Intracranial hypertension in 2 cases of craniometaphyseal dysplasia: differing surgical options

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Craniometaphyseal dysplasia (CMD) is a very rare bone disorder characterized by abnormally developed metaphyses in long bones and sclerosis of the craniofacial bones. In this paper, the authors report 2 cases of children diagnosed with CMD and chronic intracranial hypertension with deletion in exon 9 of the human ANK gene (ANKH). After intracranial monitoring, a different treatment was chosen for each patient. One of the patients was treated using CSF shunting because ventriculomegaly in the absence of a Chiari malformation was also observed on cerebral MR imaging. The other patient underwent cranial expansion and decompressive craniotomy of the posterior fossa, because ventriculomegaly was excluded after cerebral MR imaging and cervical MR imaging showed a Chiari malformation Type I. The origin of intracranial hypertension in CMD is multifactorial. Previous intracranial pressure monitoring and a thorough understanding of neuroimaging studies are essential to achieve an accurate diagnosis and effective treatment. (DOI: 10.3171/2011.4.FOCUS1126)

KEY WORDS • Chiari malformation • craniofacial remodeling • craniometaphyseal dysplasia • hydrocephalus • intracranial hypertension

Craniometaphyseal dysplasia is a rare genetically transmitted bone disorder characterized by abnormally developed metaphyses in long bones and sclerosis and hyperostosis of the craniofacial bones. Other rare bone disorders with similar clinical and radiological features are metaphyseal dysplasia (Pyle disease), frontometaphyseal dysplasia, and craniodiaphysial dysplasia.1,4,5

Diffuse sclerosis of skull bones can lead to cranial nerve compression that may eventually result in severe visual and neurological impairment, such as facial palsy and hearing loss. Signs of intracranial hypertension may be the result of jugular foramen stenosis together with hyperostosis of the cranial vault and compression of the superior sagittal sinus.2-6 We present 2 rare cases of intracranial hypertension of multifactorial origin treated using different therapies.

Summary of Cases

In this paper we present 2 patients with CMD who were treated at the Department of Pediatric Neurosurgery of Virgen del Rocio Hospital in Seville, Spain. Both patients showed distinctive craniofacial features of CMD: wide nasal bridge, secondary dystopia canthorum, and scaphocephaly. They also reported progressive loss of bilateral vision and hearing due to cranial nerve compression.

Plain radiographs of these patients revealed abnormalities in the metaphyses of the long bones (Fig. 1), as well as multiple diaphyseal and skull base scleroses. Computed tomography scans of the skull demonstrated thickening of the diploe and sclerosis of the skull base. A 3D cranial CT scan obtained later also demonstrated dolichocepha and severe stenosis of the skull base foramina (Fig. 2). However, the evolution of the clinical course and cerebral MR imaging findings necessitated different treatments for each patient.

Case Reports

Case 1

This patient was a 9-year-old girl and a carrier of a mutation in the ANKH gene (position 1192 of the CCT in exon 9). She presented with a cephalic perimeter of 35 cm at birth (< 90th percentile); 7 months later, her cephalic perimeter had increased by 3.5 standard deviations to 45.5 cm.

A cranial 3D CT scan also demonstrated dolichocephaly and severe stenosis of the skull base foramina (Fig. 2 left). Ventriculomegaly in the absence of periventricular lu-
Cerebellar hypoplasia was also observed on cerebral MR imaging without Chiari malformation Type I (Fig. 3A and B). A bilateral auditory prosthesis was required due to progressive loss hearing.

Intracranial pressure monitoring was performed by means of external ventricular drainage after the patient experienced referred continuous headache and loss of visual acuity. Intracranial hypertension was then confirmed and controlled using a ventriculoperitoneal shunt when the patient was 4 years old, and the right optic foramen were drilled widely to achieve decompression using a supraciliary approach. Overdrainage complications were documented and successfully corrected when the previously placed valve was replaced by a programmable valve with an extra fluid flow control device. After surgical intervention, visual acuity improved. At present, the patient shows normal neurological and psychomotor development for her age.

Case 2

This 6-year-old boy presented with headache and bilateral loss of visual acuity, which was progressive and became more intense. Intracranial pressure monitoring was performed using an epidural sensor. Continuous sleep recording confirmed a basal intracranial pressure value > 25 cm H2O and a high incidence of B-waves (> 20%), which led us to perform anterior and middle cranial fossa decompression.

Ventriculomegaly was excluded after reviewing cerebral MR imaging results, which showed bone remodeling and sagittal suture diastasis due to extremely high pressure of the superior sagittal sinus (Fig. 3C). Cerebral MR angiography showed an abnormal venous drainage pattern from the superior sagittal sinus into dilated subcutaneous veins (mimicking sinus pericranii), explained by the increasing pressure and size of the superior sagittal sinus and the jugular venous outflow resistance (Fig. 4). Cervical MR imaging showed a Chiari malformation Type I.

We performed cranial vault expansion using multiple and bilateral osteotomies in the frontal, parietal, and temporal bones, as well as orbital bar advancement and superior sagittal sinus decompression. Optic foramina were drilled widely to achieve optic nerve decompression. Sev-
eral dural tears were observed during the surgical procedure as a result of dural digitiform projections on the bone caused by chronic intracranial hypertension.

After surgery, supratentorial intracranial pressure normalized and ventricle size increased slightly (Fig. 5 left). However, basal cisterns remained collapsed on the follow-up cranial CT scan. Five days after surgery, a CSF leak appeared. In view of these events, we proceeded with surgical decompression of the posterior fossa to solve the foramen magnum obstruction caused by the presence of a Chiari malformation (Fig. 5 right). The patient underwent lumboperitoneal shunt placement in a third surgical intervention. He was finally discharged home when the initial headache resolved, supratentorial intracranial pressure registry returned to normal values, and the CSF leak disappeared.

**Discussion**

Craniometaphyseal dysplasia, or leontiasis, is a rare bone disorder that affects normal bone synthesis and resorption. A thorough genetic study must be performed to obtain an accurate diagnosis of this disorder, because it may be confused with other pathological entities such as Pyle disease, metaphyseal dysplasia, Gaucher disease, Niemann-Pick disease, or fibrous dysplasia. There are 2 types of CMD that are distinguished by their pattern of inheritance. These 2 types are known as the autosomal dominant and autosomal recessive types. Autosomal recessive CMD is typically more severe than the autosomal dominant form, although in single cases it may be almost impossible to distinguish the real pattern one is facing.4

Mutations have been found in the human ankylosis gene (ANKH) for autosomal dominant CMD and some simplex cases. The phenotypic severity (expressivity) in autosomal dominant CMD is variable even among affected members of the same family. Penetration is close to 100% in both sexes. Males and females are equally affected.3

Mutations located in cytoplasmic domains close to the C terminus of the Ankh gene were identified for the autosomal dominant form of CMD. The Ank gene is proposed to act as a pyrophosphate transporter to channel intracellular pyrophosphate into the extracellular matrix. Extracellular pyrophosphate transporter in a physiological concentration acts as a potent inhibitor of mineralization. Low concentrations of extracellular pyrophosphate transporter lead to excess hydroxyapatite deposition, while supersaturation of extracellular pyrophosphate transporter promotes calcium pyrophosphate dehydrate crystal formation. On the other hand, pyrophosphate is a major component and a promoter of hydroxyapatite formation. A tightly controlled balance between extracellular pyrophosphate and extracellular pyrophosphate transporter is required to maintain normal bone mineral content. Homeostasis of pyrophosphate/ pyrophosphate transporter is primarily maintained by the concerted activities of Ankh and other regulators: plasma cell membrane glycoprotein 1, a protein encoded by Enpp1, which generates pyrophosphate transporter; and TNAP, a protein encoded by Tnp1, which hydrolyzes the extracellular nucleoside triphosphate; and TNAP, a protein encoded by Tnp1, which hydrolyzes the extracellular nucleoside triphosphate; and TNAP, a protein encoded by Tnp1, which hydrolyzes the extracellular nucleoside triphosphate.

Progressive sclerosis of the skull base causes stenosis of cranial foramina and cranial nerve compression that may result in hearing loss, loss of visual acuity, or impaired deglutition. In the cases reported in this paper, the initial symptom in both patients was progressive neurosensorial deafness accompanied by severely impaired visual acuity. Optic foramina were decompressed, unilaterally in Case 1 and bilaterally in Case 2.

Sclerosis of the cranial vault may lead to an abnormal increase in the cephalic perimeter or even dolichocephalic morphology. An increase in the cranial vault thickness may result in extremely high pressure of the dural sinuses and thus an increase in intracranial pressure.

In the first case reported in this paper, the patient presented with progressive lateral and third ventricle size increases while the posterior fossa remained unaltered. In view of these findings, we decided to place a ventriculoperitoneal shunt device.5

In the second case, the ventricles were normal in size, the skull showed digitiform projections, and the superior sagittal sinus protruded through the sagittal suture with anomalous cutaneous drainage veins, mimicking sinus pericranii; possibly this extracranial venous drainage reduces venous pressure within the longitudinal sinus, and resorption of CSF is not altered; therefore, ventricular

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**Fig. 3.** Magnetic resonance images from the 2 cases. A: Axial image showing ventriculomegaly in the absence of periven- tricular lucencies in Case 1. B: Sagittal image demonstrating no Chiari malformation in Case 1. C: Sagittal image in Case 2 showing the skull with digitiform projections and the superior sagittal sinus protruding through the sagittal suture, as well as a Chiari malformation.
size may be normal. The patient also presented with Chiari malformation Type I.\textsuperscript{2,7} As a result of all these events, the origin of hypertension became multifactorial and the treatment became more complex: an increase in skull thickness and dolichocephalic morphology caused cranioencephalic disproportion, diminution in the skull foramina diameter (including the jugular foramen), and resistance to venous return. As a result, superior sagittal sinus pressure increased, as later confirmed on cerebral MR angiography. In view of these events, we decided to perform internal cranial expansion to release the superior sagittal sinus and both optic foramina. However, the result of this procedure was determined to not be effective, because CSF flow obstruction at the foramen magnum was also present. Diffuse bone sclerosis and diminution of the posterior fossa diameter led to the Chiari malformation, explaining the disturbances observed in CSF flow. At that point, posterior fossa expansion was achieved, as well as resection of the arch of C-1 (Fig. 5). After this second surgical intervention, the ventricles increased in size but the CSF leak remained. Consequently, a lumboperitoneal shunt was placed. At discharge from the hospital, the ventricles were bigger in size than in previous studies as a result of surgical cranial expansions, which led to an increase in intracranial capacity and diminution of venous congestion, and resulted in the disappearance of diffuse brain edema and improvement in cerebral compliance.

Intracranial findings determined surgical treatment in each case. In Case 1, a shunt was placed because there was hydrocephalus without a Chiari malformation; in Case 2, with decreased intracranial volume, small ventricles, Chiari malformation Type I, and intracranial hypertension, the chosen treatment was whole cranial vault expansion in 2 phases (frontoorbital advancement and suboccipital decompression; Fig. 5).

Despite presenting with the same pathological entity, patients who suffer from CMD and chronic intracranial hypertension may manifest a wide variety of signs and symptoms that can be managed by means of different therapies, varying from shunt placement to cranial expansion.

Fig. 4. Case 2. Magnetic resonance angiography showing an abnormal venous drainage pattern from the superior sagittal sinus into dilated subcutaneous veins (upper), mimicking sinus pericranii shown in the photograph (lower).

Fig. 5. Case 2. Three-dimensional cranial CT scans showing bilateral osteotomies in frontal, parietal, and temporal bones, orbital bar advancement, and superior sagittal sinus decompression (left), as well as surgical decompression of the posterior fossa (right).
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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.

Author contributions to the study and manuscript preparation include the following. Conception and design: Rivero-Garvía, Márquez-Rivas. Acquisition of data: Rivero-Garvía, García-Iglesias, Gutiérrez-González. Drafting the article: Rivero-Garvía, García-Iglesias, Gutiérrez-González. Critically revising the article: Márquez-Rivas. Reviewed submitted version of manuscript: Márquez-Rivas, García-Iglesias, Gutiérrez-González. Approved the final version of the manuscript on behalf of all authors: Rivero-Garvía.

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Manuscript submitted January 27, 2011.
Accepted April 28, 2011.
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