 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 ANKH 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

**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-
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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 foramina 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 H$_2$O 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-

Fig. 1. Case 2. Plain radiograph revealing abnormal development and osteopenia of the metaphyses in the long bones as well as multiple diaphyseal scleroses.

Fig. 2. Case 1 (left) and Case 2 (right). Computed tomography scans of the skull showing thickening of the diploe, dolichocephaly, sclerosis of the skull base, and severe stenosis of the skull base foramina in both cases.

Fig. 3.
eral dural tears were observed during the surgical pro-
cEDURE 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 under-
went lumboperitoneal shunt placement in a third surgical
intervention. He was finally discharged home when the
initial headache resolved, supratentorial intracranial pres-
sure 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 re-
sorption. 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 re-
cessive 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 af-
fected 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 pro-
posed to act as a pyrophosphate transporter to channel
intracellular pyrophosphate into the extracellular matrix.
Extracellular pyrophosphate transporter in a physiologi-
cal concentration acts as a potent inhibitor of mineraliza-
tion. 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 extra-
cellular pyrophosphate and extracellular pyrophosphate
transporter is required to maintain normal bone mineral
content. Homeostasis of pyrophosphate/pyrophosphate
transporter is primarily maintained by the concerted ac-
tivities of ANK and other regulators: plasma cell mem-
brane glycoprotein 1, a protein encoded by Enpp1, which
generates pyrophosphate transporter from extracellular
and intracellular nucleoside triphosphate; and TNAP, a
protein encoded by Tnap, which hydrolyzes the extracel-
ular pyrophosphate transporter to generate pyrophos-
phate. Deficiency of any of these 3 proteins can lead to
mineral-related pathological conditions in bone.3

Progressive sclerosis of the skull base causes steno-
sis 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 neu-
sensorial deafness accompanied by severely impaired
visual acuity. Optic foramina were decompressed, unilat-
erally 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 dolichocephal-
ic 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 ventricu-
loperitoneal shunt device.3

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
size may be normal. The patient also presented with Chiari malformation Type I.27 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.

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