Incidence of basioccipital hypoplasia in Chiari malformation Type I: comparative morphometric study of the posterior cranial fossa

Clinical article

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Object. The chronic tonsillar herniation defining Chiari malformation Type I (CMI) is thought to result from overcrowding of a normally developing hindbrain within a congenitally small posterior cranial fossa (PCF) due to occipital hypoplasia. The goals in the present study were to authenticate the cranioencephalic disproportion in a group of patients with CMI and to discuss new developmental aspects according to which part of the occipital bone was underdeveloped.

Methods. The authors retrospectively examined a group of 17 patients with CMI. Measurements of osteotentorial and neural structures of the PCF were made on MR images of the brain. The results were compared with findings in 30 healthy controls by using the Mann-Whitney U-test.

Results. Dimensions of the neural structures did not differ between the 2 groups of patients. The mean length of the basiocciput was significantly shorter in the CMI group (19.4 mm) compared with the control group (25.7 mm; p = 0.0003). The mean diameter of the foramen magnum was larger in the CMI group, but this difference was not statistically significant. The dimensions of the supraocciput and the mean angle of the cerebellar tentorium were identical in the 2 groups.

Conclusions. Data in this study support the idea that occipital hypoplasia is the main cause of overcrowding within the PCF. Basioccipital shortness is a cardinal feature of the resultant shallow PCF and could proceed from a congenital disorder of the cephalic mesoderm of the parachordal plate or occur later in the infancy because of premature stenosis of the sphenoccipital synchondrosis. (DOI: 10.3171/2009.2.JNS08284)

Key Words • Chiari malformation Type I • posterior cranial fossa • morphometric study • basioccipital hypoplasia • hindbrain-related syringomyelia

Abbreviations used in this paper: CM0 = Chiari malformation Type 0; CMI = CM Type I; CTH = chronic tonsillar herniation; PCF = posterior cranial fossa.

result from isolated constriction of a PCF that is not capacious enough to house the developing hindbrain, which defines the classic form of CMI.19 Experimental models14,15,23 supported by morphometric studies2,9,19,20,25,29,33 have shown that the CTH occurring in classic CMI mainly results from overcrowding of a normally developing hindbrain within a congenitally small and shallow PCF due to occipital bone underdevelopment. Given the somitic origin of the occipital bone, a very early paraxial mesodermal defect of the parachordal plate or occur later in the infancy because of premature stenosis of the sphenoccipital synchondrosis.
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The goals in the present study were to properly investigate overcrowding of the PCF in patients with classic CMI and to determine the degree and location of occipital bone hypoplasia. We found that significant underdevelopment of the occipital bone was restricted to the basiociput, and we discuss alternative developmental mechanisms according to which part of the occipital bone was hypoplastic.

Methods

Patient Population

In this study, we retrospectively reviewed the morphometric results in 17 patients (7 males and 10 females) with a symptomatic CMI as compared with 30 healthy controls (12 men and 18 women). The average age among patients with CMI was 33.2 years (range 16–55 years), and among controls 38.7 years (range 18–67 years).

All patients had been referred to our department between 2002 and 2006 and are still undergoing clinical-urological follow-up. The diagnosis of CMI was based on the identification of a tonsillar herniation of at least 5 mm below the foramen magnum on midsagittal T1-weighted MR images. Seven patients had CMI only (41%), whereas 10 patients had CMI with syringomyelia (59%). Patients with any other cranioencephalic disorder, such as hydrocephalus or a history of ventricular shunt, basilar impression or platybasia, and craniosynostosis-related hindbrain hernia, were excluded. Eleven patients presented with a typical history of posterior paroxystic headaches, 9 patients with syringomyelia had radicular pains and various degrees of thermoalgesic dissociation, 8 patients displayed oculomotor disturbances or neurootological signs, and 2 patients had cerebellar symptoms.

The control group included 30 patients who underwent brain MR imaging studies for headaches or migraine between January 2001 and September 2006. In all of these cases, the MR imaging results were entirely normal and remained so 1 year after this study.

Morphometric MR Imaging Studies of the Contents of the PCF

The structures of the brain and skull base were investigated using high-field MR imaging (Signa 1.5-T, General Electric). Seven measurements from several recent morphometric studies were obtained on midsagittal T1-weighted MR images by the same investigator for the 2 groups of patients (Figs. 1 and 2).

The morphology of the occipital bone within the PCF was estimated based on the length of the basiocciput (a in Fig. 1) as determined from the distance of the basioccipital synchondrosis to the basion, the length of the supraocciput (b in Fig. 1) from the internal occipital protuberance to the opisthion, and the anteroposterior diameter of the foramen magnum as determined from the distance of the McRae line between the basion and opisthion (foramen magnum). To estimate the steepness of the cerebellar tentorium, the angle of the tentorium was measured to a line connecting the internal occipital protuberance and the opisthion (c in Fig. 1). The dimensions of the neural structures were calculated based on the length of the brainstem (pons and medulla oblongata) between the midbrain-pons junction and the cervicomедullary junction (d in Fig. 2), and the length of the cerebellar hemisphere from the highest to lowest point (e in Fig. 2). In addition, for the CMI group the degree of tonsillar descent was assessed according to the Aboulezz et al. method by measuring the distance between the tip of the cerebellar tonsils and the foramen magnum along a perpendicular line to the McRae line (f in Fig. 2). We searched for statistical correlations between the value of the tonsillar descent and other measured parameters of the PCF.

Compression of the CSF cisterns posterior and lateral to the cerebellum was identified by the absence of the hypointense at the lowest point of the cerebellar hemisphere on sagittal T2-weighted MR images (Fig. 3).

Statistical Analysis

Statistical analysis was performed with the aid of SPSS software for Windows (version 11, SPSS, Inc.). The values of all morphometric parameters were comparatively assessed within the CMI group and the control group by using the nonparametric Mann-Whitney U-test. Correlations between the different quantitative measurements were determined using the linear regression test. A p < 0.05 was considered statistically significant.

Results

Table 1 shows a summary of PCF measurements for the 17 patients and 30 controls. The average length of the basiocciput was significantly shorter in the CMI group (19.4 mm, range 10–28 mm) as compared with controls (25.7 mm, range 15–35 mm; p = 0.0003), whereas no significant difference was found in the dimensions of the measured neural structures, brainstem, and cerebellar hemisphere.
The average anteroposterior diameter of the foramen magnum was larger in the CMI group (37.1 mm, range 25–53 mm) than in the control group (35.4 mm, range 28–41 mm), but the difference was not statistically significant (p = 0.61). The average length of the supraocciput and angle of the cerebellar tentorium were not different between the 2 groups.

In the CMI group, statistical analysis failed to reveal any significant correlation between the degree of tonsillar herniation and any of the measured parameters.

Overall, compression of the retrocerebellar CSF spaces of the cisterna magna was the most constant MR imaging finding, being present in 100% of our patients.

Discussion

Cranioencephalic Disproportion Within the PCF

The pathogenesis of classic CMI results from a cranioencephalic disproportion between the underdeveloped bony structures of the PCF and the normal-sized rhombencephalic derivatives. In the present study, overcrowding of the normally developing hindbrain within a congenitally small PCF was demonstrated by significant shortness of the basiocciput, whereas no significant difference was found in the dimensions of the hindbrain structures. From the experimental models of Marin-Padilla and Marin-Padilla, it has become unanimously accepted that CMI is a disorder of the cephalic paraxial mesoderm of the parachordal plate that leads to occipital bone underdevelopment. Previous morphometric studies have confirmed that the clivus and other parameters are hypoplastic both in patients with CMI and in those with CM1 and in those with CM0, although no neural structure abnormalities are displayed in the PCF.

The resulting small PCF is first occupied and then overfilled during the postnatal growth spurt of the cerebellum, which is forced to grow into the available space of the upper cervical canal. Despite the lack of significant abnormality of any other osseous structure of the PCF in our study, it has been shown that caudal displacement of the hindbrain can enlarge the foramen magnum diameter and simultaneously shift upward the cerebellar tentorium. Furthermore, our results confirm that the most consistent MR imaging finding is compression of the retrocerebellar CSF spaces of the cisterna magna by the herniated tonsils, which provides substantial evidence of overcrowding (17 patients [100%]; Fig. 3). Consequently, most clinical symptoms result from displacement of newly formed CSF from the subarachnoid spaces of the PCF into available spaces within the supratentorial and spinal compartments. Current evidence suggests that hindbrain-related syringomyelia, observed in 59% of our patients, is also a complication resulting from obstructed CSF flow between the cranial and spinal compartments. The spinal cord cavity fills from the spinal subarachnoid space as a consequence of CSF waves produced by the piston-like effect of impacted cerebellar tonsils driving CSF through the extracellular spaces of the spinal cord into the central canal. Other clinical disturbances are believed to result from direct compression of the lower brainstem and the upper cervical cord by the herniated tonsils. The considerable delay in the occurrence of neurological symptoms could be explained by the relatively late, mainly postnatal, growth spurt of the cerebellum within a small and inadequate PCF.

Reliability of the Index of Cranioencephalic Disproportion

To estimate overcrowding in the PCF, we measured...
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TABLE 1: Comparison of average values for measured parameters between patients with CMI and controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CMI Group</th>
<th>Control Group</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>no. of patients</td>
<td>17</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>basiocciput (mm)</td>
<td>19.4</td>
<td>25.7</td>
<td>0.0003</td>
</tr>
<tr>
<td>foramen magnum (mm)</td>
<td>37.1</td>
<td>35.4</td>
<td>0.61</td>
</tr>
<tr>
<td>supraocciput (mm)</td>
<td>40.7</td>
<td>40.9</td>
<td>0.85</td>
</tr>
<tr>
<td>tentorial angle (°)</td>
<td>85.3</td>
<td>84.6</td>
<td>0.93</td>
</tr>
<tr>
<td>brainstem (mm)</td>
<td>40.7</td>
<td>43.2</td>
<td>0.13</td>
</tr>
<tr>
<td>cerebellum (mm)</td>
<td>52.7</td>
<td>49</td>
<td>0.11</td>
</tr>
</tbody>
</table>

the dimensions of 7 anatomical parameters, which have proven to be reliable indicators of the degree of cranioencephalic disproportion. The neuroradiological methodology we used was first developed by Nishikawa et al. in 1997 and has since been widely reproduced under the same conditions for morphometric analysis of the PCF in patients with CMI. Using a similar methodology in previous comparative morphometric studies, authors have found significant underdevelopment of the bony structures of the PCF with normal dimensions of the hindbrain structures; therefore, they concluded that overcrowding of the PCF is a ubiquitous finding in CMI and is specifically related to occipital hypoplasia.

Volume analysis was not performed in our study because the results of previous volumetric reports on the assessment of cranioencephalic disproportion have been discordant whatever the methodology of PCF volume calculation. Using the Cavalieri method, Milhorat et al. have confirmed the disproportion, showing a significant reduction of PCF volume in patients with CMI but no differences in brain volumes compared with controls. With a different methodology, Vega et al. have demonstrated a significant reduction in PCF volumes only in males. Despite the use of advanced image segmentation techniques for PCF volume calculation, the results remain controversial. Nishikawa et al. have found no significant difference in the PCF volume between CMI and control groups, but they did determine that the volume ratio between PCF brain and cranial volumes was significantly increased in CMI. Using a similar methodology in a study of pediatric patients with CMI, Sgouros et al. showed that a significant reduction in PCF volume was restricted to cases of CMI with associated syringomyelia. Given these dissimilar results, PCF volume analysis does not thoroughly reflect the degree of cranioencephalic disproportion. According to Stovner et al., the depth of the PCF and the length of the clivus as seen in midsagittal sections are better estimations of the initial PCF abnormality than the actual PCF volume.

Neither does the degree of tonsillar herniation seem to be representative of the cranioencephalic disproportion. Our data failed to show any significant correlation between the extent of tonsillar ectopia and any other measured parameter of the PCF, as in 2 previously published studies. However, Schady et al. have found an inverse relationship between the size of the PCF and the degree of cerebellar herniation, whereas Stovner et al. have shown a strong positive correlation. Furthermore, the extent of tonsillar herniation has never been satisfactorily correlated with the severity of symptoms. Many observations have confirmed that a high percentage of patients with tonsillar herniation of at least 5 mm below the foramen magnum can be asymptomatic, whereas symptomatic patients with CM0 harbor no significant tonsillar descent on radiography. As a result, CTH can be encountered as an incidental finding and is definitely not a reliable index of specific overcrowding within the PCF.

TABLE 2: Literature review of morphometric studies of the posterior cranial fossa*

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Radiographic Studies</th>
<th>Clivus or Basiocciput</th>
<th>SO</th>
<th>PCF Area</th>
<th>PCF Volume</th>
<th>Tentorial Angle</th>
<th>Neural Structures</th>
<th>Cisterna Magna</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schady et al., 1987</td>
<td>radio + CT</td>
<td>↓ (NS for women)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Vega et al., 1990</td>
<td>radio + CT</td>
<td>↓</td>
<td>—</td>
<td>↓ (NS for women)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Nishikawa et al., 1997</td>
<td>MRI</td>
<td>↓ (for CMI + BI)</td>
<td>↓</td>
<td>—</td>
<td>↓ NS</td>
<td>↑ normal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Milhorat et al., 1999</td>
<td>MRI</td>
<td>↓</td>
<td>↓</td>
<td>—</td>
<td>↓</td>
<td>↑ normal</td>
<td>absent</td>
<td>—</td>
</tr>
<tr>
<td>Karagöz et al., 2002</td>
<td>MRI</td>
<td>↓</td>
<td>—</td>
<td>—</td>
<td>↑</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Aydin et al., 2005</td>
<td>MRI</td>
<td>↓</td>
<td>↓ NS</td>
<td>—</td>
<td>—</td>
<td>↑ normal</td>
<td>absent</td>
<td>—</td>
</tr>
<tr>
<td>Sekula et al., 2005†</td>
<td>MRI</td>
<td>↓</td>
<td>↓ NS</td>
<td>—</td>
<td>—</td>
<td>↑ normal</td>
<td>absent</td>
<td>—</td>
</tr>
<tr>
<td>present study</td>
<td>MRI</td>
<td>↓</td>
<td>↓ NS</td>
<td>—</td>
<td>—</td>
<td>↑NS normal</td>
<td>absent</td>
<td>—</td>
</tr>
</tbody>
</table>

* Black arrows (↓ or ↑) indicate decreasing or increasing changes in a parameter between patients with CMI and controls. Abbreviations: BI = basilar impression; NS = not significant; radio = radiographic studies; SO = supraocciput; — = not available.
† Chiari malformation Type 0.
Incidence of Basioccipital Hypoplasia in CMI

Our results revealed that the underdevelopment of the bony structures of the PCF in the CMI group is only significant for the basiocciput, whereas no significant abnormality was found in any other measured parameter (Table 1).

Underdevelopment of the basiocciput was also a cardinal feature in the experimental model (vitamin A-induced) described by Marin-Padilla and Marin-Padilla.15 The authors concluded that the shortness of the basiocciput resulted in a short, inadequate, and funnel-shaped PCF, leading to compression of the growing cerebellum. Our results also confirmed the prevalence of basioccipital hypoplasia as reflected by shortening of the basiocciput or the clivus length in earlier morphometric studies.2,11,19–21,25,26,30,33 As shown in Table 2, the difference between patients and controls was always significant or more significant as regards the clivus.2,11,25,33 Basiocciput19–21,26 or PCF depth diminution11,29 than the PCF volume and other parameters. Given the vertical orientation of the basiocciput, shortening of this structure is likely to cause the resulting shallow and lordotic PCF, leading to parallel caudal displacement of the cerebellar tonsils. In addition, a short basiocciput has been recognized as the main predictive factor associated with the morphogenesis of CMI. According to Vega et al.,33 the most discriminative variable between patients with CMI and controls is the clivus length, which allows accurate identification of 76% of patients as belonging to the CMI group.

Two main elements may be responsible for the predominance of basioccipital and/or clival shortness: early underdevelopment of the bony structures of the clivus, basiocciput, and/or basisphenoid and premature closure of the sphenoccipital synchondrosis later in infancy.

Changes in the anterior or middle skull base have been seen as part of the original mesodermal defect associated with distortion of the basiocciput and hindbrain herniation in craniofacial syndromes6,15 and recently in a subgroup of children with CMI.28 However, Marin-Padilla14 has shown that in CMI only the subtemporal portion of the axial basicranium is smaller than normal, whereas the ethmoid and sphenoid bones are essentially normal.

Chiari malformation Type I is thus supposed to result mainly from an underdevelopment of the occipital bone. Arising from the early concentration of mesodermal cells around the cephalic end of the notochord in the 3rd week of gestation, occipital bone development follows the same rules of segmentation and induction as vertebrae.15–23 Normal growth of vertebral bodies depends on the proximity of the notochord, whereas the posterior arches require an inductive signal from the neural tube.2,34 The basioccipital region arises at the anterior part of the cephalic paraxial mesoderm from a pair of cartilaginous precursors, the parachordal plates, and represents a modified vertebral body resulting from the induction of growth factor secreted by the notochord. Therefore, a failure of notochordal induction may result in an anterior cephalic mesodermal defect leading to the underdevelopment of the basiocciput only, whereas the exo- and supraoccipital portions will develop normally because the neural tube has closed normally in cases of CMI.24,25 However, Nishikawa et al. have found that both the exo- and supraoccipital bones were underdeveloped in patients with CMI, which would suggest a failure of neural tube induction. This discrepancy illustrates the distinct developmental patterns between the anterior and posterior portions of the occipital bone and lends weight to the hypothesis that an isolated basioccipital defect is sufficient to induce CTH in patients with classic CMI.

Close to the embryological mesodermic origin of the occipital bone, intraoccipital synchondrosial growth is an important feature of PCF expansion and is active until the end of the 2nd decade of life.12,18 Stovner et al.29 have suggested that a mechanism for the development of a small PCF could be premature synostosis of the foramen magnum synchondroses. The sphenoccipital synchondrosis is prone to be affected by a single craniosynostosis because of its long exposure to growth impairment mechanisms due to a very tardive closure of the suture between the ages of 16 and 20 years. Moreover, the underdevelopment of the basiocciput is frequently involved in cases of CMI induced by multiple craniosynostosis. In 1988 Venes34 described the case of a newborn with Pfeiffer syndrome and CMI, suggesting that it was caused by basioccipital hypoplasia. The high incidence of CTH in Crouzon syndrome, up to 70%, is also representative of the potential impact of impaired synchondrosial growth in the occurrence of CMI and is believed to result from the vertical orientation of the basiocciput due to bilateral lambdoid craniosynostosis.6

In addition, CMI has been reported in various metabolic disorders such as deficient or excessive growth hormone24,32 and rickets,31 in which the fundamental anomaly specifically affects the basioccipital portion. Pediatric patients with growth hormone deficiency have a shorter-than-normal clivus, especially with regard to the basiocciput, which is supposed to result from a disorder of synchondrosial growth. The sphenoccipital synchondrosis in patients with thyroid hormone deficiency can remain open up to the 40th year of life.12

The constant involvement of basiocciput hypoplasia and/or sphenoccipital synostosis in such general pathological conditions associated with CMI is evocative of the extreme vulnerability of the sphenoccipital synchondrosis. In classic forms of CMI, a transient and more restricted process of craniosynostosis is at risk of preferentially affecting this area and thus explains the postnatal development of basiocciput hypoplasia leading to CMI.

Even if CTH can occur in many anatomical abnormalities of the craniovertebral skeleton, the incidence of basioccipital hypoplasia in classic CMI is especially high and may result from long exposure to developmental abnormalities from the embryonic stage of the parachordal plates until the very tardive closure of the sphenoccipital synchondrosis. Similarly, the association with exo- or supraoccipital shortness may occur because of a failure of neural tube induction in the embryological period or premature synostosis of intraoccipital synchondrosis.29

Variations in the degree and time of occurrence of the paraxial mesodermal insufficiency or sphenoccipital craniosynostosis will determine final morphological changes and may explain the delay in neurological symp-
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toms and the heterogeneity of the ages at presentation. More than a pathogenic continuum, CM0 and -I could represent the variable association between several skeletal developmental mechanisms: neurological anomalies will arise later in development when inadequate growth of the cerebellum within the abnormal cranial encasement leads to compression of the hindbrain structures and retrocerebellar CSF spaces. Surgical decompression of the PCF is therefore not directly performed to correct the original basioccipital hypoplasia but to compensate for the lack of cisterna magna that is the most common pathological consequence.3,26

Conclusions

The results of our study support the notion that CMI results from a cranioencephalic disproportion in the PCF due to occipital hypoplasia. The originality of our study lies in the demonstration of the preferential involvement of basioccipital hypoplasia. For the first time, we focused on the specific role of basioccipital hypoplasia in the pathogenesis of CMI, which can proceed either from an early paraxial mesodermal insufficiency due to a failure of notochordal induction in intrauterine life or from premature stenosis of the sphenoccipital synchondrosis occurring later in infancy. The type, moment, and duration of the initial defect will determine the severity and time of clinical revelation. The final result will be compression of the cisterna magna, common to CM0 and -I, whatever the degree of tonsillar herniation. Even if the understanding of CMI evolves, further morphometric studies with large patient series will help to define more accurately the complex physiopathological mechanisms at play in the occurrence of classic CMI.

Disclaimer

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

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