The natural history of the Chiari malformation Type I (CM-I) is incompletely understood. The authors report on the outcome of a large group of patients with CM-I that were initially selected for nonsurgical management.

Methods. The authors identified 147 patients in whom CM-I was diagnosed on MR imaging, who were not offered surgery at the time of diagnosis, and in whom at least 1 year of clinical and MR imaging follow-up was available after the initial CM-I diagnosis. These patients were included in an outcome analysis.

Results. Patients were followed clinically and by MR imaging for a mean duration of 4.6 and 3.8 years, respectively. Of the 147 patients, 9 had new symptoms attributed to the CM-I during the follow-up interval. During this time, development of a spinal cord syrinx occurred in 8 patients; 5 of these patients had a prior diagnosis of a presyrinx state or a dilated central canal. Spontaneous resolution of a syrinx occurred in 3 patients. Multiple CSF flow studies were obtained in 74 patients. Of these patients, 23 had improvement in CSF flow, 39 had no change, and 12 showed worsening CSF flow at the foramen magnum. There was no significant change in the mean amount of cerebellar tonsillar herniation over the follow-up period. Fourteen patients underwent surgical treatment for CM-I. There were no differences in initial cerebellar tonsillar herniation or CSF flow at the foramen magnum in those who ultimately underwent surgery compared with those who did not.

Conclusions. In patients with CM-I that are selected for nonsurgical management, the natural history is usually benign, although spontaneous improvement and worsening are occasionally seen. (DOI: 10.3171/2011.5.PEDS11122)

Key Words • Chiari malformation • syrinx • natural history

Abbreviations used in this paper: CM-I = Chiari malformation Type I; EMERSE = Electronic Medical Record Search Engine.
Natural history of Chiari malformation Type I

CM-I surgically if a syrinx is present has made natural history analysis of this subgroup particularly challenging. We hope that an analysis of a large group of patients with CM-I with or without associated spinal cord syrinx that have been selected for nonsurgical management will improve our understanding of the natural history of these conditions, and ultimately improve surgical management decisions for this group of patients.

Methods

Medical Records Search

Following approval by the Institutional Review Board at the University of Michigan, we performed a retrospective review of the electronic medical records of all patients ≤ 18 years of age who underwent brain or cervical spine MR imaging at the University of Michigan between November 1997 and August 2008. Brain or cervical spine MR images were obtained in 14,116 individual children during this period. All MR images were performed on either a 1.5- or 3-T MR imaging device. Electronic records were reviewed using the Electronic Medical Record Search Engine (EMERSE), a search engine that queries all free-text documents within the electronic medical records of a specified patient population. In this study, we used EMERSE to identify a population in whom the terms “tonsillar ectopia,” “tonsillar herniation,” “tonsillar descent,” “syrinx,” “myelomeningocele,” “hydromyelia,” and “Chiari” were used in any part of the medical record. We then reviewed the records of all patients identified by EMERSE to select those who met the criteria for inclusion.

All included patients had cerebellar tonsillar ectopia measured as ≥ 5 mm below the foramen magnum. Also, to be included in the analysis, all patients who were treated nonsurgically must have had at least a 1-year interval between the first and last clinical assessment and at least a 1-year interval between the first and last MR imaging session. Any patient who underwent surgical treatment for a CM-I on the basis of a recommendation made at the initial neurosurgical consultation was excluded from analysis. Patients who were treated surgically at an interval following an initial recommendation for nonsurgical management were included, even if the interval between the initial evaluation and surgical treatment was < 1 year. Patients were excluded if the cerebellar tonsillar descent was believed to be secondary to mass effect from other intracranial or cranial conditions such as tumor, cerebral edema, arachnoid cyst, or craniosynostosis. Any patient who met criteria for CM-II, -III, or -IV, including a history of myelomeningocele repair, was excluded from analysis. Finally, any patient who had undergone surgical treatment for CM-I prior to MR imaging evaluation at our institution was excluded.

We identified 509 patients who met the initial inclusion criteria for a diagnosis of CM-I on MR imaging at our institution. Of these, 120 patients were excluded because a recommendation for surgical treatment was made at the first clinical assessment. Another 242 patients were excluded because they had < 1 year of clinical and MR imaging follow-up. A total of 147 patients met all inclusion criteria for the natural history analysis. For these patients, we recorded age and sex, neurological symptoms, other clinical diagnoses, other radiological diagnoses, the indication that was provided for performing the initial MR imaging, and any surgical treatment. In addition, we recorded imaging characteristics of the CM-I, including the amount of cerebellar tonsillar descent, CSF flow at the foramen magnum, and the presence of any spinal cord syrinx. If a patient had more than 2 MR imaging studies, we considered only the studies performed at the time of CM-I diagnosis as well as the most recent ones in nonsurgically treated patients, or the MR imaging studies performed immediately preceding surgery in surgically treated patients. Not all patients underwent complete spine imaging at the time of CM-I diagnosis; therefore, for those patients with a spinal cord syrinx, the initial MR imaging study that demonstrated a syrinx was considered to be the initial spine study for these patients. The CSF flow was categorized as normal, decreased anteriorly or posteriorly at the foramen magnum, or decreased at the foramen magnum with abnormal tonsillar pulsations.

For the purpose of this analysis, the presence of a syrinx was defined as a spinal cord cyst (hypointensity on T1-weighted images, with corresponding T2 hyperintensity) ≥ 3 mm in maximal anteroposterior diameter on sagittal or axial imaging. Presyrinx states (T2 hyperintensity, indistinct T1 prolongation, without cavitation) were classified separately. If a syrinx was present, we recorded its diameter in millimeters at the widest diameter as viewed on sagittal imaging. The length of the syrinx was recorded according to the number of corresponding vertebral levels.

Statistical Analysis

Statistical significance calculations were obtained using ANOVA, the chi-square test, and Tukey multiple comparisons. Univariate logistic regression was used to evaluate change over time. Data were analyzed using SPSS version 16.0 software (SPSS, Inc.).

Results

Patient Population

Included in the analysis were 147 patients ≤ 18 years of age (mean age 7.7 years). The mean duration of MR imaging follow-up was 3.8 years. The mean length of clinical follow-up by a neurosurgeon or neurologist was 4.6 years, and the mean duration of clinical follow-up by any physician at our hospital was 6.5 years. In the study population, 76 (51.7%) patients were female. Other clinical conditions and imaging findings diagnosed in the study group are summarized in Table 1.

Tonsillar Descent

There was no change in mean cerebellar tonsillar herniation for the group as a whole over a mean follow-up of 3.8 years. The mean tonsillar herniation was 9.53 mm at presentation and 9.34 mm at follow-up (p = 0.4). Considered individually, however, many patients did have a change in the amount of tonsillar descent (Fig. 1).
J. Strahle et al.

Changes in tonsillar herniation ≤ 2 mm over the follow-up interval were seen in 103 patients (73%). Interval improvement in the amount of tonsillar descent was seen in 45 patients (31%), and 7 patients had a follow-up MR imaging study with < 5 mm tonsillar descent, and were therefore no longer considered to have a CM-I by our criteria. An increase in tonsillar herniation of at least 4 mm was seen in 6 patients (4%). Of the 14 patients who were surgically treated, 11 had interval MR imaging studies prior to surgery. Those patients who were not treated surgically over the follow-up interval had a mean decrease in tonsillar herniation of 0.32 mm, and those treated with surgical decompression during the follow-up interval had a mean increase in tonsillar herniation of 0.93 mm prior to surgery.

Evaluation of CSF Flow

The CSF flow at the foramen magnum was evaluated on MR images obtained in 74 patients at the time of CM-I diagnosis as well as at the time of the most recent follow-up MR imaging session or the MR imaging studies performed prior to surgery. Interval improvement in CSF flow was seen in 23 patients, 39 patients had no change in CSF flow, and 12 patients had decreased CSF flow on the follow-up study compared with the initial MR imaging. The patient’s age at time of CM-I diagnosis was not predictive of changes in CSF flow over the follow-up interval. Of the 14 patients who were treated surgically, 7 had interval CSF flow studies for comparison, and all 7 of these patients had stable (5 patients) or improved (2 patients) CSF flow. Of the 12 patients with decreased CSF flow on follow-up imaging, none had worse symptoms or a new syrinx, and none were treated surgically. A change in CSF flow analysis was never used as a surgical indication in this series of patients.

Syrinx Characteristics

A spinal cord syrinx of at least 3 mm diameter was

![Fig. 1. Bar graph illustrating change in tonsillar herniation in 147 patients with CM-I.](image1)

![Fig. 2. Scatterplot demonstrating change in tonsillar herniation by age at the time of CM-I diagnosis (regression slope estimate −0.15; p = 0.007).](image2)
Natural history of Chiari malformation Type I

...found in 20 patients (13.5%). In 13 of these patients, the syrinx was present at the time of CM-I diagnosis. Development of a syrinx during the follow-up interval occurred in 7 patients, with a mean time to syrinx development of 28 months (range 2–74 months). One patient with a thoracic syrinx developed a new cervical spine syrinx during follow-up. Of the 7 new syringes, 2 developed from a previously identified presyrinx state (hyperintensity on T2-weighted MR imaging studies without cavitation), 3 developed from what had been considered a dilated central canal < 3 mm in diameter, and 2 patients had normal results on prior spine MR images (Fig. 3). In the 13 patients with a syrinx at the time of CM-I diagnosis, 6 lesions were unchanged in size, 5 were smaller, and 2 were larger on follow-up MR imaging. Of the 5 patients with spontaneous improvement in syrinx size, 3 demonstrated complete syrinx resolution on follow-up MR imaging.

Despite these examples of individual changes in syrinx dimensions, when the group was analyzed as a whole there was no change in average initial (4 vertebral levels) and final syrinx length (p = 0.88; Fig. 4 left). In addition, there was no significant change in the mean initial (4.25 mm) and final (3.56 mm) syrinx width (p = 0.16; Fig. 4 right). All 5 patients who had a decrease in syrinx size were female. Patients with syrinx progression (mean age 6.7 years) or regression (mean age 5.6 years) were younger (p = 0.05) compared with those whose syrinx remained stable (mean age 11.6 years). Patients with new syrinx formation over the follow-up interval had a mean initial tonsillar herniation of 13.5 mm. Those patients with larger syringes on follow-up imaging had a greater mean initial tonsillar herniation (14.5 mm) compared with those with a stable (8.6 mm) or decreased (8.6 mm) syrinx size (p = 0.04).

Of the 20 patients with a spinal cord syrinx, 6 were treated surgically during the follow-up interval. Of these 6, concern for the syrinx was documented as a primary issue...
consideration in the decision to recommend surgery in 4 cases. The remaining 2 patients underwent surgery for reasons thought to be unrelated to changes in the syrinx. There was an association between eventual surgical treatment and a prior increase in syrinx width (0.7 mm, p = 0.05) and length (2.2 levels, p = 0.08).

**Symptoms of CM-I**

A patient was designated as being symptomatic from their CM-I if either the primary neurologist or neurosurgeon treating the individual at our institution thought that the complement of presenting symptoms was attributable to the lesion. There was no significant difference in the number of symptomatic patients between the time of initial presentation and the most recent follow-up. There were 5 patients who remained symptomatic throughout the follow-up interval. The 6 patients who were symptomatic at presentation were not so at last follow-up. Another 9 patients who had symptoms that were initially not thought to be due to the CM-I were considered to be symptomatic at the time of the most recent evaluation.

**Rationale for Surgery**

Of the 147 patients in the study group, 14 underwent surgery for CM-I (Table 2). The most common reasons for surgical treatment during the follow-up interval were medically refractory and persistent headaches, sleep apnea, and changes in a syrinx. For these 14 patients, the mean time to surgery after CM-I diagnosis was 2.1 years (Fig. 5). There was no significant difference in the initial tonsillar herniation in the group that ultimately underwent surgery compared with those individuals who did not undergo surgery. In addition, there were no significant differences in the change in CSF flow at the foramen magnum between the group that underwent surgery and the group that did not have surgery.

**Discussion**

We analyzed the outcome of a group of 147 children with CM-I that was initially managed without surgery. Of these, 14 patients eventually underwent surgical intervention, and 133 patients remained asymptomatic or minimally symptomatic. Spontaneous clinical and radiological improvement was seen in some cases. These data support a generally benign natural history for those patients with CM-I that meet the usual criteria for conservative management.

There is very little existing information on the natural history of CM-I. Novegno et al. recently reported on a series of 22 patients for whom nonsurgical management was recommended. Over a mean follow-up interval of 5.9 years, they found that 5 patients had symptomatic worsening, and 3 of these required surgery. Spontaneous improvement was seen in 3 of their patients, and 1 patient had complete resolution. They concluded that a conservative approach to asymptomatic or minimally symptomatic patients could be justified based on their data. Nishizawa et al. reported on 9 adults with CM-I and a spinal cord syrinx in whom the entity was managed without surgery, and found that 8 of these patients had a benign natural course. There are several reported cases of CM-I with spontaneous improvement in cerebellar tonsillar herniation. In many of these cases, improvement in the degree of tonsillar herniation was associated with a decrease in the size or resolution of the associated syrinx. Because the presence of CM-I on imaging does not have any pathological consequences in many cases, several surgeons have recently suggested a preference for the term “Chiari Type I anomaly” rather than “Chiari malformation.”

**TABLE 2: Results in 14 patients receiving surgical treatment for CM-I following an initial decision for conservative management**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Preop Symptoms</th>
<th>Time to Op (days)</th>
<th>Descent (mm)</th>
<th>Syrinx Initial</th>
<th>Syrinx Final</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>syrinx progression</td>
<td>179</td>
<td>8.0</td>
<td>ND yes; new</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>worsening HAs</td>
<td>183</td>
<td>20.0</td>
<td>20.0 no</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>sleep apnea</td>
<td>214</td>
<td>16.0</td>
<td>16.0 no</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>sleep apnea</td>
<td>232</td>
<td>15.0</td>
<td>20.0 no</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>worsening HAs</td>
<td>367</td>
<td>16.0</td>
<td>ND no</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>HA refractory to medical therapy</td>
<td>434</td>
<td>15.0</td>
<td>ND no</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>rapid progression of scoliosis</td>
<td>474</td>
<td>8.0</td>
<td>8.0 yes; new</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>central sleep apnea</td>
<td>526</td>
<td>10.0</td>
<td>10.0 yes</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>new syrinx</td>
<td>812</td>
<td>17.0</td>
<td>20.0 yes</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>concern for neurological decline</td>
<td>849</td>
<td>12.0</td>
<td>15.0 yes</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>concern for neurological decline</td>
<td>1152</td>
<td>12.0</td>
<td>9.0 no</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>worsening HAs, occipital neck pain</td>
<td>1316</td>
<td>5.5</td>
<td>5.5 no</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>sleep apnea</td>
<td>1744</td>
<td>12.8</td>
<td>16.0 no</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>new syrinx</td>
<td>2449</td>
<td>30.0</td>
<td>29.0 yes; new</td>
<td></td>
</tr>
</tbody>
</table>

* For the 3 patients marked “ND,” no interval brain MRI was obtained prior to surgical treatment. Abbreviations: HA = headache; ND = not done.

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natural history of Chiari malformation Type I
terminology may help to emphasize the generally benign
natural history in many cases.

The pathophysiological mechanism underlying the
relationship between CM-I and spinal cord syrinx is well established,
and therefore there are few reports on the natural history of syrinx in the setting of CM-I. The
presence of a syrinx is an indication for surgical treatment of CM-I
at many centers, and there are few reports
that surgery may not be necessary in all cases of CM-I
other than the syrinx. Other series have also suggested
that for more symptomatic patients, for whom surgery is more
frequently offered. At our center, we do not follow a strict
protocol to determine if a CM-I will be treated surgically.
In general, we have offered surgery for patients with spi-
nal syrinx, patients with neurological deficits, and patients
with symptoms that are concordant with typical CM-I
symptoms and that have substantially interfered with the
patient’s quality of life. In some cases, patients were
initially recommended for nonsurgical management and then
later underwent Chiari decompression despite a lack of any
new symptoms or radiological findings. In these cases, the
decision to offer surgery was made because symptoms had
persisted despite conservative management.

Our criteria for recommending surgical treatment of
CM-I must be considered in any analysis of those who were
treated without surgery at our institution. Based on
the results of this series, there is no basis for making any
assumptions about the natural history of the lesions in pa-
patients who did meet our usual surgical criteria and were
treated surgically. Given the widespread acceptance of
Chiari decompression in patients with either neurologi-
cal deficits or severe symptoms, it will be difficult to per-
form a natural history analysis of that group of patients
with CM-I. Nevertheless, we hope our analysis will help
to clarify the natural history of CM-I for the subgroup of
patients with CM-I that are considered to be asympto-
matic or minimally symptomatic and without neurological
deficits. The mean duration of clinical follow-up by any
physician was only 6.5 years in this series. This follow-up
interval may be insufficient to capture all cases of clinical
deficits. The mean duration of clinical follow-up by any
physician was only 6.5 years in this series. This follow-up
interval may be insufficient to capture all cases of clinical
or radiographic deterioration that could be seen over lon-
ger follow-up intervals. Further study over longer time in-
tervals will be necessary to clarify the natural history of
CM-I over the lifetime of individuals with this diagnosis.
The mean tonsillar descent is known to decrease with
advancing age in the normal population. This should be
considered in any interpretation of the natural history of
CM-I over long periods of time. Furthermore, it should
be noted that for this analysis, measurements of tonsillar
herniation were made without taking into account small
changes that may be seen in the degree of tonsillar descent
during the cardiac cycle. We believe that the changes in
tonsillar descent seen during the cardiac cycle (< 1 mm)
would not substantially alter our results or conclusions.

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during the cardiac cycle. We believe that the changes in
tonsillar descent seen during the cardiac cycle (< 1 mm)
would not substantially alter our results or conclusions.

Any attempt to consider the natural history of CM-I
will need to account for selection bias in the decision to
pursue surgical treatment. The group of patients presented
here was selected for nonsurgical management. Therefore,
this analysis should only apply to the group of patients with
CM-I that is managed nonsurgically. Any conclusions
that may be derived from these asymptomatic or minimally
symptomatic patients should not be applied to symptom-
atic patients that are ordinarily considered good surgical
candidates. It is possible that the natural history is worse
for these patients because surgery is more
frequently offered. At our center, we do not follow a strict
protocol to determine if a CM-I will be treated surgically.
In general, we have offered surgery for patients with spi-
nal syrinx, patients with neurological deficits, and patients
with symptoms that are concordant with typical CM-I
symptoms and that have substantially interfered with the
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tonsillar descent seen during the cardiac cycle (< 1 mm)
would not substantially alter our results or conclusions.
Conclusions

The natural history of CM-IIs for those patients selected for conservative management is generally benign. Symptoms and MR imaging findings are stable over time in most cases, although spontaneous improvement and worsening of both the CM-I and the spinal syrinx do occur.

Disclosure

Dr. Muraszko is a consultant for Stem Cells, Inc. The remaining authors report no other conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Maher, Muraszko, Garton, Strahle. Acquisition of data: Strahle, Kapurch, Maher, Muraszko, Garton. Analysis and interpretation of data: all authors. Drafting the article: Maher, Strahle. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Maher. Study supervision: Maher, Muraszko, Garton.

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Chiari malformation Type I and syrinx in children undergoing magnetic resonance imaging

Clinical article

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Departments of 1Neurosurgery and 2Radiology, University of Michigan, Ann Arbor, Michigan

Object. Chiari malformation Type I (CM-I) with an associated spinal syrinx is a common pediatric diagnosis. A better understanding of the relative age-related prevalence and MR imaging characteristics of these associated conditions may lead to improved treatment decisions.

Methods. The authors performed a retrospective review of 14,116 consecutive individuals 18 years of age or younger who had undergone brain or cervical spine MR imaging at the University of Michigan between November 1997 and August 2008. In the patients with CM-I, demographic, clinical, and radiographic information was recorded.

Results. Five hundred nine children (3.6%) with CM-I were identified. Among these patients, 23% also had a spinal cord syrinx, and 86% of the syringes were found in the cervical spine. The MR imaging prevalence of CM-I with a syrinx was 1.2% in girls and 0.5% in boys (p < 0.0001). The severity of impaired CSF flow at the foramen magnum was associated with the amount of tonsillar herniation (p < 0.0001) and conformation of the tonsils (p < 0.0001). Patients with CM-I were treated surgically in 35% of cases; these patients exhibited more severe tonsillar herniation (p < 0.0001) and impaired CSF flow (p < 0.0001) as compared with those who did not undergo surgery. On imaging, 32% of all the patients with CM-I were considered symptomatic by the treating physician. Patients were more likely to be considered symptomatic if they were female, had a syrinx, displayed abnormal tonsillar pulsations, or had a greater amount of tonsillar herniation.

Conclusions. In this study the authors describe the age-related prevalence and MR imaging characteristics of CM-I and its association with a syrinx and other abnormalities in a large group of children who underwent MR imaging for any indication. Syringes are more common in older children, in girls, and in patients with a greater degree of tonsillar descent and CSF flow impairment. (DOI: 10.3171/2011.5.PEDS1121)

Key Words • Chiari malformation Type I • syrinx • prevalence • magnetic resonance imaging

Chiari malformation Type I (CM-I) is a common pediatric referral diagnosis. The relationship between CM-I and a spinal cord syrinx is well established.6,8,47,50 Chiari malformation Type I can lead to spinal cord syrinx formation as a result of abnormal flow of the CSF at the foramen magnum.6,8,10,18,24,27,35,36,38,47 The true prevalence of syrinx in CM-I is not well defined, as most estimates have been derived from case series of patients undergoing surgery.4,14,26,27,38,42 Studies describing groups of patients that have been surgically treated for CM-I tend to have a bias for including symptomatic cases and excluding those that are more minimally affected. Syringomyelia is found in as many as 75% of patients undergoing surgical treatment for CM-I.9,26,27,29,32,43 Since surgeons are more likely to recommend surgery if a spinal syrinx is present, the true prevalence of a syrinx in patients with CM-I is lower.17,41

The radiographic characteristics of CM-I and syrinx have not been described in a large series, with the exception of descriptions of surgical outcomes following decompression.4,27,38,42 The relationship between patient age and other clinical and imaging characteristics, and the prevalence of syrinx in CM-I has never been properly studied. An improved understanding of these relationships may lead to better treatment decisions for children with CM-I.25,41

Abbreviations used in this paper: CM-I = Chiari malformation Type I; EMERSE = Electronic Medical Record Search Engine.
Methods

Following approval by the University of Michigan Institutional Review Board, we performed a retrospective review of the electronic medical records of all patients 18 years of age or younger who had undergone brain or cervical spine MR imaging at the University of Michigan between November 1997 and August 2008. Brain or cervical spine MR imaging was performed in 14,116 children during this period. All MR images were obtained on either a 1.5- or 3-T MR imaging device. All electronic records were reviewed using the Electronic Medical Record Search Engine (EMERSE),16 a search engine that queries all free-text documents within the electronic medical records of a specified patient population. We used EMERSE to identify a population in which the terms “tonsillar ectopia,” “tonsillar herniation,” “tonsillar descent,” “syrinx,” “syringomyelia,” “hydromyelia,” or “Chiari” were used in the text of the medical record. We then manually reviewed the medical and imaging records of all patients identified by EMERSE to select those who met the inclusion criteria. Cerebellar tonsillar descent ≥ 5 mm below the foramen magnum was considered diagnostic of CM-I. Patients were excluded from the study if tonsillar ectopia was believed to be caused by tumor mass effect, hydrocephalus, cysts, or cerebellar edema or was associated with craniosynostosis. Any patient who met the criteria for CM Type II, III, or IV, including a history of myelomeningocele repair, was excluded from the study. Any patient who had received surgical treatment for CM-I prior to their first MR imaging review at our institution was also excluded.

For patients who met all inclusion criteria, we recorded age, sex, presenting symptoms, associated radiological diagnoses, syrinx characteristics, indication given for the initial MR imaging, and any surgical treatment. We reviewed the MR images from each of the patients with CM-I and recorded the imaging characteristics of the malformation, including the degree of tonsillar descent in millimeters as well as tonsillar morphology. If a single patient had more than 1 MR image during the study period, the initial MR image on which the malformation was diagnosed was used for analysis.

Tonsillar descent was assessed by identifying the line from the basion to opisthion and then by measuring from this line to the inferior margin of the cerebellar tonsils on sagittal MR imaging. Tonsillar morphology was classified as either rounded or pegged. Cerebrospinal fluid flow data were recorded for all patients who had dedicated CSF flow sequences on MR imaging. At our institution, changes in signal intensity on sagittal phase-contrast CSF flow studies are observed in the CSF spaces anteriorly and posteriorly at the level of the cervicomedullary junction. The alternating bright and dark signals seen in the CSF spaces in the cine mode are diminished or absent when there is abnormal flow. On the axial and sagittal phase contrast images, any change in signal intensity of the cerebellar tonsils in the cine mode suggests tonsillar pulsations. Cerebrospinal fluid flow was categorized as normal, decreased anteriorly or posteriorly at the foramen magnum, or decreased at the foramen magnum with abnormal tonsillar pulsations, based on the initial report of the radiologist. The presence of scoliosis, defined as a > 10° lateral Cobb angle on upright radiography, was recorded. Patients without adequate spine radiographs in our system were also designated as having scoliosis if a prior diagnosis of scoliosis was in the medical record. We noted any additional abnormal findings on the radiology report following MR imaging of the brain or spine, including retroverted dens or basilar invagination. Determining basilar invagination or retroflexed dens was based on the radiologist’s original interpretation of the images.

For the present analysis, a syrinx was defined as a spinal cord cyst (T1 hypointensity and T2 hyperintensity) ≥ 3 mm in width in the anteroposterior dimension on sagittal or axial MR imaging. Patients who had a presyrinx state (T2 hyperintensity within the cord parenchyma without cavitation) were considered separately. Either a neurologist or a neurosurgeon at our hospital had performed the clinical evaluation in 443 patients (87%). Patients were considered symptomatic if the treating physician thought the patient had symptoms caused by a CM or spinal syrinx.

Statistical significance calculations were obtained using ANOVA, chi-square, and Tukey multiple comparisons as well as univariate logistic regression. Data were analyzed using SPSS version 16.0 software (SPSS, Inc.).

Results

At our institution, 14,116 children underwent MR imaging of the brain or cervical spine over an 11-year interval. Of these, 509 patients (3.6%) met our imaging criteria for CM-I. Brain MR imaging had been performed in all of these patients, whereas cervical spine MR imaging had been performed in 397 (78%). At least one MR image of the entire spine had been obtained in 256 patients (50%). On imaging, 117 patients (0.83%) had both CM-I and spinal syrinx. The prevalence of CM-I in those who underwent MR imaging did not vary significantly by age (p = 0.54; Fig. 1). However, a spinal syrinx was more commonly found in older children with CM-I (p =

![Fig. 1. Line graph reflecting the percentage of children, according to age (in years), in whom a diagnosis of CM-I was made at the time of MR imaging.](image-url)
Chiari malformation Type I and syrinx on MR imaging

**Fig. 2.** Line graph depicting the percentage of children with CM-I, according to age (in years), in whom spinal syrinx was diagnosed on MR imaging.

...This age-related increase was most pronounced in the first 5 years of life (Fig. 2). There was no significant increase in the prevalence of syrinx in patients with CM-I as a function of advancing age after 5 years of age. The prevalence of CM-I did not differ significantly by sex (p = 0.15; Table 1).

In those with CM-I, the mean tonsillar descent measurement was 10.2 mm below the foramen magnum. Cerebrospinal fluid flow studies were obtained at or near the time of CM-I diagnosis in 308 patients (61%). An increasing amount of tonsillar herniation was associated with more severe alterations in CSF flow at the foramen magnum. Patients with abnormal tonsillar pulsations had a mean tonsillar descent of 13.5 mm as compared with a mean of 11.5 mm in patients with decreased flow anterior or posterior to the foramen magnum without abnormal tonsillar pulsations and a mean of 7.9 mm in those with normal CSF flow at the foramen magnum (p < 0.0001). Abnormal tonsillar pulsations were also associated with a pegged tonsillar morphology. Pegged tonsils were found in 77 (93%) of 83 patients with abnormal tonsillar pulsations as compared with 46 (51%) of 91 patients with normal CSF flow (p < 0.0001). Additional imaging findings are listed in Table 2. Associated conditions such as retroverted dens and basilar invagination were found in 6.5% and 4.7% of patients with CM-I, respectively. Other incidental findings, such as arachnoid cysts, were found at the expected rate in a cohort of children undergoing MR imaging.3

Magnetic resonance imaging of the entire spine (cervical, thoracic, and lumbar regions) was performed in 256 patients (50%), and 397 patients (78%) underwent cervical

**TABLE 1: Syrinx and scoliosis in 509 pediatric patients with CM-I**

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>% MRI†</td>
<td>% CM‡</td>
</tr>
<tr>
<td>CM-I</td>
<td>249</td>
<td>3.4</td>
<td>NA</td>
</tr>
<tr>
<td>CM-I &amp; syrinx</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ scoliosis</td>
<td>22</td>
<td>0.3</td>
<td>8.8</td>
</tr>
<tr>
<td>w/o scoliosis</td>
<td>15</td>
<td>0.2</td>
<td>6.0</td>
</tr>
<tr>
<td>total</td>
<td>37</td>
<td>0.5</td>
<td>14.8</td>
</tr>
<tr>
<td>CM-I &amp; scoliosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>w/ syrinx</td>
<td>22</td>
<td>0.3</td>
<td>8.8</td>
</tr>
<tr>
<td>w/o syrinx</td>
<td>13</td>
<td>0.2</td>
<td>5.2</td>
</tr>
<tr>
<td>total</td>
<td>35</td>
<td>0.5</td>
<td>14.0</td>
</tr>
</tbody>
</table>

* NA = not applicable.
† Percentage of patients 0–18 years of age undergoing MR imaging.
‡ Percentage of patients 0–18 years of age with CM-I on MR imaging.

**TABLE 2: Incidental or associated findings on MR imaging in patients with CM-I**

<table>
<thead>
<tr>
<th>Finding</th>
<th>No. (%)</th>
<th>Tonsillar Herniation</th>
<th>Syrinx</th>
<th>CSF Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>retroverted dens</td>
<td>33 (6.5)</td>
<td>&lt;0.00001</td>
<td>0.30</td>
<td>0.006</td>
</tr>
<tr>
<td>basilar invagination</td>
<td>24 (4.7)</td>
<td>&lt;0.00001</td>
<td>0.006</td>
<td>0.001</td>
</tr>
<tr>
<td>arachnoid cyst</td>
<td>18 (3.5)</td>
<td>0.21</td>
<td>0.58</td>
<td>0.81</td>
</tr>
<tr>
<td>callosal dysgenesis</td>
<td>15 (2.9)</td>
<td>0.85</td>
<td>1.00</td>
<td>0.31</td>
</tr>
<tr>
<td>venous angioma</td>
<td>15 (2.9)</td>
<td>0.60</td>
<td>1.00</td>
<td>0.81</td>
</tr>
<tr>
<td>Klippel-Feil syndrome</td>
<td>14 (2.7)</td>
<td>0.64</td>
<td>1.00</td>
<td>0.56</td>
</tr>
<tr>
<td>absent septum pellicidum</td>
<td>12 (2.4)</td>
<td>0.86</td>
<td>0.31</td>
<td>0.081</td>
</tr>
<tr>
<td>hemivertebra</td>
<td>12 (2.4)</td>
<td>0.086</td>
<td>1.000</td>
<td>0.22</td>
</tr>
<tr>
<td>platybasia</td>
<td>9 (1.8)</td>
<td>0.002</td>
<td>0.44</td>
<td>0.13</td>
</tr>
<tr>
<td>butterfly vertebrae</td>
<td>8 (1.6)</td>
<td>0.14</td>
<td>0.086</td>
<td>0.18</td>
</tr>
<tr>
<td>spina bifida occulta</td>
<td>8 (1.6)</td>
<td>0.85</td>
<td>0.086</td>
<td>0.34</td>
</tr>
</tbody>
</table>

* In each category, patients in whom these additional diagnoses had been made were tested against all other patients with CM-I for the amount of tonsillar herniation (in mm), the presence of a syrinx, or abnormal CSF flow at the foramen magnum. Significant p values suggest that a greater amount of tonsillar herniation, the presence of a syrinx, or more severe CSF flow alterations at the foramen magnum were associated with the listed clinical condition as compared with patients with CM-I but without the listed condition.
spine imaging. Girls were more likely than boys to have undergone complete spine imaging. Of the patients with CM-I who had undergone at least cervical and thoracic spine imaging, 155 were girls (155 [60%] of 260 girls) and 108 were boys (108 [43%] of 249 boys). A syrinx was found in 117 patients (23%) with CM-I (Table 1). In contrast to CM-I alone, CM-I together with syrinx was more common in girls (1.2%) as compared with boys (0.5%; p < 0.0001). More girls had both CM-I and scoliosis (1.2%) as compared with boys (0.5%; p < 0.0001). There was overlap between patients with syrinx and those with scoliosis. Seventy-three patients had CM-I, spinal syrinx, and scoliosis. Chiari malformation Type I with scoliosis but no syrinx was found in 41 patients. Chiari malformation Type I with spinal syrinx but no scoliosis was found in 44 patients (Table 1).

The mean syrinx width was 7.8 mm, and the average length was 9 vertebral levels. Individuals with a syrinx had a greater amount of tonsillar descent at the time of CM-I diagnosis. Those with a syrinx had a mean tonsillar descent of 12.6 mm; those without a syrinx had a mean tonsillar descent of 9.5 mm (p < 0.0001; Fig. 3). More severe CSF flow alterations at the foramen magnum occurred in patients with a syrinx: 52% of patients with abnormal tonsillar pulsations had a syrinx compared with 13% of patients with normal CSF flow at the foramen magnum (p < 0.0001). Furthermore, only 6% (7 of 126) of patients with rounded tonsils had a syrinx compared with 31% (109 of 357) of patients with pegged tonsils (p < 0.0001). Patients with basilar invagination were more likely to have an associated syrinx (p = 0.006). A syrinx was found in 46% of patients with basilar invagination compared with 22% (106 of 485) of patients without.

Although the degree of tonsillar herniation did correlate with the presence of a syrinx, the degree of tonsillar herniation was not associated with syrinx width (p = 0.6). Similarly, alterations in CSF flow were not associated with syrinx dimensions such as length or width (p = 0.15 and 0.28, respectively). Syrinx length was not associated with the degree of tonsillar descent. A test of slope was conducted using linear regression to determine whether an increase in tonsillar herniation was associated with a linear increase or decrease in syrinx length. The slope was not significantly different from 0 (p = 0.9). Tonsillar descent was also evaluated for a relationship with the cranial extent of the syrinx by comparing tonsillar descent in groups of syringes with a cranial extent at C-3 or above, between C-4 and C-7, and in the thoracic spine. The tonsillar descent was not significantly different between these groups (p = 0.6). Syringes were found to have their cranial extent within the cervical spine in 86% of cases (Fig. 4). In the 16 patients with a syrinx that was entirely within the thoracolumbar spine, 5 had scoliosis and 11 did not.

Of those patients with CM-I on MR imaging, 32% were considered to be symptomatic at the time of CM-I diagnosis by the treating physician. A higher proportion of girls (41%) were considered to be symptomatic as compared with boys (22%; p < 0.0001). Patients who were symptomatic were more likely to have a syrinx (p < 0.0001). Older children were more likely to be classified as symptomatic (p = 0.0002). The mean age of asymptomatic patients at diagnosis was 8.0 years, and the mean age of symptomatic patients at diagnosis was 9.9 years. Symptomatic patients had more severe alterations in CSF flow at the foramen magnum (p < 0.0001). Finally, symptomatic patients had a greater amount of tonsillar descent (p < 0.0001). Patients with symptoms had a mean tonsillar descent of 13 mm, whereas those without had a mean descent of 9 mm. Associated clinical conditions discovered at the time of CM-I diagnosis are presented in Table 3.

![Fig. 3. Bar graph illustrating the number of patients with CM-I alone (black bars) versus those with both CM-I and syrinx (gray bars), according to the measurement (in mm) of tonsillar descent below the foramen magnum. Those with greater amounts of tonsillar descent were more likely to have an associated syrinx.](image-url)
Chiari malformation Type I and syrinx on MR imaging

Treatment by decompression occurred in 180 patients (35%). The mean tonsillar descent in these patients was 12.9 mm, and the mean descent in those treated without surgery was 8.7 mm (p < 0.0001). The severity of CSF flow alterations at the foramen magnum was also associated with the surgical treatment of CM-I. Sixty-five (78%) of 83 patients with abnormal tonsillar pulsations had decompression surgery compared with 25 (27%) of 91 patients with normal CSF flow. Patients treated using decompression were older at the time of CM-I diagnosis compared with those whose disease was managed without surgery, but this difference was not statistically significant (p = 0.1). Patients who underwent surgery for CM-I had a mean age of 9.3 years at diagnosis, and those without surgery had a mean age of 8.4 years at diagnosis (Fig. 5).

The indications for obtaining the initial MR image as provided by the ordering physician are listed in Table 4. In many cases, the indication for imaging was considered a potential diagnosis that was not confirmed on MR imaging. Chiari malformation Type I was diagnosed at the time of the first MR image in 482 patients (95%). Another 27 patients had an initial MR image that was not diagnostic for CM-I but later had at least 1 other MR image that met our criteria for CM-I diagnosis. In these patients, the mean interval between the first and the subsequent scan demonstrating a CM was 1087 days.

**Figure 4.** Bar graph showing the cranial extent of syrinx in patients at the time of the initial syrinx diagnosis, according to the adjacent vertebral level.

**TABLE 3: Additional clinical diagnoses in patients at the time of CM-I diagnosis**

<table>
<thead>
<tr>
<th>Condition</th>
<th>No. (%)</th>
<th>Tonsillar Herniation</th>
<th>Syrinx</th>
<th>CSF Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>scoliosis</td>
<td>114 (22.4)</td>
<td>0.001</td>
<td>&lt;0.00001</td>
<td>0.001</td>
</tr>
<tr>
<td>sleep apnea†</td>
<td>65 (12.9)</td>
<td>0.002</td>
<td>0.009</td>
<td>‡</td>
</tr>
<tr>
<td>seizure disorder</td>
<td>64 (12.6)</td>
<td>0.020§</td>
<td>0.0007§</td>
<td>0.140</td>
</tr>
<tr>
<td>shunted hydrocephalus</td>
<td>42 (8.3)</td>
<td>0.310</td>
<td>0.010</td>
<td>0.007</td>
</tr>
<tr>
<td>autism</td>
<td>26 (5.1)</td>
<td>0.21</td>
<td>0.34</td>
<td>0.29</td>
</tr>
</tbody>
</table>

* In each category, patients with these additional conditions were tested against all other patients with CM-I for the amount of tonsillar herniation (in mm), the presence of a syrinx, or abnormal CSF flow at the foramen magnum. In most cases, the p values indicate that a greater amount of tonsillar herniation, the presence of a syrinx, or more severe CSF flow alterations at the foramen magnum were associated with the listed clinical condition as compared with patients with CM-I but without the listed condition.
† Fifty-seven patients were diagnosed with obstructive sleep apnea; 4 patients each had central sleep apnea or combined obstructive and central sleep apnea.
‡ Insufficient data available for statistical analysis.
§ Patients had less tonsillar herniation, no syrinx, and less severe CSF flow at the foramen magnum.

**Discussion**

Cerebellar tonsillar descent of at least 5 mm below the foramen magnum is usually considered consistent with an imaging diagnosis of CM-I.1,3,39,45 Several prior studies estimated the prevalence of CM-I to be between 0.6% and 1% in those undergoing imaging.2,25,48 Meadows et al.25 found CM-I in 0.77% of patients undergoing MR imaging at a single referral center. All age groups were included in their analysis, but children composed a relatively small proportion of their study participants. Age-specific or even age group–specific prevalence is not reported by Meadows et al., and it is not clear whether the prevalence is different in children as compared with adults in their series. Their report is remarkable for the relatively few asymptomatic cases of CM-I discovered on imaging; only 25 (14%) of 175 patients with CM-I were thought to be asymptomatic. In contrast, we found a much higher percentage of asymptomatic cases (68%) at the time of CM-I diagnosis. It is certainly possible that this percentage reflects differences between institutions in the relative sensitivity of CM-I diagnosis as well as in referral biases for imaging. Our determination of symptom-
atic or asymptomatic CM-I was made according to the judgment of the treating physician. The complex clinical presentation of CM-I as well as the retrospective nature of this study does not allow for a more precise definition. In general, at our institution, patients with headaches are considered symptomatic if the headaches have at least some of the features considered compatible with CM-I headaches, including a tussive component, a short duration, and a lack of migrainous features. Other symptoms assigned to CM-I include sleep apnea, swallowing difficulty, scoliosis, and motor or sensory disturbances in the extremities of patients with spinal syrinx.

In our series as well as in several prior reports, asymptomatic cases in our series reflects our focus on children rather than on a group consisting mostly of adults.

Patient sex appears to be an important factor in CM-I presentation. Some groups have reported a female predominance for CM-I, but this finding is not universal. Although our results do not support any sex predilection for CM-I diagnosis on imaging, we did find that girls are more likely to be considered symptomatic, to have an associated spinal syrinx, and to have associated scoliosis. As a result, girls appear to be more likely to present for neurosurgical treatment, probably explaining the female predominance in some series. In our own series, girls were more likely to undergo surgical treatment of CM-I.

Chiari malformation Type I is known to cause spinal cord syrinx in some patients. Most surgical studies report that between 60% and 85% of patients with CM-I have an associated syrinx. Because the presence of a syrinx is an indication for surgery at many centers, published surgical studies have overestimated the frequency with which a syrinx occurs in patients with CM-I. Therefore, the true age-related prevalence of spinal syrinx in children with CM-I is not well established. Meadows et al. found only 1 patient with a spinal syrinx in their series of 25 asymptomatic patients with CM-I. It is possible that syringes were uncommon in their study because of screening methods that may have been less sensitive in detecting spinal syringes. Most of the patients in our series underwent cervical spine MR imaging to screen for syrinx, and half of our patients underwent complete spine imag-

![Graph showing the patients treated with decompression (black bars) versus without surgery (gray bars), according to age (in years).](image)

**TABLE 4: Indication for initial MR imaging in patients with diagnosed CM-I**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>headache</td>
<td>111 (22.8)</td>
</tr>
<tr>
<td>scoliosis</td>
<td>77 (15.8)</td>
</tr>
<tr>
<td>neurological change</td>
<td>60 (12.3)</td>
</tr>
<tr>
<td>seizure</td>
<td>58 (11.9)</td>
</tr>
<tr>
<td>hydrocephalus/macrocephaly*</td>
<td>43 (8.8)</td>
</tr>
<tr>
<td>other</td>
<td>29 (6.0)</td>
</tr>
<tr>
<td>cranial nerve palsy</td>
<td>27 (5.6)</td>
</tr>
<tr>
<td>developmental delay</td>
<td>22 (4.5)</td>
</tr>
<tr>
<td>trauma</td>
<td>22 (4.5)</td>
</tr>
<tr>
<td>pituitary/endocrine</td>
<td>19 (3.9)</td>
</tr>
<tr>
<td>tumor/cyst/mass*</td>
<td>18 (3.7)</td>
</tr>
<tr>
<td>total</td>
<td>486† (100)</td>
</tr>
</tbody>
</table>

* Indication for imaging was provided on the MR imaging requisition. In many cases, the indication for imaging was considered a possible diagnosis that was not confirmed on MR imaging.
† Indication for initial imaging was unknown in 23 patients.
Chiari malformation Type I and syrinx on MR imaging

We found on initial imaging that a syrinx was present in 23% of all patients with CM-I. It is possible that even this rate represents an overestimate of the true population prevalence of syrinx in children with CM-I, especially given that a population of children undergoing spine imaging may have an increased likelihood of harboring an associated syrinx as compared with children with CM-I who do not come to medical attention. In patients with CM-I, age appears to be a relevant factor in spinal syrinx prevalence. In contrast to CM-I, which was found throughout the pediatric age range with a similar age-related prevalence, syringes were much less common during the first years of life but do appear to reach a stable age-related prevalence by 5 years of age. This finding supports our current understanding of the causal relationship between the malformation and the spinal syrinx and suggests some potential utility for spine imaging follow-up in the children with CM-I diagnosed at a very young age.

The relevance of the degree of tonsillar herniation and the likelihood of syrinx formation is controversial. Although some studies have shown that syringes are associated with a greater amount of tonsillar herniation, others have suggested that an intermediate degree of herniation between 9 and 14 mm is more likely to be associated with a syrinx than either lesser or greater degrees of tonsillar descent. In contrast, we found that an increased amount of tonsillar herniation was associated with a greater likelihood of an associated spinal syrinx (Fig. 3). It seems possible that the prior report assigning pathophysiological significance to an intermediate degree of tonsillar herniation may have suffered from a small sample size.

In our series, in addition to increased tonsillar descent, syringes were associated with pegged tonsillar morphology and decreased CSF flow at the foramen magnum. Not surprisingly, we also found that patients with basilar invagination and hydrocephalus were more likely to have a spinal syrinx (Tables 2 and 3). Furthermore, a retroverted dens and basilar invagination were both associated with increased tonsillar descent. These associations are consistent with current morphometric theories of CM-I pathogenesis.

For the present analysis, we used the radiological interpretation as the basis for determining the presence of basilar invagination and retroflexed dens. It is possible that the presence of basilar invagination or a retroflexed dens is more likely to be noted by a radiologist when a syrinx is present, a potential source of bias in this analysis. The negative correlation that was found between spinal syrinx and seizures, a diagnosis that is unrelated to CSF flow at the foramen magnum, may be a result of a selection bias for children with this condition who were undergoing MR imaging (Table 3).

Although CM-I–associated syringomyelia can occur at any level of the spine, even as low as the conus, the cervical spine is most frequently affected. This tendency follows a general principle for syrinx formation at or immediately caudal to any pathological narrowing of the subarachnoid space within the craniovertebral junction or spinal canal. We found that most syringes had their cranial extent in the cervical spine, but a significant number of patients had a syrinx only in the lower segments (Fig. 4). This finding should be considered when ordering imaging studies. If the presence of a syrinx would change the treatment recommendation, total spine imaging should be considered in patients with CM-I. Of the 16 patients with a spinal syrinx entirely within the thoracic or lumbar spine, 11 did not have associated scoliosis.

Patients with CM-I were identified by examining medical and imaging records from a cohort of patients undergoing MR imaging at our institution. This method allowed an analysis of all patients with a diagnosis on MR imaging without respect to their ultimate treatment or clinical evaluation. The 509 patients with CM-I described here reflect the selection bias that is anticipated for a group that has been referred for imaging at a medical center. This bias is evident in the indications provided for obtaining the initial MR image as well as the frequency of comorbidities in this patient group. Although there are many reasons to obtain an MR image in a child, the population of children undergoing MR imaging is different from the general population. Therefore, our reported prevalence estimate for CM-I should be considered the MR imaging prevalence rather than the true population prevalence. It seems likely that MR imaging prevalence is an overestimate of CM-I prevalence in the general population. Several groups have reported on intracranial findings in healthy adult volunteers. Although each of these studies was small, a meta-analysis by Morris et al. revealed CM-I on 71 of 15,559 MR imaging studies from combined data of multiple reports in adults. The sensitivity for detecting CM-I in each of these studies and in the subsequent meta-analysis is not clear, and in some reports contained in the meta-analysis, no cases of CM-I were found. Given these concerns about the sensitivity of CM-I detection, it is possible that the estimated prevalence of CM-I provided by those studies may be less than the true population prevalence. Vernooij et al. recently studied 2000 healthy adults over the age of 45 years and found 18 volunteers (0.9%) with CM-I. To obtain a true age-based population prevalence of CM-I in children, screening the general pediatric population with MR imaging would be preferable to reviewing a cohort of children for whom scanning was thought to be medically necessary. Nevertheless, an analysis of MR imaging prevalence in the group undergoing MR imaging for any reason can provide insight into associated conditions, age and sex differences, and imaging characteristics of CM-I and syrinx.

Conclusions

At our institution, 3.6% of children undergoing MR imaging of the brain or cervical spine had CM-I, with a near equal sex distribution. Syrinx and scoliosis were much more common in girls with CM-I than in boys with CM-I. A greater amount of tonsillar herniation and pegged tonsillar morphology were associated with spinal cord syrinx and more severe alterations in CSF flow at the foramen magnum. A syrinx was found in 23% of children with CM-I and was found much less frequently in the first 5 years of life.

Disclosure

Dr. Muraszko is a consultant for Stem Cells, Inc.
Author contributions to the study and manuscript preparation include the following. Conception and design: Maher, Muraszko, Garton. Acquisition of data: Maher, Muraszko, Strahle, Kapurch. Analysis and interpretation of data: all authors. Drafting the article: Maher, Strahle, Kapurch. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Maher. Study supervision: Maher, Muraszko, Garton.

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The association between Chiari malformation Type I, spinal syrinx, and scoliosis

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Departments of 1Neurosurgery and 2Radiology, University of Michigan, Ann Arbor, Michigan

OBJECT Chiari malformation Type I (CM-I) is often found in patients with scoliosis. Most previous reports of CM-I and scoliosis have focused on patients with CM-I and a spinal syrinx. The relationship between CM-I and scoliosis in the absence of a syrinx has never been defined clearly. The authors sought to determine if there is an independent association between CM-I and scoliosis when controlling for syrinx status.

METHODS The medical records of 14,118 consecutive patients aged ≤ 18 years who underwent brain or cervical spine MRI at a single institution in an 11-year span were reviewed to identify patients with CM-I, scoliosis, and/or syrinx. The relationship between CM-I and scoliosis was analyzed by using multivariate regression analysis and controlling for age, sex, CM-I status, and syrinx status.

RESULTS In this cohort, 509 patients had CM-I, 1740 patients had scoliosis, and 243 patients had a spinal syrinx. The presence of CM-I, the presence of syrinx, older age, and female sex were each significantly associated with scoliosis in the univariate analysis. In the multivariate regression analysis, older age (OR 1.02 [95% CI 1.01–1.03]; p < 0.0001), female sex (OR 1.71 [95% CI 1.54–1.90]; p < 0.0001), and syrinx (OR 9.08 [95% CI 6.82–12.10]; p < 0.0001) were each independently associated with scoliosis. CM-I was not independently associated with scoliosis when controlling for these other variables (OR 0.99 [95% CI 0.79–1.29]; p = 0.9).

CONCLUSIONS A syrinx was independently associated with scoliosis in a large pediatric population undergoing MRI. CM-I was not independently associated with scoliosis when controlling for age, sex, and syrinx status. Because CM-I is not independently associated with scoliosis, scoliosis should not necessarily be considered a symptom of low cerebellar tonsil position in patients without a syrinx.

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KEY WORDS Chiari malformation Type I; scoliosis; spinal syrinx

Chiari malformation Type I (CM-I) is often associated with a spinal syrinx.26,33 Patients who have both CM-I and a syrinx are more likely to undergo surgery than those with CM-I alone.28 For this reason, surgical series tend to overestimate the true prevalence of syringes associated with CM-I.24,33 When all patients with CM-I discovered on imaging are considered without selecting for those who are symptomatic or undergoing treatment, a syrinx is found in a smaller, but still substantial, percentage of those with CM-I.30 Spinal syrinx is associated with scoliosis in some individuals,5,18,19,38 perhaps as a result of asymmetrical injury to the spinal cord from an expanding cyst.16

Although most researchers agree that CM-I can cause a spinal syrinx and that a spinal syrinx can cause scoliosis,3,5,6,11,12,15,20 the association of CM-I and scoliosis in the absence of a syrinx has never been defined properly and remains controversial. Some researchers have speculated that asymmetrical compression of the cervicomедullary junction by the cerebellar tonsils can result in scoliosis even in the absence of a spinal syrinx.5,6,34,37 Nevertheless, there is scant existing evidence for such a causal relationship between CM-I and scoliosis in the absence of a syrinx. Arguing in favor of such a relationship are several case reports of patients with CM-I and scoliosis in the absence of a syrinx.13,22,34 However, given the high preva-
lence of both CM-I\textsuperscript{23,30} and scoliosis,\textsuperscript{2,35} both conditions in an individual can occur by chance in many instances. Therefore, the existence of reports of individual patients or even small series of patients with both findings does not prove a causative relationship. In addition, there are case series in which CM-I as a cause of scoliosis has been examined.\textsuperscript{11,20,34} Unfortunately, a majority of these patients also have a spinal syrinx, making it impossible to draw any conclusion on the relationship between CM-I and scoliosis in the absence of a syrinx. To examine this relationship, we analyzed a large cohort of children who, over an 11-year span, underwent brain or cervical spine MRI. We then performed multivariate regression analysis to determine if there was an independent relationship between CM-I and scoliosis when we controlled for syrinx status.

**Methods**

After approval by the University of Michigan Institutional Review Board, we examined the medical records of 14,118 consecutive children aged ≤18 years who underwent brain or cervical spine MRI at the University of Michigan in an 11-year span. Electronic records, including radiology reports, surgical reports, all office consultation notes, and hospital chart entries, were reviewed by using the Electronic Medical Record Search Engine (EMERSE)\textsuperscript{14} to identify patients with CM-I, syrinx, and/ or scoliosis by searching for the key words “tonsillar ectopia,” “tonsillar herniation,” “tonsillar descent,” “tonsil,” “syrinx,” “syringomyelia,” “hydromyelia,” “Chiari,” or “scoliosis” in any part of the electronic medical record. All imaging records and all other medical records for patients selected in this way were reviewed to confirm the diagnoses.

Each patient was assigned to a category on the basis of his or her syrinx status, CM-I status, and scoliosis status. For the purpose of this analysis, CM-I was defined on imaging as a cerebellar tonsil position at least 5 mm below the foramen magnum.\textsuperscript{1,4,29,30} A spinal syrinx was defined as a spinal cord cyst (hypointense signal on T1-weighted images and hyperintense signal on T2-weighted images) of at least 3 mm wide seen on an axial image.\textsuperscript{30} Scoliosis was defined as at least a 10° Cobb angle seen on a radiograph. Although radiographs were available for most of the patients with a diagnosis of scoliosis, those without radiographs but with a clear description and diagnosis of scoliosis in the medical record were also included in the scoliosis category.

There were 554 patients excluded from analysis. Patients were excluded if they had Chiari malformation Type II or III or any risk factors for low cerebellar tonsil position other than idiopathic CM-I, including mass effect from tumor, hydrocephalus, intracranial cysts, cerebral edema, or craniostenosis. Patients who received surgical treatment for CM-I before their first MRI at our institution were excluded. Patients with a syrinx and Chiari malformation Type 0, intramedullary spinal cord tumor, or open myelomeningocele were also excluded. The final analysis included 13,564 patients.

Statistical significance calculations were obtained using the chi-square test, the t-test, ANOVA, and multivari-ate regression analysis. Multivariate regression analysis for scoliosis was performed while taking into account CM-I status, syrinx status, sex, and age. Raw odds ratios (ORs) were produced using 2 × 2 tables and chi-square testing. Data were analyzed using SAS 9.3 (SAS Institute, Inc.) and StatPlus (AnalystSoft, Inc.) software. For the multivariate regression analysis, we analyzed CM-I as a categorical variable rather than a continuous variable; patients with a cerebellar tonsil position of ≥5 mm below the foramen magnum were analyzed together. Scoliosis and syrinxes were also analyzed as categorical variables for multivariate regression analysis.

**Results**

In this cohort of 13,564 patients, 52% were male, and the mean age at the time of MRI was 7.7 years. Scoliosis was present in 1740 patients (12.8%), 509 patients (3.8%) had a cerebellar tonsil position of ≥5 mm below the foramen magnum, and 243 (1.8%) had a syrinx of ≥3 mm in maximal diameter. Of the 1740 patients with scoliosis, 114 (6.6%) had CM-I, 137 (7.9%) had a syrinx, and 72 (4.1%) had both CM-I and a syrinx.

Of the 114 patients with both CM-I and scoliosis, 72 had a syrinx and 42 did not (Table 1). The mean age at the time of the scoliosis diagnosis was 9.5 years (Fig. 1). There was no difference in the mean ages at diagnosis between those with and those without a syrinx. There was a similar sex distribution for those with a syrinx (69.4% female) and those without a syrinx (69.0% female). The patients with both CM-I and a syrinx had a lower cerebellar tonsil position (mean 12.9 mm) than those with CM-I and no syrinx (mean 9.1 mm; p < 0.001). Patients with a syrinx were more likely to have a curve of >20° (70.8%) than those without a syrinx (45.2%; p < 0.01). The locations of the curve with the largest Cobb angle for the group as a whole were distributed similarly between the thoracic (51%) and thoracolumbar (46%) regions, with a minority in the lumbar spine (2.6%). Thirteen patients (11.4%) had a left thoracic curve. Neither the presence of a syrinx (p = 0.9) nor the syrinx width (p = 0.3) was related to the presence of a left thoracic curve. The average greatest curve was 31°. There was no association between cerebellar ton-

<table>
<thead>
<tr>
<th>TABLE 1. Characteristics of the study patients with CM-I and scoliosis (n = 114)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristic</strong></td>
</tr>
<tr>
<td>Female (no. [%])</td>
</tr>
<tr>
<td>Mean age at scoliosis diagnosis (yrs)</td>
</tr>
<tr>
<td>Lt thoracic curve (no. [%])</td>
</tr>
<tr>
<td>Degree of greatest curve (*)</td>
</tr>
<tr>
<td>Patients w/ ≤20° curve (no. [%])</td>
</tr>
<tr>
<td>Patients w/ &gt;20° curve (no. [%])</td>
</tr>
<tr>
<td>Mean cerebellar tonsil position (mm)*</td>
</tr>
</tbody>
</table>

* Below the foramen magnum.
Chiari malformation Type I and scoliosis

Discussion

Patients with both CM-I and scoliosis are frequently referred to neurosurgeons for consideration of Chiari decompression surgery. When a syrinx is also present, the decision to proceed with Chiari decompression is not controversial, because the association between CM-I and syringes is well established. It is also clear that those patients with both CM-I and a syrinx are at risk for scoliosis. Our data confirmed this well-established association between syringes and scoliosis. The management of a patient with scoliosis and an otherwise asymptomatic CM-I is not as clear in the absence of an associated syrinx. Our goal was to evaluate this relationship in the absence of a syrinx by analyzing the independent association between CM-I and scoliosis while controlling for syrinx status. ORs from the multivariate analysis indicate that syringes, female sex, and age have associations with scoliosis. Because the OR for older age was close to 1, we believe that this finding is unlikely to be clinically significant. Most important is that CM-I was not independently associated with scoliosis in our multivariate analysis.

Some reports have suggested that there is an independent relationship between low cerebellar tonsil position and scoliosis, perhaps as a result of dorsal compression of the cervicomedullary junction by the tonsils. However, much of the existing evidence that could be used to suggest an independent association for CM-I and scoliosis in the absence of a syrinx is inconclusive. First, there have been several reports of patients with CM-I and sco-

TABLE 2. Odds ratios for scoliosis in the study cohort

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariate Analysis</th>
<th>Multivariate Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p Value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Female sex</td>
<td>&lt;0.0001</td>
<td>1.76(1.59–1.95)</td>
</tr>
<tr>
<td>Syrinx</td>
<td>&lt;0.0001</td>
<td>9.45(7.29–12.24)</td>
</tr>
<tr>
<td>CM-I</td>
<td>&lt;0.0001</td>
<td>2.03(1.64–2.51)</td>
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scoliosis without syringomyelia; however, most of these cases were drawn from larger case series that included a majority of patients with a syrinx and CM-I.12,13,22,34 Because both low cerebellar tonsil position and scoliosis are common, it is not surprising that many individuals with both conditions have been identified.2,23,30,35 Others have cited an improvement in scoliosis after CM-I decompression in patients without an associated syrinx;12,17,34 however, most patients in these series had a syrinx, making it difficult to support any independent effect of CM-I without a syrinx.17 Also, the natural history of scoliosis is variable, so it is not clear whether a few examples of postsurgical improvement in patients without a syrinx differs from the natural history of this condition seen in other individuals.34 Minor curve improvements are not unusual within groups of patients with scoliosis followed without treatment,21 and on the basis of the existing literature, it is difficult to make a case for the therapeutic benefit of Chiari decompression surgery to treat scoliosis in the absence of a syrinx.

Other evidence that has been cited to support the notion that CM-I may cause scoliosis in the absence of a syrinx is the prevalence of CM-I on screening MR images of patients undergoing scoliosis repair.18,25 Several studies have noted an association of low cerebellar tonsil position and idiopathic scoliosis.2,8,9,18,25,31 Cerebellar tonsil position, however, is distributed in an approximately normal distribution pattern across all age groups, and low tonsil position is not rare, even in healthy individuals.29 Furthermore, some groups have used definitions for tonsil ectopia in patients with scoliosis that fall within the range of normal tonsil position as it is usually defined.8,27,31 These reports confirm only that CM-I is found in a small percentage of patients with scoliosis, not that there is an independent association between CM-I and scoliosis. It is notable as well that these studies found no association between low tonsil position and the severity of curve or the presence of an atypical curve.2,31

We analyzed a large number of patients in an MRI database to study the relationship between CM-I and syrinxes. Patients in this cohort were categorized by CM-I, syrinx, and scoliosis status. When we controlled for known risk factors for scoliosis, including presence of a syrinx, female sex, and age, there was no longer an independent association between CM-I and scoliosis. When CM-I is associated with a syrinx, there is an increased risk for scoliosis and, on the basis of our analysis, this increased risk is most likely from the syrinx. In cases of CM-I without a syrinx, no association with scoliosis was found. We conclude that although CM-I is associated with syrinxes and syrinxes are associated with scoliosis, the syrinx is a necessary intermediary in most cases. When CM-I is present without a syrinx, there does not seem to be a significantly increased risk of scoliosis.

There are several limitations to our study. The patients we analyzed are representative of those who underwent MRI at a tertiary referral center and therefore do not represent a true population cohort. The cohort of patients in the study was derived from all individuals who underwent brain or cervical spine imaging in an 11-year span, which ensured that cerebellar tonsil position could be assessed accurately in every case. Because patients with scoliosis are more likely to be referred for diagnostic imaging, there was a detection bias for scoliosis in this study. For this reason, the number of detected cases of scoliosis in this group was higher than would be expected in the population as a whole. The original imaging interpretation was performed by unblinded observers and, therefore, was subject to observer bias. Finally, the multivariate regression included CM-I status, presence of a syrinx, sex, and age but did not include other potentially important factors such as a history of meningitis, subarachnoid hemorrhage, or bony abnormalities.

We did not find an independent association between CM-I and scoliosis after controlling for syrinx status. The lack of an independent association indicates that CM-I is unlikely to be causative for scoliosis in the absence of a spinal syrinx. Finally, and most important, the lack of an independent association casts some doubt on the existence of any putative therapeutic benefit of CM-I decompression surgery for treating scoliosis alone in the absence of a syrinx or other symptoms.

Conclusions

There is a strong association between syrinxes and scoliosis, but there does not seem to be a significant relationship between CM-I and scoliosis when controlling for the presence of a syrinx.

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References


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**Author Contributions**

Conception and design: Maher, Strahle. Acquisition of data: all authors. Analysis and interpretation of data: Maher, Strahle, Smith. Drafting the article: Maher, Strahle, Garton, Muraszko. Critically revising the article: Maher, Strahle. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Maher. Study supervision: Maher.

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Syrinx location and size according to etiology: identification of Chiari-associated syrinx

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OBJECT Syrinx size and location within the spinal cord may differ based on etiology or associated conditions of the brain and spine. These differences have not been clearly defined.

METHODS All patients with a syrinx were identified from 14,118 patients undergoing brain or cervical spine imaging at a single institution over an 11-year interval. Syrinx width, length, and location in the spinal cord were recorded. Patients were grouped according to associated brain and spine conditions including Chiari malformation Type I (CM-I), secondary CM (2°CM), Chiari malformation Type 0 (CM-0), tethered cord, other closed dysraphism, and spinal tumors. Syringes not associated with any known brain or spinal cord condition were considered idiopathic. Syrinx characteristics were compared between groups.

RESULTS A total of 271 patients with a syrinx were identified. The most common associated condition was CM-I (occurring in 117 patients [43.2%]), followed by spinal dysraphism (20 [7.4%]), tumor (15 [5.5%]), and tethered cord (13 [4.8%]). Eighty-three patients (30.6%) did not have any associated condition of the brain or spinal cord and their syringes were considered idiopathic. Syringes in patients with CM-I were wide (7.8 ± 3.9 mm) compared with idiopathic syringes (3.9 ± 1.0, p < 0.0001) and those associated with tethered cord (4.2 ± 0.9, p < 0.01). When considering CM-I–associated and idiopathic syringes, the authors found that CM-I–associated syringes were more likely to have their cranial extent in the cervical spine (88%), compared with idiopathic syringes (43%; p < 0.0001). The combination of syrinx width greater than 5 mm and cranial extent in the cervical spine had 99% specificity (95% CI 0.92–0.99) for CM-I–associated syrinx.

CONCLUSIONS Syrinx morphology differs according to syrinx etiology. The combination of width greater than 5 mm and cranial extent in the cervical spine is highly specific for CM-I–associated syringes. This may have relevance when determining the clinical significance of syringes in patients with low cerebellar tonsil position.


KEY WORDS Chiari malformation; scoliosis; syrinx; congenital

SYRINGOMYELIA is a common reason for neurosurgical referral. Syringes may be associated with a number of different brain or spinal cord conditions including Chiari malformation Type I (CM-I), CM secondary to other intracranial pathology such as craniostenosis (secondary CM, 2°CM), Chiari malformation Type 0 (CM-0), tethered cord, other closed dysraphism, trauma, and spinal tumors. Some syringes are not associated with any of these conditions and may be considered idiopathic. It is well established that large cervical cord syringes in patients with typical-appearing CM-I are causally linked in many cases. Decompression of the CM-I leads to a reduction in syrinx size in a significant majority of cases. In our view, the causative relationship for CM-I and syrinx is less certain for small syringes or syringes located more caudally in the spinal cord. The assignment of causation of a spinal syrinx to concurrent low position of the cerebellar tonsils, however, is clinically relevant. Surveys of pediatric neurosurgeons consistently show that surgeons are more willing to recommend CM-I decompression when a syrinx is present, even in the absence of other symptoms of CM-I. In one survey, 28% of pediatric neurosurgeon respondents recommended CM-I decompression in an oth-
erwise asymptomatic patient with CM-I and a 2-mm-wide “syrinx,” a substantially higher percentage than those who would recommend surgery for the same patient without this finding on spine MRI. If the syrinx in this hypothetical asymptomatic patient was 8 mm wide, then 75% of respondents recommended surgery. A more recent survey confirmed that most pediatric neurosurgeons continue to recommend surgery for otherwise asymptomatic patients with CM-I and syrinx. Because both CM-I and syringomyelia are not uncommon incidental findings on imaging, and decompression is frequently recommended for CM-I patients with syrinx found on MRI, it is important to address whether all such syringes are likely related to the CM-I, or whether in some cases other forces are at work that may not necessarily respond to posterior fossa decompression. Our goal was to analyze syrinx size and location of syringes associated with CM-I and other brain and spine conditions as well as idiopathic syringes to better define differences between syrinx types. We hope that this information will allow clinicians to more accurately predict the likelihood of a causative or coincidental relationship when evaluating a patient with CM-I and a syrinx.

Methods

Following University of Michigan Institutional Review Board approval, all patients with a syrinx were identified from a group of 14,118 consecutive patients who underwent brain or cervical spine MRI over an 11-year interval at the University of Michigan. The most frequent indication for imaging was scoliosis, followed by pain and weakness. Electronic records were reviewed using the Electronic Medical Record Search Engine (EMERSE) to identify patients with syrinx using the key words “syrinx,” “syringomyelia,” and “hydromyelia.” Syrinx was defined as an intramedullary spinal cord cyst that was hypointense on T1-weighted imaging and hyperintense on T2-weighted imaging, without contrast enhancement. Syrinx size and location were recorded. To be included in this analysis, the syrinx must have measured at least 3 mm in its maximum dimension on axial imaging. Intramedullary cavitations measuring less than 3 mm were excluded from analysis. Syrinx characteristics were recorded, including cranial and caudal extent and syrinx width. Syrinx level was evaluated according to the adjacent vertebral body or disc space, and the cranial and caudal extent of the syrinx were recorded according to the number of levels from the foramen magnum.

Patients were divided into 9 groups according to any associated brain or spinal cord condition (Table 1, Fig. 1). Those patients with cerebellar tonsil position 5 mm or more below the foramen magnum were assigned to the CM group. If low tonsil position was thought to be secondary to another associated intracranial condition, such as brain tumor or craniosynostosis, patients were assigned to the 2°C group. All cases of 2°C in this cohort were secondary to craniosynostosis. In rare cases, patients were considered to have CM-0 by the treating physician. These patients were also considered separately. We considered the diagnosis of CM-0 in patients with a syrinx who had evidence of cerebellar tonsil impaction and distortion at the foramen magnum with evidence of CSF flow impairment but did not meet the usual imaging criteria for CM-I in that the cerebellar tonsil position was less than 5 mm below the foramen magnum as defined by the basion-opisthion line. Associated spinal conditions included closed spinal dysraphism and simple tethered cord. These were considered as two separate groups—the closed “spinal dysraphism” group included patients with lipomyelomeningocele, diastematomyelia, intradural lipoma not confined to the filum terminale, myelocystocele, and meningocoele, while the “tethered cord” group included only those patients with low conus position below the L-2 vertebral body and fatty filum terminale without other features of closed dysraphism. For this analysis, patients were considered to have simple tethered cord if they were not included in the other closed dysraphism group and if the treating physician made a diagnosis of tethered cord. This diagnosis was made on the basis of patient symptoms as well as the presence of a low-lying conus or a fatty filum. A conus position below the inferior margin of the L-2 body is generally considered low-lying at our institution. Patients with syringes that were secondary to spinal tumor, spinal trauma, and other conditions such as infection and spinal arachnoid cyst were also considered separately. Patients were excluded if there was a history of CM Type II or open spinal dysraphism. Patients who received surgical treatment for CM-I prior to their first MRI at our institution were also excluded. Scoliosis was defined as a lateral Cobb angle of at least 10° on radiography.

Statistical significance calculations were obtained using 2-tailed $t$-test for continuous variables and Fisher exact test for categorical variables, and $p$ values < 0.05 were considered significant. Sensitivity and specificity calculations were performed with 95% confidence intervals. Data were analyzed using StatPlus software (AnalystSoft Inc.).

Results

A total 271 patients (1.9%) with a syrinx at least 3 mm in maximum axial dimension were identified. CM-I was the most frequent associated condition (present in 117 patients [43.2%]), followed by spinal dysraphism (20 [7.4%]), tumor (15 [5.5%]), tethered cord (13 [4.8%]), and 2°C (13 [4.8%]) (Table 1, Fig. 1). No associated brain or spinal cord condition was found in 83 patients (30.6%), and syringes in these patients were considered idiopathic.

Syrinx characteristics differed according to associated condition. In general, syringes associated with CM-I, 2°C, tumor, and dysraphism were wide compared with idiopathic syringes (Fig. 2). Syringes in patients with CM-I had a mean maximum width of 7.8 ± 3.9 mm, similar to those in patients with CM-0 (8.3 ± 3.7 mm) or 2°C (7.9 ± 3.6 mm). In contrast to CM-I–associated syringes, idiopathic syringes had a mean maximum axial dimension of only 3.9 ± 1.0 mm ($p < 0.0001$). Syringes associated with tethered cord were also narrower than CM-I–associated syringes (4.2 ± 0.9 mm, $p < 0.01$). Syringes associated with spinal dysraphism were wider (5.7 ± 3.0 mm) than idiopathic syringes and syringes associated with simple tethered cord, but narrower than CM-I–associated syringes.
Almost all idiopathic syringes were less than or equal to 5 mm in maximum axial dimension (79 syringes [95.2%]). In patients with CM-I, only 31.6% of syringes (37 syringes) were 5 mm or less in maximum axial dimension (Figs. 2 and 3).

Syrinx location within the spinal canal also differed according to associated condition (Fig. 4). Syringes associated with CM-I, CM-0, or 2°CM had a more superior cranial extent, usually in the cervical spine. Syringes associated with tethered cord and spinal dysraphism were more likely to have their cranial and caudal extents located more caudally. Idiopathic syringes had an intermediate position within the spinal canal. CM-I–associated syringes were longer than idiopathic syringes (8.3 ± 5.9 vs 6.6 ± 4.8 levels, respectively; p < 0.05) (Fig. 5). In 12 patients, the syringes were limited to the T-12 segment or below. Nine of these 12 patients had a tethered cord, and 3 had a normal conus position.

Scoliosis, defined as a Cobb angle of at least 10°, was found in 144 patients (53.1%). The incidence of scoliosis did not differ significantly by associated condition, with the exception that patients with 2°CM were less likely to have scoliosis (Fig. 6). The mean age at scoliosis diagnosis was 9.6 ± 4.5 years. Those with spinal dysraphism (7.9 ± 5.2 years) and tethered cord (6.2 ± 5.5 years) were diagnosed with scoliosis at a younger age (Table 1). For idiopathic syrinx, there was a similar number of patients with and without scoliosis for a given syrinx width. For patients with CM-I–associated syrinx with narrower widths (<9 mm), there were similar numbers of patients with and without scoliosis for a given syrinx width. However, most CM-I patients with wide syringes (>9 mm) had scoliosis (Fig. 7).

We evaluated conus level to rule out occult spinal cord tethering in patients with idiopathic syrinx, as their width morphology was similar to those with tethered cord. We found a normal mean conus position in patients with idiopathic syrinx, in contrast to those with tethered cord and those with spinal dysraphism (Fig. 8), in whom a low conus position was expected. The mean conus position for patients with CM-I and syrinx was in the normal range.

When looking at the cranial extent of syringes, we found that it was in the cervical spine in 88% of patients with CM-I–associated syringes compared with 43% of patients with idiopathic syringes (p < 0.0001). A small number of patients with CM-I had narrow syringes with cranial extent in the thoracic or lumbar spine, more similar in morphology to that of an idiopathic syrinx than a typical CM-I–associated syrinx. Despite these outliers, however, the combination of syrinx width greater than 5 mm and cranial extent in the cervical spine had 99% specificity (95% CI 0.92–0.99) and 64% sensitivity (95% CI 0.55–0.73) for CM-I–associated syrinx. Conversely, syrinx width of 5 mm or less and cranial extent in the thoracic or lumbar spine had 92% specificity (95% CI 0.86–0.96) and 54% sensitivity (95% CI 0.42–0.65) for idiopathic syrinx.

The mean age at the time of syrinx diagnosis, including patients in all groups, was 9.3 ± 5.3 years. Syringes associated with tethered cord and spinal dysraphism were diagnosed earlier, with a mean age at the time of diagnosis of 4.6 ± 4.7 years for tethered cord–associated syrinx, and
4.3 ± 4.7 years for syringes associated with spinal dysraphism. The mean age at diagnosis of syringes associated with CM-I was 10.2 ± 4.8 years, and for idiopathic syringes the mean age at diagnosis was 9.8 ± 5.2 years. Syringes associated with 2°CM were also diagnosed at a young age (7.1 ± 4.4 years).

Discussion

Syringomyelia may result from several possible etiologies or, in idiopathic cases, may have no discernible etiology at all.10,11 It is well established that CM-I may lead to syrinx formation.2,5,8,10,20,28,30 Most contemporary reports have suggested that abnormal flow of CSF at the cranio-cervical junction leads to syrinx formation.4,5,10,17,20,27,28,31 However, given the relatively common incidence of CM-I and syrinx found in patients undergoing MRI, it is also possible that in some cases, a patient with low tonsil position also will have an intramedullary spine cyst for reasons unrelated to the CM-I. This idea is reinforced by clinical experience, in that syringes are quite variable in terms of size and position within the spinal canal. When a patient with a syrinx also has a CM-I, can we determine how likely it is that the CM-I has actually caused the syrinx? This determination is clinically important, since the presence of a syrinx may be used as a justification for CM-I decompression in some cases.1,22,25,26

Since syringes may be caused by multiple associated conditions or even, for idiopathic syringes, have no known cause at all, it follows that not all syringes found in patients with CM-I are necessarily caused by the CM-I. There are several facts that establish the relationship between CM-I and syringomyelia. First, syringes occur with significantly increased frequency in those with CM-I and reliably improves following CM-I decompression.13,28,30 Many groups have plausibly described how changes in CSF flow at the foramen magnum can lead to syrinx formation.10,20 We have

FIG. 1. Number of patients with syrinx according to associated pathology.

FIG. 2. Syrinx width according to associated pathology. Mean maximum width values and SDs are shown. *p < 0.0001, **p < 0.01.
shown that CM-I–associated syringes are also usually distinct in location and size. We found that CM-I–associated syringes had a larger mean axial dimension compared with other types and were more likely to have a cranial extent in the cervical spine. These findings are consistent with prior reports of CM-I–associated syringes.10,28 Taken together, these facts imply that the mechanism of syrinx formation in CM-I–associated cases is likely to be different than in syringes of a different morphological appearance. Mean syrinx length, however, was not useful in differentiating CM-I–associated syringes from idiopathic syringes.

Thin, idiopathic syringes have a benign natural history and almost certainly have a pathophysiology distinct from that of CM-I–associated syringes.12,23,26 In general, idiopathic syringes have a different morphology and location, tending to be narrower than CM-associated syringes and not as frequently located in the cervical spine.3,12,14,18,23 They are usually asymptomatic, incidental findings, and in most cases require no treatment.12,14,18,23,26 All patients in this series had a syrinx width of at least 3 mm. There is no consensus definition for distinguishing a narrow syrinx from the very common finding of a dilated central canal on imaging. Some groups have used a minimum width threshold of 2 mm for an imaging diagnosis of syrinx; we used 3 mm width as the inclusion criterion for syrinx in this analysis.18,21 We prefer the 3-mm definition, since it is more likely to exclude very thin central spinal fluid collections that blend into the category of dilated central canal.

Conus level was evaluated, as it has previously been suggested by others that some patients with CM-I have a low-lying conus.30–32 We did not find any difference in conus position in patients with CM-I–associated syrinx compared with patients with idiopathic syrinx. The fact that tethered cord syringes are narrow and usually located caudally in the spine suggests a distinct pathophysiology

**FIG. 3.** Patients with idiopathic and CM-I–associated syrinx grouped according to maximum syrinx width and cranial extent of syrinx. Figure is available in color online only.

**FIG. 4.** Cranial and caudal extent of syrinx (mean number of levels). Error bars indicate SDs.
for this group as well. Nine of the 12 patients with a syrinx confined to the lowest segments (T-12 or below) had a low conus position. Three patients with a syrinx at or below the T-12 level had no evidence of tethered cord, and their cases may be consistent with a diagnosis of a benign distal syrinx, although for the purposes of this analysis, we made no attempt to separate these patients from the idiopathic syrinx group. Our finding that these syringes tend to be located caudally in the spinal cord is consistent with the small series previously reported by Kulwin et al.\textsuperscript{16} In our cohort, patients with tethered cord were diagnosed earlier. Ten of the 22 patients in our series with a cutaneous mark on the back had a tethered cord. It is possible that this association with cutaneous stigmata led to an earlier mean age of diagnosis in the group with tethered cord.

Although we may conclude that most syringes in patients with CM-I are caused by the CM-I, it is likely that a small number of syringes in these patients may be idiopathic or caused by another agent. For the purposes of this analysis, we treated all syringes in patients with CM-I as “CM-I–associated syringes.” Nevertheless, there are clearly syringes within this group that do not share the typical features of the group, either because they are narrow or because they are inferiorly located or for both reasons. It is possible that these outliers represent patients who could be considered to have another syrinx type and coincidentally low cerebellar tonsil position. Our data support a strong link between wide, rostrally located syringes and CM-I, but no such strong link for thin, inferiorly located syringes.

On the basis of these results, when an otherwise asymptomatic patient with CM-I presents with a syrinx that is not typical for a CM-I–associated syrinx, we would not offer CM-I decompression in our practice. We would be more likely to consider prophylactic CM-I decompression for a patient with a typical wide, cervical CM-I–associated syrinx.

While the pathophysiology for CM-I–associated syrinx has received much attention,\textsuperscript{20} less attention has been given to idiopathic syringomyelia. As idiopathic syringes are clearly different both in their behavior\textsuperscript{18} and morphology, it

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**FIG. 5.** Syrinx length (mean number of levels) according to syrinx etiology. Error bars indicate SDs. *p < 0.05.

**FIG. 6.** Fraction of patients with scoliosis according to syrinx etiology, stratified by sex.
is possible that their pathophysiology is different. We can speculate that idiopathic syringes may arise from stretch on the canal from the denticulate ligaments, with passive accumulation of fluid in the spinal cord.

The passive formation of thin syrinx cavities resulting from stretch could theoretically also be applied to those patients with scoliosis, whose spinal cord and ligaments may be under more tension. Scoliosis is also seen in patients with CM-I–associated syringes, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider. For the group of patients with syrinx cavities, which, as our data demonstrate, are typically wider.
we acknowledge that some will undoubtedly consider patients that we have considered to have a thin syrinx to instead harbor a dilated central canal.12 Idiopathic syrinx is essentially impossible to distinguish from a dilated central canal on imaging.18 Despite this limitation, it is necessary to choose an arbitrary minimum diameter for this inclusion criterion. We chose to exclude from analysis those with a maximum axial dimension of less than 3 mm, since smaller cavitations are rarely clinically relevant.

There are several other limitations to this retrospective analysis. All patients in this analysis were selected from a population undergoing imaging; therefore, selection bias must be considered in any interpretation of these results. We recorded conus position without respect to patient age. We do not expect this to have a meaningful impact on our conclusions since, in most individuals, the conus position is not expected to ascend to any significant extent beyond infancy.7,15,33,34 The categorization of patients with CM-0 deserves mention also, as these patients might otherwise have been grouped with the idiopathic group. We believe that CM-0, although very rare, is a distinct entity and should be considered as a separate diagnostic category. Only 4 such patients were included in this study, and placing them within the idiopathic group would not substantially change the character of the group if these patients had been reclassified as having idiopathic syringes. Logically, however, if the syrinx morphology is strongly related to the pathophysiology of syrinx formation, then the presence of wide cervical syrinx should prompt a search for cervicomedullary CSF flow interruptions. Our methodology does not allow for any analysis of the natural history of these lesions from the data presented here. We have previously reported on the natural history of a small group of patients with CM-I and syrinx that had been selected for nonoperative management.35 We excluded patients with open spinal dysraphism. Those with open dysraphism are unique in that the diagnosis is always well established by patient history. Furthermore, we believe that the treatment recommendations made for syringes in this category of patients are different due to the distinct pathophysiology of patients with open dysraphism. Finally, it must be noted that although we found associations between various conditions and syrinx size and location, this does not definitely prove causation. Prospective studies will be necessary to confirm our findings.

Conclusions

Syrinx morphology, including width and location, differs according to syrinx etiology. This suggests a distinct pathogenesis for syringes with different associated conditions. When considering CM-I and idiopathic syrinx, the combination of width greater than 5 mm and cranial extent in the cervical spine is highly specific for CM-I–associated syrinx. Conversely, the combination of width of 5 mm or less and a cranial extent in the thoracic or lumbar spine has high specificity for idiopathic syrinx. This finding may assist with assigning causation when evaluating a patient with both CM-I and syringomyelia.

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References


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Conception and design: Maher, Strahle. Acquisition of data: Maher, Strahle, Smith, Starr, Kapurch. Analysis and interpretation of data: Maher, Strahle, Garten. Drafting the article: Maher, Strahle. Critically revising the article: Maher, Muraszko, Garten, Strahle. Reviewed submitted version: all authors. Approved the final version: Maher. Statistical analysis: Strahle, Maher, Smith. Study supervision: Maher.

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With any measurement, a definition of normal is necessary before any determination of abnormality can be made. This is especially relevant for abnormal measurements that may lead to further testing, specialty consultation, or treatment. The definition of normalcy for any morphometric measurement may be influenced by an understanding of both the frequency of values in the population and the pathological consequences of outliers.

Chiari malformation is frequently diagnosed on imaging based on the extent of tonsil location below the foramen magnum. Most often, CM is defined as tonsil location at least 5 mm below the basion-opisthion line.1,7,12,23–25,33 Unfortunately, studies on the normal cerebellar tonsil position, especially as it relates to normal population distribution with advancing age, are extremely limited.1,7,25,28 Understanding the distribution of normal cerebellar tonsil position is a basic prerequisite when determining a potentially abnormal position. Prior attempts at defining a normal cerebellar tonsil position have been limited by the very small number of patients precluding normative analysis by age. Our objective in the present study was to provide normative data on cerebellar tonsil positions across every age range with the hope that this information would allow clinicians to determine the relative importance of an abnormal tonsil position in patients of all ages.

Methods

After approval was obtained from the University of Michigan Institutional Review Board, we performed a database search for consecutive patients who had undergone brain or cervical spine MRI for any reason over an 11-year interval at our institution. From 62,533 consecutive patients, 300 in each of 8 age cohorts (in years) were randomly selected: 0–10, 11–20, 21–30, 31–40, 41–50, 51–60, 61–70, and ≥71. Ages at the time of MRI were used to
Cerebellar tonsil position

categorize patients. Imaging evidence of any significant posterior fossa comorbidity precluded participation in the study: posterior fossa tumor (26 patients), posterior fossa arachnoid cyst (45 patients), prior posterior fossa surgery other than Chiari decompression (23 patients), prior Chiari decompression (17 patients), significant mass effect from a primarily supratentorial process (17 patients), volume loss from prior stroke (9 patients), or developmental abnormality including Chiari Type II (14 patients). Magnetic resonance images for 2551 patients were reviewed to assemble 8 groups of 300 patients each (2400 total patients) for analysis.

Of the 2400 patients selected for examination, 1380 were females and 1020 were males, reflecting a female preponderance in the overall group of 62,533 patients undergoing MRI examination at our institution. Magnetic resonance images for each of the 2400 selected patients were reviewed, and tonsil position measurements were recorded. For each patient, the lowest tonsil position was determined by first drawing a line from the basion to the opisthion on a midsagittal T1-weighted MR image. Next, a line was drawn perpendicular to the basion-opisthion line and extending either superiorly or inferiorly to the tip of the cerebellar tonsils. The length of this second line from the tonsil tip to the basion-opisthion line was recorded as the tonsil position. For purposes of this analysis, tonsils extending caudally to the basion-opisthion line were assigned positive values, and tonsils that ended rostrally to the basion-opisthion line were assigned negative values. Tonsils that ended at the basion-opisthion line were assigned a value of 0. Measurements were recorded to the nearest millimeter. Two tonsil measurements were taken for each patient: one in the midsagittal plane and one in the parasagittal plane that corresponded to the lowest tonsil position on the left or right side. Coronal images were then examined to determine if there was a difference in tonsil position between the left and right side. Finally, tonsil morphology for each patient was assigned to one of 3 categories: rounded, pegged, or intermediate (Fig. 1). Each image was measured, and measurements were agreed on by 2 investigators, one of whom was a board-certified pediatric neurological surgeon.

Clinical data for each patient was reviewed, and patients with a clinical diagnosis of CM were identified. Of the 2400 patients, 22 had a clinical diagnosis of CM according to the treating physician. For certain portions of our analysis, these 22 patients were excluded and the remaining 2378 patients were considered separately. Most of the 22 patients with a clinical diagnosis of CM were in the youngest age groups: 14 in the 0–10 years group, 2 in the 21–30 years group, 4 in the 31–40 years group, and 2 in the 41–50 years group.

The SAS 9.2 statistical software (SAS Institute Inc.) was used to generate reports and figures based on the data. Simple descriptive statistics were generated using the means procedure. Histograms were generated using the univariate procedure. The lowest tonsil position for each patient, without respect to laterality, was used for analysis of tonsil position.

Results

The lowest measurement for cerebellar tonsil position varied according to age group (Tables 1 and 2). In general, the mean tonsil height decreased slightly with advancing age into young adulthood and increased gradually with advancing age in adulthood (Fig. 2 upper). This trend persisted when 22 patients with a clinical diagnosis of CM were excluded from analysis (Fig. 2 lower). An increasing age in the adult age range was significantly associated with a decreased likelihood of a tonsil position 5 mm or more below the foramen magnum (p = 0.0004).

In general, distribution of the lowest tonsil position in each age group followed a normal-type distribution. An exception to this pattern was found in the 1st decade of life (Fig. 3A) in which the normal distribution pattern was skewed toward higher tonsils, although a small group of outliers had very low tonsils. Each of the adult age cohorts followed an essentially normal distribution pattern with a gradual shift of the curve toward a higher mean tonsil position with advancing age (Fig. 3C–H). Female sex was associated with a lower mean tonsil position (Table 3; p < 0.0001). Among all age groups, 47 females (2%) and 27 males (1%) had tonsils at least 5 mm below the foramen magnum. Given that only 20 patients with pegged tonsils were included in the study, female sex was not significantly associated with pegged tonsil morphology in this group (p = 0.2).

Most patients had rounded tonsil morphology. Two thousand three hundred thirty-five patients (97%) had rounded tonsils, 45 (2%) had intermediate morphology, and 20 (1%) had pegged morphology. Patients with pegged

![Fig. 1](image-url) Magnetic resonance images depicting examples of cerebellar tonsil morphology: pegged (A), intermediate (B), or rounded (C).
morphology were more likely to have a tonsil location at least 5 mm below the foramen magnum (85%), as compared with those with intermediate (38%) or rounded (2%) morphology (p < 0.0001). Three patients with a tonsil position less than 5 mm below the foramen magnum had pegged tonsils. Of the 74 patients with a tonsil position at least 5 mm below the foramen magnum, 40 (54%) had a rounded configuration. Patients with a tonsil position 3–5 mm below the foramen magnum were unlikely to exhibit pegged morphology. Only 1 (0.5%) of 212 patients in that group had pegged morphology and 4 (2%) had intermediate morphology.

In most cases (84%), the right and left tonsils had symmetric locations with respect to the foramen magnum. Two hundred seventy-four patients had a lower right tonsil (11%), and 101 patients (4%) had a lower left tonsil. Patients with a lower tonsil position tended to have an asymmetric tonsil position, usually lower on the right (p < 0.0001). Of the 212 patients with the lowest tonsil 3–5 mm below the foramen magnum, 141 (67%) had symmetric tonsils, 52 (25%) had a lower right tonsil, and 19 (9%) had a lower left tonsil. Of the 74 patients with a tonsil position 5 mm or more below the foramen magnum, 38 (51%) had a symmetric tonsil position, 29 (39%) had a lower right tonsil, and 7 (9%) had a lower left tonsil.

**Discussion**

We evaluated a random sample of patients undergoing neuroimaging at our institution to assess the position and morphology of the cerebellar tonsils. Our data support several conclusions regarding tonsil position. The position of the cerebellar tonsils with respect to the foramen magnum follows a normal distribution pattern in most age groups. A normal distribution is characterized by a symmetrical curve centered around the mean value, indicating that the data points are evenly distributed around the average. This pattern is evident in our study's age groups, with the highest percentage of tonsil positions occurring around the mean value, and fewer at the extremes. This distribution pattern helps in understanding the variability and typical positioning of the tonsils, which is crucial for clinical assessment and patient management. The observed asymmetry in the lower tonsil positions also provides insights into potential neurological implications, such as the risk of developing hindbrain herniation, which is a critical concern in neurosurgical practice.
Cerebellar tonsil position

<table>
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<th>Age Group in Yrs</th>
<th>0%</th>
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<th>10%</th>
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* Excluded from this secondary analysis were 22 patients in whom CM was diagnosed at any time during their clinical encounter. Negative numbers correspond to a more rostral tonsil location with respect to the foramen magnum.

The mean tonsil height decreases during childhood and young adulthood and then increases gradually with advancing age. Females have, on average, a lower tonsil position than males, and the right-sided tonsil is lower more often than the left. The distribution pattern of tonsil position suggests a multifactorial inheritance pattern similar to other normally distributed morphometric features such as height or head circumference. Given this pattern, it is still possible to account for the emergence of familial tendencies in CM, perhaps as a result of multifactorial inheritance tendencies for posterior fossa dimensions. Although the identification of a genetic locus for CM inheritance remains an area for investigation, we believe that a discrete genetic cause that accounts for most cases of CM is unlikely to be found given the population distribution pattern that we report.

While prior publications with small sample sizes have addressed the position of the cerebellar tonsils in individuals undergoing imaging studies, our study is the first to provide age- and sex-specific distributions using a much larger sample. In 1985, Aboulezz et al. studied 82 patients and concluded that none of the patients without posterior fossa abnormalities had tonsil position more than 3 mm below the foramen magnum. Patients with any posterior fossa abnormality on MRI were excluded from that analysis. In 1986, Barkovich et al. analyzed 200 selected “normal” patients and found a mean tonsil position of 1 mm above the foramen magnum and a range of 8 mm above to 5 mm below. Ishikawa and colleagues reported on 50 patients whose mean tonsil position was just above the foramen magnum. Finally, 2 recent studies reported on 170 and 203 patients to evaluate the relationship between cerebellar tonsil position and scoliosis.

Initial studies that attempted to define cerebellar ton-
sil position in normal individuals were limited by a very small number of patients, which precluded normative analysis by age. Mikulis et al. were the first to analyze age-related changes in normal tonsil position. They studied the MR images of 221 patients between 5 months and 89 years of age, with 18–30 patients in each age decade. They found a trend toward a more cranial tonsil position with advancing age. Unfortunately, because of the relatively small number of patients included in that study, they were unable to perform a detailed analysis of the distribution of tonsil location in specific age groups. They suggested that tonsil height increased during childhood, remained relatively static during adult life, and then increased again in late adulthood, although they acknowledged that they had an insufficient number of patients to prove that theory. Our observations suggest that mean cerebellar tonsil position changes associated with advancing age differ from the pattern that was postulated by Mikulis et al. in two important ways. First, we found that mean tonsil height follows a pattern of decrease, not increase, early in life. Mikulis et al. speculated that early in life, cranial volume is often insufficient for the posterior fossa contents, and as a result the tonsils are frequently displaced through the foramen magnum. Although we found many instances of such morphology, we found several instances of high tonsil position in the 1st decade as well. We noted that tonsil position in the 1st decade was extremely variable, with a relatively high mean position as well as a sizable group of low-lying outliers. Another difference between our results and the theory advanced by Mikulis et al. is found in the adult age range. Rather than abruptly increasing in the elderly after a long static period in the middle-age decades, mean cerebellar tonsil height increases steadily with advancing age throughout the adult age range.

Chiari malformation Type I is more frequently diagnosed in females. Sex differences in tonsil position in the normal population have not been extensively studied. Sun et al. found that girls with scoliosis had a slightly lower mean tonsil position compared with boys, although the difference was not statistically significant in their small sample. We found that female sex was significantly associated with a lower mean tonsil position in all age groups. Although most patients had symmetric right and left tonsil positions, we found that the right tonsil tended to be lower than the left in patients with lower tonsils. This right-sided predominance was also noted by Tubbs et al. in a prior series of 42 patients with CM. The finding that the right-sided tonsil is generally lower than the left in patients with a low tonsil position is of uncertain significance and joins a list of other similarly unexplained side preferences including dominance of the right transverse sinus, left vertebral artery, and left middle fossa arachnoid cysts.

It is probable that Chiari symptoms and the formation of spinal syringes are the result of crowding at the foramen magnum, thus leading to abnormal CSF movement at the craniocervical junction. Since crowding is difficult to quantify, CM has usually been diagnosed on imaging by determining a cerebellar tonsil position at least 5 mm below the basion-opisthion line, with some groups even considering a tonsil position 3–5 mm below the foramen magnum as evidence of a “borderline” CM. General acceptance of this definition followed the publication of several (previously discussed) clinical studies at the dawn of the MRI era. It is worth noting that the imaging definition for CM was based on studies involving very small numbers of patients. First, in 1985, Aboulezz et al. evaluated 82 patients and concluded that none of the patients without posterior fossa abnormalities had a tonsil location more than 3 mm below the foramen magnum. Patients with any posterior fossa abnormality on MRI were excluded from that analysis. In another study, these authors found that all of 13 patients with CM had a tonsil position more than 5 mm below the foramen magnum. One year later, Barkovich et al. reported the MRI findings for 200 selected “normal” patients and 25 patients who were considered to have symptomatic CM. In that small and selected sample, they found that the range of tonsil position in “normal” patients varied between 8 mm above to 5 mm below the foramen magnum. Tonsil position for CM patients in that study varied between 3 and 29 mm below the foramen magnum. With these results in mind, Barkovich et al. determined that a 3-mm definition for CM would result in 96% sensitivity and 99.5% specificity. These authors suggested that it is better to err on the side of a false-positive diagnosis when determining the most proper cutoff for
Cerebellar tonsil position

Normal versus pathological cerebellar descent. Their initial studies indicated that one could be confident that a patient with a tonsil position 5 mm beneath the foramen magnum was different from the normal population in a way that implied a distinctly pathological anatomy. In contrast to these initial reports, several groups have found that many patients with tonsils located more than 5 mm below the foramen magnum are asymptomatic. In 1992, Elster and Chen found that 30% of patients with descent between 5 and 10 mm were asymptomatic. More recent reports have shown an even larger percentage of asymptomatic individuals who meet the diagnostic criteria for CM-I on imaging. Thus, the use of a discrete 5-mm boundary for a clinical syndrome is not as specific as early investigators had suggested.

In normal individuals, the position of the cerebellar tonsils falls along a normally distributed continuum, and a position 5 mm below the foramen magnum falls on the low side of that continuum. A group of individuals presenting with common complaints is likely to contain many whose tonsil position is part of the tail of the normal distribution. Unfortunately, the current clinical tendency appears to be unreservedly admitting such patients to a pathoanatomical group we call CM-I based on tonsil position alone. In view of our results, we believe that this should be reconsidered. Although cerebellar tonsil position in scoliosis is controversial, several studies have provided additional insight into the distribution of cerebellar tonsil position in this context. Sun et al. revealed that the lowest tonsil position in patients with scoliosis followed a normal distribution, which is consistent with our own finding of an essentially normal distribution of tonsil position in all age ranges.

In our previous publication detailing the prevalence of CM-I in children undergoing imaging, we found that 3.6% of the children had a tonsil position ≥ 5 mm below the foramen magnum. In the present study, however, we found a slightly higher prevalence for the same age group. The previous cohort was generated based on radiology re-
ports with direct review of images in only those cases that were initially identified by a key word search of the medical and radiographic record. In that study, a patient with a tonsil position 5 mm or more below the foramen magnum but with no recorded comment on tonsil position or CM would not have been identified. The current study involved a random sample of our imaging database without regard to identified pathology. In fact, of the patients with tonsils 5 mm or more below the foramen magnum, CM was mentioned in the radiology report of only 39 (53%) of 74 patients.

Several groups have shown that patients with CM have a reduced posterior fossa volume resulting in craniocerebral disproportion, or crowding, in the posterior fossa.6,15,17,26,30–32,37 Although cerebellar tonsil measurements are a convenient marker for crowding at the foramen magnum, the correlation is far from exact. In some cases, patients with tonsils less than 5 mm below the basion-opisthion line can have clinical presentation of Chiari syndrome and even syringomelia due to crowding at the foramen magnum. This is consistent with recent studies that have found no clinical differences between CM-I and CM-0.21,36 Conversely, many patients with a tonsil location more than 5 mm below the basion-opisthion line are asymptomatic and do not demonstrate evidence of crowding at the foramen magnum.5,27,33,34 Given the relatively small number of patients with pegged tonsil morphology, sex was not associated with an increased likelihood of pegged tonsils. An analysis that includes more patients with pegged morphology will be necessary to better understand that relationship. Furthermore, we confined our measurements to tonsil position with respect to the foramen magnum. Future study will be required to understand the relationship between tonsil position and posterior fossa volume and cerebroval volume in those without CM. We hope the findings in the present study will stimulate more investigation in these areas.

Selection bias must be considered in any interpretation of these results. Most importantly, our patients were randomly selected from a population of those undergoing imaging rather than the entire population. All patients in this series were selected for intracranial imaging, and the distribution of tonsil position in this group cannot be expected to exactly match that of the population as a whole. To mitigate this bias, we attempted to identify any patient in whom CM had been clinically diagnosed and excluded them from portions of our analysis. Nevertheless, by excluding these patients, it is possible that we introduced yet another bias, especially given the prevalence of CM in the population. We believe that the best estimate of true tonsil position in the population can be made by considering both sets of results; thus, we have presented both. Furthermore, it is worth noting that the percentile estimates and general trends do not differ substantially whether or not the CM patients are included, reflecting the fact that relatively few patients were excluded from our secondary analysis because of a clinical diagnosis of CM. Patients with posterior fossa arachnoid cysts were also excluded. These cysts are common in the general population and usually asymptomatic.3,4 Nevertheless, since these cysts are occasionally associated with tonsillar ectopia, we chose to exclude patients with these lesions from our analysis.8,18

Conclusions

Cerebellar tonsil position follows an essentially normal distribution and varies significantly by age. This finding has implications for advancing our understanding of CM-I.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Maher, Smith. Acquisition of data: Maher, Smith, Strahle, Bapuraj, Muraszko, Garton. Analysis and interpretation of data: Maher, Smith, Strahle. Drafting the article: Maher, Smith, Strahle, Muraszko, Garton. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Maher. Statistical analysis: Smith. Study supervision: Maher.

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Cerebellar tonsil position


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INTRACRANIAL PSEUDOTUMORS

Anne G. Osborn, M.D.

DISCLOSURES

- Elsevier (consultant, author)
- Mallinckrodt (speaker)

INTRACRANIAL PSEUDOTUMOR SYNDROMES

- CSF pressure
  - Primary idiopathic
  - Secondary pseudotumor cerebri syndrome
- Inflammatory pseudotumors
  - A.k.a. “plasma cell granulomas”
  - Idiopathic
  - Known/presumed etiology
    - Granulomatosis
    - Histiocytosis
    - IgG4-related
  - Not tumor-related


CLINICAL PRESENTATION

- Age, gender
  - Adults >> children
- Common
  - Headache, pain
  - Cranial nerve palsy
  - Visual symptoms


The REALLY Maddening Mystery Of...

Inflammatory Pseudotumors

- Inflammatory pseudotumors (IIP)
  - Uncommon
  - Can be virtually indistinguishable from true neoplasms
  - Body (lung) >> head and neck
    - 5-8% of orbital masses
  - Skull base, intracranial rare but a huge diagnostic dilemma!
- Idiopathic (etiology unknown)
  - Exaggerated immunological response?
  - Mediated by B- and/or T-cell lymphocytes
  - Role of viral infection (EBV)?
  - Can they be “premalignant”??
- Known etiology
  - IgG4-related
- Clinical presentation
  - Fever, weight loss, pain common

- Location
  - Meninges (60%), especially basal
  - Cavernous sinus (often from orbit)
  - Parenchyma (usually 2nd invasion)
  - Ventricles (choroid plexus)
- Gross pathology
  - Masslike dura-arachnoid thickening
  - Firm, yellowish
  - Lobulated
  - 1% invade underlying brain
- Microscopic features
  - Myofiibroblastic cells
  - Polyclonal lymphocytes, plasma cells
  ± Scattered histiocytes

Courtesy R. Hewlett, MD

INTRACRANIAL INFLAMMATORY PSEUDOTUMORS

- Location
- Gross pathology
- Microscopic features

Page 1
**INTRACRANIAL INFLAMMATORY PSEUDOTUMORS**

- **Microscopic pathology**
  - Inflammatory infiltrate
    - Lymphocytes (no atypical ones!)
    - Plasma cells
    - Variable histiocytes, fibroblasts
    - No granulomas
  - May cause vasculitis
    - Can be necrotizing
  - Can be IgG4-related
    - Many IIPs are IgG4-induced pseudotumors

**Imaging**

- Dural-based
- BOS > calvarium
- May invade skull
- May involve underlying brain
- T2 hypointense
- Uniform enhancement

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**INTRACRANIAL PSEUDOTUMOR**

- **58yF vertical strabismus, diagnosed Tolosa-Hunt**
  - Rx steroids
  - 3 yrs later…..

**SKULL/SCALP/SURAL LESION**

- Biopsy disclosed B-cell lymphoma!
  - So . . . Are some pseudotumors “pre-malignant”??

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**62yM with seizure, RUE weakness**

- Initial imaging studies nonspecific mild dural thickening . . .meh!
  - But 6 months later, worsened ….

**REPEAT MR SCAN PERFORMED**

- Biopsy showed **benign polyclonal** lymphocytes → pseudotumor!
**IgG4-Related Disease**

- **Pathology**
  - Plasma cell infiltrate
  - IgG4+ immunoreactivity

- **Location**
  - Most common = pancreas
  - Head-neck
    - Lacrimal gland
    - Orbital pseudotumors
    - Cranial nerves
  - Intracranial
    - Pituitary gland
    - Infundibulum

- **Significance**
  - Most “idiopathic” hypertrophic pachymeningitis?

Lu et al: IgG4-related hypertrophic pachymeningitis. JAMA Neurol 6: 785-93, 2014

**ORBITAL/INTRACRANIAL “IDIOPATHIC” PSEUDOTUMOR**

- **Initial Presentation**
  - Headaches x 8 months
  - Increasingly severe
  - Occipital radiating to front
  - Initially relieved with ibuprofen

- **ED**
  - Worsening HA
  - Visual loss x 1 week

**DURAL BIOPSY**

- H&E dural thickening, fibrosis, lymphoplasmacytic infiltrate
- Perivascular, interstitial distribution of lymphoplasmacytic infiltrate

**NEUROSARCOID**

- **Terminology, etiology**
  - Multisystem inflammation CD4+ cells
  - Noncaseating epithelioid granulomas

- **Location**
  - CNS in 5%
  - Of these, isolated CNS in 5-10%
  - Meninges (pia, dura-arachnoid)
  - Hypothalamus, infundibulum
  - CNs
  - Brain parenchyma (PVSs)

- **Clinical**
  - Worldwide
  - Adults

**NEUROSARCOID**

- Dura-Arachnoid + Brain Invasion

**DURAL BIOPSY**

IHC plasma cell stain + for IgG4

IgG:IgG4 ratio > 40% so diagnosis = IgG4-related disease
NEUROSARCOID
Nasopharynx, BOS/Dura-arachnoid/Brain

INTRACRANIAL INFLAMMATORY PSEUDOTUMORS: DDX

• “Real” tumor
  - Dural-based lymphoma
  - Metastases
  - Lymphoplasmacytic-rich meningioma
  - Grows “flat” along meninges, may invade

• Benign mimics
  - Langerhans cell histiocytosis (LCH)
  - Non-LCH disorders
    - Rosai-Dorfman disease
    - Erdheim-Chester disease
    - Hemophagocytic lymphohistiocytosis
    - Juvenile xanthogranuloma
    - IgG4-related disease
  - Neurosarcoïd
  - Infection (tuberculosis)
  - Extramedullary hematopoiesis
Spontaneous Intracranial Hypotension Diagnosis and Treatment

Spontaneous Intracranial Hypotension

- Loss of CSF volume
  - resulting in headache syndrome, typically postural in nature
  - occurring in all age groups, but typically middle-aged females
- CSF fistula at thoracic or cervicothoracic junction
  - perineural cyst or HNP/osteophyte that erodes dura
  - Collagen defect
- CSF opening pressure is often but not always low,
  - Pressures may be within normal limits (6-20cm)
- Imaging is usually diagnostic, but can be subtle (MR>CT)
  - Slow CSF leak may result in "normal" CT myelogram
  - Fast leak may require dynamic myelography w C1-2 puncture
- Epidural blood patch is curative in ~75% of cases

Key Take Home Points

- The diagnosis of "Chiari 1" requires one to consider the alternative diagnosis of SIH
- SIH may be present without a demonstrable leak
  - Frustrating cases? CSF Venous fistula, slow leak?
- Spine disc pathology is the etiology in many cases and can be difficult to identify on MRI
- Complications of SIH can be life threatening (coma and death) or result in dementia like syndromes
- Neuroradiology plays a significant role in the diagnosis and treatment of SIH patients

8-year-old girl presents with headaches of a postural nature since the age of 2
Chiari decompression performed at age 2 1/2

CSF fistula secondary to Gorham’s Vanishing Bone Disease AJNR
**What's inside the skull ...**

- **The Brain floats**
  - Weight ~ 1400 grams in air / 50g in water

- **Vascular structures**
  - Cerebrospinal fluid ~ 250cc
    - Intracranial volume ~ 150-200cc
    - Spinal volume 50cc
  - 0.3 ml/min in adults (500 ml/24h)
  - Opening pressure: 6-20 cm water (in lateral decubitus position)
  - Pressure at vertex when erect < 0cm

10% reduction volume = headache

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**Monro-Kellie Doctrine**

*The total volume within an intact skull is constant*

The volume of brain, blood, and CSF are in reciprocal relationship

If one component increases (or decreases) in volume, the other two elements compensate (in the intact skull).

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**SIH: CLINICAL FEATURES**

- **Headache**
  - Usually Postural, often abrupt in onset
  - Headache becomes constant if chronic or if SDH occur

- **Neck Pain**: suboccipital, upper neck and arms, intrascapular

- **Visual**:
  - Horizontal diplopia (unilateral or bilateral 6th nerve palsy)
  - Inferior Quadrantanopia field defects (superior binasal field defects)

- **Auditory**:
  - Tinnitus (postural), vertigo (nausea), hyperacusis, hearing loss

- **Mentation**: memory loss, stupor, coma

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**SPONTANEOUS INTRACRANIAL HYPOTENSION: MR Findings**

- **Diffuse Dural Enhancement (95%)**

- **Brain Sag (80% ~ severity)**
  - Downward Displacement Of Pons, Cerebellum, Chiasm, Cisterns

- **Venous distention (80%)**
  - Cranial and Spinal veins

- **Pituitary Gland Prominence**

- **Subdural Hygroma / Hematomas**

- **Midbrain compression / dementia**

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**MR findings may rapidly correct after treatment of SIH**

- **Pre-therapy**

- **Post-therapy**

Venous Distension Sign

Farb et al

AJNR 28:1489, 2007
**Etiologies of SIH**

- “Acquired Chiari 1”
- Ruptured perineural cyst
- Transdural HNP/osteophyte
- Traumatic or surgical durotomy
  - Lumbar Shunt or drainage
  - CSF-Pleural fistula
- Connective tissue disorders
  - Ehlers-Danlos II
  - Marfan’s
  - ? Other

**SIH: VENOUS PROMINENCE**

**Spinal Manifestations of SIH**

- Extradural collections of CSF
- Enlarged epidural veins
- Dural enhancement
- HNP/cysts

- Rare:
  - Siderosis (rare)
  - Syrinx or Pre-syrinx secondary to tonsillar impaction

**False Localizing C1-2 leakage**

- Ligamentum Flavum extends from C2-Sacrum

**SIH: DIFFERENTIAL DIAGNOSIS OF DURAL ENHANCEMENT**

- Metastatic disease- focal
- VP or LP Shunting
- “Pachymeningitis” (focal)
- Craniotomy- usually focal
- Wegener’s, sarcoid, meningioma (focal)

Burtis et al: Spinal manifestations of SIH AJNR 26:34-38, 2005

**Why errors in SIH diagnosis?**

- 30% underwent unnecessary procedures
  - angios, craniotomies, dural and brain biopsies
- Why??
  - Lack of understanding of this disease
  - Inadequate history
  - Findings may be subtle at presentation
  - History and CSF analysis confused with other Dx
    - "Aseptic Meningitis"
      - Lymphocytic pleocytosis / Protein elevation
      - Subtlety of MR or CT studies

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**37-year-old previously healthy man with abrupt onset of non-postural headache**

Initial CT at time of initial headache:
- Normal

Diagnosis in ED = “migraine”

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**9 weeks later re-presents to ER with postural headache, normal mentation**

ER ordered CTA to rule out SAH

Tonsils low, "tight brain," bilateral subdural hematomas, but… prominent venous structures

Diagnosis of SIH suggested by radiologist, blood patch performed – more

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**Headache returns after three days**

Thoracic blood patch, 20cc

(Not the large transdural thoracic disc herniation)

Postural headaches resolve, but persistent headache requires subdural evacuation, with resolution of sx

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**23-year-old woman with 2 days of postural headaches**

*Dx in Emergency Dept: Migraines*

MR very subtle, enlarged Dural sinus

? slight dural enhancement

Radiologist Dx: ? SIH confirm with spinal MR

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**23 yr old, cont..Spine MR shows extradural CSF, Thoracic osteophyte/HNP resulting in SIH, EBP x 2, caffeine infusion= HA better**

Extradural CSF on T2 spine

CT guided EBP
66-yr-old woman with one year of intermittent short term memory loss.

- MRI Brain was ordered, which showed signs of intracranial hypotension and compression around the brainstem.

- Of note, she had no experienced chronic headaches, cranial nerve deficits, or gait difficulty.

Opening Pressure 5 cm water
?

Fistula on left

C1-2 needed to define level of leak

Surgery found transdural HNP

Dynamic Myelography

Hoxworth et al
SIH Syndrome without detectable leak

- Frustrating
- What are we missing?
  - Intermittent, or very slow leak?
  - Increase compliance of spinal dura?
  - CSF-venous/lymphatic fistula?
- "Treatment" in these cases is symptomatic:
  - Vitamin A, caffeine

Treatment of SIH

- CT guided epidural blood patch 10-20cc
  - 9cc of blood mixed with 1cc 240% contrast
  - Or Fibrin glue
  - Repeat 2 or 3 times, best at the site of leak
- If not cured, then localize leak
  - MR, CT myelography (C1-2) in CT
  - Direct Blood Patch to site of leak
- Cure ~ 75% after two EBP

Treatment : SIH
20cc Epidural Patch
Outcome: Resolution of HA 10 hours

9cc blood: 1 cc 240% omnipaque
Slow injection, reverse Trendelenberg
Rotation on sides and back

Transforaminal leak unresponsive to epidural blood patch

42-year-old with postural headaches and back pain

No leak, multiple perineural cysts
Blood patch – no effect
Treatment Vitamin A

Courtesy of David Malfair MD
University British Columbia
**SIH, MR myelogram shows slow leakage at 7 hours**

*Human spinal arachnoid villi revisited: immunohistological study and review of the literature Tubbs et al J Neurosurg Spine 7:328–331, 2007*

Arachnoid villi exist and are morphologically associated with radicular veins. CSF absorption occurs not only intracranially but also along the spinal axis.

**COMPLICATIONS of SIH**

- Venous sinus thrombosis +/- Dural AVF
- Central midbrain herniation syndromes – Stupor, Stroke and Death
- Myelopathy
  - Pre or real syrinx
  - Thoracic Cord Herniation
  - Siderosis
- Rebound intracranial hypertension

**SIH, Venous thrombosis and Ventral Osteophyte**

Difficult management as patient was on heparin

**Pre-syrinx and SIH Marfan’s with progressive SIH**

Initial presentation with postural HA

Follow up: obtundation and myelopathy

**38-yr-old patient 1 year prior to onset of SIH MR performed 2005 for neck mass: normal tonsils 2006 Postural Headaches>2007 tingling in fingers**
**Myelo 2008**

Transdural herniation with CSF leak

**Blood Patch-T5 and lumbar Headaches resolved x 1 year**

**Thoracic cord herniation**

*Etiology?*

- Spontaneous herniation of thoracic cord >> progressive myelopathy
- Upper thoracic level, where cord is closest to ventral dural surface
- Cord herniates through defect left by transdural HNP (note: location at disc level in most reports)

**Rebound Intracranial Hypertension**

Headache different from SIH, but can be confusing
- Papilledema/loss of Spontaneous venous pulsations
- Acetazolamide, time
- Can last for months

**SPONTANEOUS “CSF HYPOVOLEMIA”**

- Often unrecognized cause of headache syndrome
  - MR IS OFTEN DIAGNOSTIC AND CAN LEAD TO THE CORRECT DIAGNOSIS AND THERAPY
- Epidural Blood patch is effective in over 75% of patients
  - first line of therapy BEFORE imaging evaluations or surgery
- Perineural cysts and transdural herniation of discs are frequent causes of leaks
  - Slow CSF leak may result in negative imaging studies
    - Delayed scans may help (1-2 hours)
    - Gad MR myelography may also show slow leaks
    - Isotope rarely useful

A 65-year-old woman with progressive walking disturbances and limping of the left leg
Additional Readings


- Wouter I. Schievink, MD Spontaneous Spinal Cerebrospinal Fluid Leaks and Intracranial Hypotension JAMA 2006; 295:2286-2296

- Sencakova D et al The efficacy of epidural blood patch in spontaneous CSF leaks Neurology 2001; 57:1921-1923

Modern Imaging Evaluation of CSF Leaks

The Foundation of the ASNR Symposium 2015

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Disclosure

• No relevant financial disclosures
• Off-label use of Gadolinium contrast will be discussed.

Goals and Objectives

• Review relevant risk factors for CSF leak
• Stress the necessity of B2-transferrin prior to imaging
• Describe pertinent findings on skull base CT
• Introduce stepwise approach for cisternography, including contrast needed

Clinical Scenario: CSF Leak

1) Unequivocal leak
   • Predisposing event (trauma, surgery, skull base tumor, intracranial hypertension, congenital)
   • + B2 protein from oto or rhinorrhea

2) Suspected leak
   • Oto or rhinorrhea
   • Meningitis

3) Maybe leak?

CSF Diagnostic Test

• First screening test “gold standard”
• Unequivocal evidence to support use
• B2-transferrin assay or
• B-trace protein assay - faster, cheaper, more sensitive

• Evidence: Strong

Clinical Scenario: CSF Leak

1) Unequivocal leak
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2) Suspected leak
   • Oto or rhinorrhea
   • Meningitis

3) Maybe leak?
CSF Leak Risk Factors

Etiology

- Post-surgical
  - Transphenoidal hypophysectomy (TSH)
  - Parasellar aneurysm clipping
  - Endoscopic sinus surgery (ESS)
- Trauma (esp closed head injury)
- Spontaneous (obesity, idiopathic intracranial hypertension)
- Skull base tumors, congenital, etc

CSF Leak After Trans-sphenoidal Hypophysectomy

- TSH by definition includes surgical defect in floor of sella turcica
- Defect patched intra-op
- Post-op CSF leak, location of leak obvious
- Often difficult to show + CTCg, CSF mixes in soft tissue used to patch surgical defect

CSF Leak After Endoscopic Sinus Surgery

- CSF leak known complication of ESS
- Usually noted during surgery, repaired immediately
- Location of leak
  - Cribiform plate
  - Lateral lamella
  - Anterior ethmoid roof
  - Junction of ant/posterior ethmoid roof
- Risk of leak ↑
  - Prior ESS
  - Polyp

CSF Leak After Endoscopic Sinus Surgery

- CSF leak known complication of ESS
- Usually noted during surgery, repaired immediately
- Risk of leak ↑
  - Prior ESS
  - Polyps

CSF Leak, Spontaneous

- Middle aged women
- Often overweight or obese (BMI > 30)
- IIH
- Relationship between spontaneous leaks & obesity
- Develop after chronic ↑↑ ICP
- May have associated encephalocele, so MR often recommended

CSF Leak, Spontaneous

Osseous dural defects
44yM Spontaneous CSF Leak

- 1 yr h/o right nasal drainage
- Lying on rt side or bending down
- 5’3” 207 lbs BMI 36

44yM Spontaneous CSF Leak

Idiopathic Intracranial Hypertension

Is High-Resolution CT Alone Adequate for Pre-Operative Repair?

- Retrospective review
- 19 pts with HRCT
- Endoscopy – 22 leaks
- CT – 20/22 (91%)
- Size of defect on CT was within 2 mm in 75% of pts

LaFata V, et al. CSF Leaks: Correlation of HR CT & multiplanar reformations w/ intraoperative endoscopic findings. AJNR 2008;29:536-551

When is MR Needed?

- If soft tissue present in nasal cavity, sinus or middle ear/mastoid
- Will best determine contents of cephalocele

Cisternography

- When is cisternography needed?
  - When more than one potential source for leak is present on HRCT
  - Rarely necessary, except for trauma or IIH
- Cisternography is performed with intrathecal contrast
  - Iodinated contrast and CT
  - 0.5-1.0 ml Magnevist and MR
CTCg: Technique

> 2 potential sites for leak on HRCT
1. Patient should be actively leaking or able to initiate leak
2. Start with pre – cisternogram HRCT
   Supine axial with coronal reformations, same day
3. LP – 5-7 cc’s intra-thecal contrast
   Head-down and provocative maneuvers
4. Repeat HRCT, in prone coronal plane
5. Repeat HRCT, in axial plane, with coronal reformations

CTCg: 3 Sets of Images

1. Pre-contrast CT
   Baseline mucosal disease, osteoneogenesis
2. Post-contrast prone coronal
   ↑ intracranial pressure to exacerbate leak
3. Post-contrast axial with reformations
   Reformations without respiratory artifact

Intrathecal Gd MRCg Technique

- Start with HRCT
- 0.5 ml Magnevist in 4 ml sterile saline or CSF
- Most series done with gadopentetate dimeglumine (Bayer HealthCare)
- Off label use consent
- Scan at 1 hour, fat sat T1 in multiple planes
- If leak is intermittent, or initial imaging is negative, consider rescan between 6 – 24 hours

28yF Obese IIH
HRCT – Multiple defects

Emory MRCg/Gad Technique

- HRCT
- Pre-Cg MR
- Fluoro guided LP (0.5 ml/2 cc’s saline)
- 6 ml intrathecal iodinated contrast
- Roll patient, Valsalva, provocative maneuvers
- CT: prone coronal CT, axial
- MR: Coronal T2 SPACE
- Coronal T1 radial VIBE or MPRAGE at 1.5T
Don’t forget to check temporal bones!

Summary

• Currently no metaanalysis on imaging CSF leak
• Randomized controlled trials are lacking
• Unequivocal data and personal experience to
  – Start with analysis of oto or rhinorrhea
  – Next step: HRCT to include sinuses, central skull base, temporal bones
  – Justification: Sensitivity of 84-95%
  – Yield of CT or MR Cg very low if likelihood is low or pt not leaking on day of procedure

References

• Chi, et al. The Yo-Yo technique to prevent CSF rhinorrhea after anterior clinoidectomy for proximal ICA aneurysms. Operative Neurosurg 2006:59

References, cont’d

• Lloyd MN, et al. Post-traumatic CSF rhinorrhea: modern HRCT is all that is required for the effective demonstration of the site of leakage. Clin Radiol 1994;49:100