Posterior fossa volume in children with Chiari malformation Type I

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Object. The authors sought to establish whether the volume of the posterior fossa in children suffering from Chiari malformation Type I (CM-I) is smaller than normal, as has been suggested previously. They also investigated the role of syringomyelia in posterior fossa development.

Methods. Both posterior fossa volume (PFV) and intracranial volume (ICV) were measured using segmentation techniques on preoperative magnetic resonance images obtained in 42 children who underwent surgery for CM-I (mean age 127 months, range 36–204 months); 25 (59%) of the patients had syringomyelia. The PFV/ICV ratio was calculated to eliminate differential supratentorial growth. Patients who had deformities potentially interfering with skull growth or who had undergone a shunt insertion procedure prior to craniovertebral decompression were excluded. The results were compared with measurements of 51 healthy children using one-way analysis of variance.

In patients with CM-I only, the mean PFV and PFV/ICV ratios were not statistically different than those for healthy children. In patients with both CM-I and syringomyelia (CM-S), the mean PFV and PFV/ICV ratios were statistically smaller than those for healthy children. The ICV was 1383 cm³ in the healthy group, 1459 cm³ in the CM-I only group, and 1400 cm³ in the CM-S group (p = 0.363); the PFV was 186 cm³ in the healthy group, 196 cm³ in the CM-I only group, and 171 cm³ in the CM-S group (p = 0.036); the PFV/ICV ratio was 0.135 in the healthy group, 0.134 in the CM-I only group, and 0.122 in the CM-S group (p = 0.004). These differences were more prominent in the first 10 years of life.

Conclusions. Children with isolated CM-I do not have a PFV smaller than normal, whereas children with both CM-I and syringomyelia have a PFV significantly smaller than normal. This result indicates that the two subgroups may represent different phenotypic expression or even a different pathogenesis.

KEY WORDS • Chiari I malformation • hindbrain hernia • syringomyelia • posterior fossa volume • pediatric neurosurgery

Chiari malformation Type I is characterized by the herniation of the cerebellar tonsils into the cervical canal; in a significant proportion of patients it is often accompanied by syringomyelia at presentation. However, the pathogenetic mechanisms underlying this syndrome and its association with the development of syringomyelia remain unclear. It has been postulated that a small PFV due to occipital bone dysplasia is the primary anomaly, resulting in overcrowding of the cerebellum and hence in caudal migration of the cerebellar tonsils. As a result, it is thought that CSF flow from the head to the spine is hindered due to cerebellar herniation, instigating the formation or propagation of a syrinx. A number of surgical techniques devised for the treatment of symptomatic hindbrain hernia are based on the premise that the posterior fossa is smaller than normal.

Since the advent of MR imaging, accurate diagnosis of this disorder and its detailed in vivo study has been possible. The knowledge base on the subject has expanded, but unanswered questions remain regarding the pathogenesis of cerebellar herniation and syringomyelia. In this study, we investigate the implication of posterior fossa size in the pathogenesis of CM-I. Our purpose is twofold: 1) to establish whether the PFV is indeed smaller in individuals with CM-I than in healthy individuals, and 2) to investigate the correlation between PFV and the presence of syringomyelia.

Clinical Material and Methods

Both PFV and ICV were measured on preoperative MR images obtained in 42 children suffering from isolated symptomatic CM-I, and the PFV/ICV ratio was calculated for each patient. This ratio expresses the percentage of the ICV that the posterior fossa occupies. It eliminates any bias...
that a particularly large or small head can introduce, negates the effects of age and sex on the volumes, and overcomes the problem that patient and control groups are not age matched. Comparisons were made with a control group of 51 healthy children of comparable age. All measurements were performed at the Neuroscience Informatics Laboratory at the Institute of Child Health at Birmingham Children’s Hospital, Birmingham, England, using segmentation software programs developed in house.

**Segmentation Technique**

Until recently, measurements of posterior fossa area and volume were obtained from lateral skull radiographs or midsagittal MR images using geometric calculations from 2D parameters. With increasingly advanced image-manipulation programs, however, the segmentation technique has evolved to an accurate and reproducible method and has been used before in similar studies. The technique of segmentation we used involves a mixture of automatic and semiautomatic “seed growing” algorithms as well as manual outlining applied on 2D axial images so that original data can be analyzed. We have used this technique in the past for measuring a variety of parameters, including intracranial compartment volumes. For all children, axial T1-weighted sequences with 5-mm slice thickness and a 1.5-mm interval were used for posterior fossa and ICV measurement. The T1-weighted MR images were chosen because they offer good contrast between the “white” CSF overlying the brain and the “black” inner table of the skull.

Some manual outlining was required at certain parts of the posterior fossa. The most caudal image included the foramen magnum. The highest slice to be outlined was the last one where the cerebellar folia were present through the tentorial hiatus. Attention was paid to the inclusion of the relevant midbrain structures inside the posterior fossa, as well as the cerebellum. The surface area of every outline was measured in each slice and the volume was calculated by multiplying the area of the outline by the slice thickness. The total volume of the posterior fossa was calculated by adding the volumes of all the slices, including the calculated interslice gaps. The ICV was outlined and measured on the same images, in a manner similar to that outlined in a previous publication from this group. The ratio of the PFV to the ICV was calculated. This ratio expresses the proportion of the ICV occupied by the posterior fossa, thereby removing the bias that a particularly high or low ICV could produce. All outlining was performed initially by one observer (M.K.) and subsequently verified independently by another observer (S.S.). The interobserver variation of the measuring software has been investigated before and has been found not to introduce statistical error because it uses accurately reproducible automatic segmentation algorithms.

**Patient Population**

Only patients with isolated symptomatic CM-I who required surgical treatment were included in this study. The definition of CM-I used in this study is the presence of prolapsed cerebellar tonsils 5 mm or more below the level of the foramen magnum on sagittal MR views. Patients with lesser degrees of tonsillar prolapse, such as those with the recently described CM Type 0, were not included in this study.

The study group included 17 children who presented with CM-I only (CM-I only group), and 25 children with both CM-I and syringomyelia (59% of all patients; CM-S group). Patients were excluded who had any abnormality that could potentially interfere with skull growth and hence possibly introduce a bias factor, such as craniosynostosis-related hindbrain hernia (for example, Crouzon syndrome), any other abnormality such as a congenital spinal deformity, or the presence of a ventricular shunt that had been placed prior to craniovertebral decompression.

Symptoms in the CM-I only group that were deemed worthy of surgical decompression of the foramen magnum were occipital headaches severe enough to interfere with normal activities (such as school and sports) and were exacerbated by effort (one patient), motor dysfunction in the arms (four patients), syncopal episodes (one patient), and papilledema in the absence of hydrocephalus (one patient). No child with atypical headaches was considered for surgical treatment. A typical example of an MR image obtained in a patient in the CM-I only group appears in Fig. 1. In children with CM-S, the symptoms that led to surgery were occipital headaches (six patients), weakness of the arms or legs (five patients), progressive scoliosis (nine patients), papilledema without hydrocephalus (two patients), respiratory problems (one patient), syncopal episodes (one patient), and asymptomatic radiologically progressive syringomyelia (one patient).

A typical example of images obtained in a patient with CM-S appears in Fig. 2. Commonly, patients had combinations of symptoms and findings. As part of our preoperative

![Fig. 1. Sagittal T1-weighted MR image of the head of an athletic 15-year-old boy suffering from worsening occipital headaches which forced him to reduce his sports activities. There is significant hindbrain herniation with the cerebellar tonsils prolapsed to the level of the C-1 vertebral arch. No syringomyelia was evident on the spinal images. Measurements revealed a normal PFV and PFV/ICV ratio.](image-url)
radiological investigations, cine phase-contrast cardiac-gated midsagittal MR sequences were obtained to illustrate the state of CSF flow in the foramen magnum. All of the patients included in the study had abnormal CSF flow patterns in this region, but analysis of the phase-contrast MR examinations was not included in this study. All included patients had foramen magnum decompression performed between 1998 and 2004 by one surgeon (S.S.) at the Birmingham Children’s Hospital, England, at some time after the diagnostic MR examination that was used for this analysis, and they are still being followed up clinically. During this period, another 21 children with radiological evidence of CM-I were not treated surgically either because they were asymptomatic or their symptoms were atypical or not severe enough to merit surgery. These patients are still undergoing regular follow up with yearly MR imaging studies, and at the time of completion of this report (February 2006), none of these patients required surgical treatment.

For all of the patients, the age of presentation used for statistical analysis was the age at the time of the preoperative MR imaging study that was used for volume calculations. The mean age at presentation was 127 months (range 36–204 months). Of the 42 patients, 24 (57%) were male. There was no statistically significant difference in the mean presentation age of the two subgroups of patients with CM, nevertheless, it is of note that patients with syringomyelia presented at a younger age (CM-I only 144 months, CM-S 116 months; p = 0.081, one-way ANOVA).

The control group of 51 healthy children (28 boys and 23 girls) had a mean age of 116 months (range 34–184 months), which was not statistically different from the mean age of the CM-I group (p = 0.270, one-way ANOVA). This control group has been used in previous comparative volumetric studies. They presented to the general pediatricians and pediatric neurologists group of our hospital between January 1995 and December 1997 with nonspecific symptoms such as headaches, dizziness, migraine, squint, and family history of brain hemorrhage. In all cases, the MR imaging studies were pronounced nondiagnostic. Children with any kind of medical or neurological disorder were excluded, irrespective of how irrelevant to head growth it might be. Therefore, children with epilepsy, head injury, meningitis, metabolic disorders, and any other structural, physiological, or mental abnormalities were excluded. All healthy children included in the study remained so until the completion of this study. It should be stated that it would have been impossible to achieve complete age and sex matching between patient and control groups, so this was not attempted.

**Statistical Analysis**

The statistical analysis of the mean PFV, ICV, and PFV/ICV ratios for each group was performed using one-way ANOVA and commercial statistical software (SPSS; SPSS Inc., Chicago, IL). A probability value of less than 0.05 was considered statistically significant. The association between these parameters and the sex, age, and descending brainstem status in each patient was analyzed. Graphic data analysis was performed as well. The PFV/ICV ratio was plotted against the age at presentation for each group, a scatterplot of the ratio against age was created, and best-fit curves were calculated using the Lowess smoothing proce-
This approach was used to identify any trends throughout the age span.

**Results**

The mean ICV, PFV, and PFV/ICV ratios for each group of children are shown in Table 1. The difference in the mean ICV between the three groups is not statistically significant, and this makes the three groups comparable. The mean PFV in children with CM-I only is similar to that in the controls, but in children with CM-S it is considerably smaller. This difference was statistically significant. Similarly, the mean PFV/ICV ratio in children with CM-I only is near normal, but in children with CM-S it is considerably smaller. This difference was also statistically significant.

**Effect of Sex on PFV, ICV, and PFV/ICV Ratio**

Within the healthy population, the PFV and ICV are statistically smaller in girls ($p = 0.002$ and 0.000, respectively, one-way ANOVA) as are most other somatometric measurements. The mean PFV/ICV ratio is not statistically different between the two sexes (girls 0.133, boys 0.136; $p = 0.391$, one-way ANOVA). Within the CM-I only group, the incidence of the two sexes between the two subgroups was not statistically different ($p = 0.445$, chi-square test). The mean PFV/ICV ratio was smaller in girls, but the difference was not statistically significant (boys 0.130, girls 0.122; $p = 0.181$, one-way ANOVA).

**Effect of Age on PFV, ICV, and PFV/ICV Ratio**

Graphical analysis using the Lowess smoothing technique indicated that after the age of 10 years the difference in the PFV/ICV ratio of the two CM subgroups may not be as great as in the first 10 years of life. For this reason, we analyzed the difference in mean values for children older and younger than 10 years of age. As has been shown in another publication from our group, skull growth stabilizes after the age of 10 years, which further strengthens the use of that age as a cutoff for this analysis. In the entire CM group, 18 children were younger than 10 years of age and 24 children were older. The CM-S subgroup had smaller PFV/ICV ratios than the CM-I only subgroup in both age groups, and the difference was statistically significant (younger than 10 years $p = 0.047$, older than 10 years $p = 0.013$, one-way ANOVA). The difference was more pronounced in the first 10 years of life, where the mean PFV/ICV ratio was 15% smaller in the CM-S group in comparison to the CM-I only group. In children older than 10 years of age, the mean PFV/ICV ratio was 5% smaller in the CM-S than in the CM-I only group. It should be noted that in children who were older than 10 years of age at presentation, the mean PFV/ICV ratio of the CM-I only group was statistically smaller than that of healthy children of the same age (CM-I only 0.130, healthy 0.138; $p = 0.046$, one-way ANOVA).

**Effect of Descended Brainstem Status on PFV, ICV, and PFV/ICV Ratio**

There were two patients, both with syringomyelia, in whom a descended brainstem was detected on sagittal MR images. This was judged by a lower than normal position of the fourth ventricle and the pontomedullary junction (5% of the entire CM-I group and 8% of the patients with CM-S). Within the latter group, the PFV/ICV ratio was statistically smaller in patients with a descended brainstem (descended brainstem 0.065, no descended brainstem 0.118; $p = 0.020$, one-way ANOVA).

**Discussion**

The obvious theory that a small posterior fossa is implicated in causing hindbrain hernia has been pursued for many years. Because it is unlikely that such patients will have "excess" cerebellar tissue, it follows logically that they should have a smaller posterior fossa, which is unable to accommodate the normal volume of the cerebellum. Authors of early 2D studies on lateral skull radiographs demonstrated that the height or the area of the posterior fossa is small in patients with CM-I. Authors of recent studies have used advanced image analysis techniques, similar to those used in the present study, to calculate PFV using computed tomography scans or MR images. Regardless of technical accuracy, in most studies a calculation of the ratio between the posterior fossa and the total intracranial or supratentorial compartment was performed, thereby eliminating any potential technical bias. All of these authors conclude that the posterior fossa is smaller than normal in patients with CM-I. To a large extent, this finding underpins the philosophy of treating hindbrain hernias with craniovertebral decompression that has evolved in the last two decades.

A careful appraisal of all these studies demonstrates, however, that none of them has featured a separation of patients who have CM-I according to the presence or absence of syringomyelia. In fact, in most studies the patients with syringomyelia form the majority of the sample. Stovner et al., analyzed data pertaining to 33 adult patients with CM-I and 40 healthy volunteers, but did not specify the percentage of patients who had syringomyelia. They conclude that the ratio of the area of the posterior fossa to the supratentorial compartment (PFV ratio) is statistically smaller in the CM-I group. In the study by Badie, et al., data pertaining to 20 patients with CM-I and 20 healthy volunteers were analyzed. Of the 20 patients with CM-I, 16 had syringomyelia. These authors grouped the results from all patients with CM-I together, regardless of the presence or absence of syringomyelia, and demonstrated that the entire group had smaller PFV ratios. Badie and colleagues made the interesting observation that patients with smaller PFVs presented at a younger age and had a better response to surgery. This observation corresponds with our finding that the CM-S group, which had smaller PFVs, also had a lower

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**TABLE 1**

Mean values for ICV and PFV, and the PFV/ICV ratios in three groups of children

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (51)</th>
<th>CM-I Only (17)</th>
<th>CM-S (25)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICV (cm³)</td>
<td>1383</td>
<td>1459</td>
<td>1400</td>
<td>0.363</td>
</tr>
<tr>
<td>PFV (cm³)</td>
<td>186</td>
<td>196</td>
<td>171</td>
<td>0.036</td>
</tr>
<tr>
<td>PFV/ICV ratio</td>
<td>0.135</td>
<td>0.134</td>
<td>0.122</td>
<td>0.004</td>
</tr>
</tbody>
</table>

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mean age at presentation. In another study, Vega, et al., analyzed data pertaining to 42 adult patients with CM-I and 46 healthy individuals. They did not specify the percentage of patients with syringomyelia, nor did they analyze their results according to its presence or absence. They demonstrated that the PFV was smaller in men but not in women with CM-I. We did not find such a difference between the sexes in our study. Milhorat, et al., analyzed the PFV in 50 patients drawn from a large cohort of 364 mostly adult patients, 65% of whom had syringomyelia, and compared it with the PFV of 50 healthy volunteers. The results were not separated according to the presence or absence of syringomyelia. The authors demonstrated that the PFV was smaller than normal in patients with CM-I, and they concluded that CM-I is secondary to the maldevelopment of the posterior fossa. In a study by Nishikawa, et al., data were analyzed pertaining to 30 adult patients with CM-I, 86% of whom had syringomyelia, and 50 healthy individuals. They did not separate their results according to the presence or absence of syringomyelia, but they demonstrated that patients with CM-I had statistically smaller PFVs in comparison to normal values. They concluded as well that the malformation was due to underdevelopment of the occipital bone in its cartilaginous phase.

When we analyzed the PFV ratios of both groups of patients with CM-I in our study, they were statistically smaller than normal. This finding agrees with the results of the previously published studies we have discussed. It is unfortunate, however, that none of the previous studies on the topic explored the effect of syringomyelia on PFV. Based on our findings, we postulate that the high proportion of patients with syringomyelia in all of these studies probably accounts for the low mean PFV for the entire group of patients with CM-I in each study. Our study is the first to demonstrate that patients with CM-I only have normal PFVs, whereas patients with CM-S have PFVs significantly smaller than normal. Because there is overlap between the two groups, caution should be exercised in interpreting the results of such a study. The difference in PFV ratio according to the presence or absence of syringomyelia was more pronounced in children who presented before the age of 10 years than that in those presenting afterwards. As our group has demonstrated in other studies, after the age of 10 years there is no significant change in the growth of the cranial vault, and little change in the growth of the skull base. It is possible that further on in adulthood a pattern of such a small difference occurs that would correspond to an extent with the findings of the studies we mentioned.

Our findings offer a new perspective on CM-I, challenging the view that the development of syringomyelia represents an evolutionary stage in the pathogenesis of the disorder. The senior author has observed newly developed syringomyelia after craniovertebral decompression as a result of arachnoiditis, but it occurs rarely in patients with CM-I only who have not undergone surgery. Currently, there are no sizeable reports in the literature of patients with nonoperated CM-I who have been followed up for a long time, so it is difficult to define clearly the risk of new syringomyelia developing. All the patients that the senior author has been following up for the last 8 years have not experienced new syringomyelia. On the other hand, the phenomenon of acquired CM-I in various circumstances (for example, after the placement of lumbar or ventricular shunts) is well recognized; hence, caution should be exercised not to generalize the conclusions of this study.

We propose that from the genesis of their malformations, most patients either have a normal posterior fossa and CM-I without syringomyelia, or a small posterior fossa and syringomyelia, resulting in a “loss” of CSF in the spine. This situation is similar to that in patients with CM Type II, in whom the open myelomeningocele is associated with a true loss of CSF and a small posterior fossa. This view is strengthened by the observation that children with syringomyelia and a descended brainstem have an even smaller PFV/ICV ratio. We postulate that the two subtypes of CM-I (that with and without syringomyelia) represent different types of malformation, and that it may even be inappropriate to refer to them using the same terminology. It may be preferable to refer to CM-S as “CM-Is,” to underscore its different disease phenotype from the variation of CM-I without syringomyelia. At this stage, it is difficult to establish whether the two subtypes of CM-I represent a difference in phenotypic expression, with the syringomyelia subgroup being more severely affected by the underlying process, or whether they are two different malformations within the CM spectrum.

The results of this study indicate that the mechanism of symptom creation in CM-I is probably not related to volume. Even in patients with syringomyelia, it has been noticed that symptoms and radiological signs have not altered following suboccipital craniectomy, leading certain authors to conclude that the underlying mechanism causing the syringomyelia is not related to volume. The presence of a normal posterior fossa in patients with CM-I only does not explain the development of tonsillar herniation. It could be postulated that localized venous hypertension and a possible altered geometry of the posterior fossa could initiate the downward migration, which is subsequently perpetuated by CSF movement and impaction. Personal observations (S.S.) during surgeries for foramen magnum decompression in patients with CM-I only indicate that soon after durotomy and division of the arachnoidal adhesions that link the impacted tonsils to the surrounding structures, the cerebellar tonsils usually ascend to their natural position, so that further coagulation or resection is not necessary. Thus, it appears that foramen magnum decompression probably works by allowing disimpaction of the tonsils from the craniovertebral junction, rather than through enlargement of the posterior fossa. The tonsils never move to occupy the newly enlarged cisterna magna; rather, they ascend to a normal location. Consequently, there is a tendency for reduction in the size of the craniectomy in the foramen magnum.

Conclusions

This study demonstrates that two distinct varieties of CM-I exist: that with and without syringomyelia. Children with CM-I only have a normal PFV and PFV/ICV ratio, whereas children with both CM-I and syringomyelia have a statistically significant smaller PFV and PFV/ICV ratio compared with that of healthy children. These differences are more pronounced in children presenting within the first 10 years of life. These observations may have implications for the classification and management of CM-I.
References


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