High incidence of cranial synostosis and Chiari I malformation in children with X-linked hypophosphatemic rickets (XLHR)

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Background

X-linked hypophosphatemic rickets (XLH) represents the most common form of hypophosphatemia and leads to vitamin D resistant rickets in children. Even though cranial vault and craniovertebral anomalies of potential neurosurgical interest, namely early closure of the cranial sutures and Chiari type I malformation- have been observed in XLH patients their actual incidence is not established. Aim of this study was to analyze the incidence of cranial and cervico-occipital junction (COJ) in children with XLH.

Patients and Methods

Retrospective study of CT scans of the head and skull in 44 XLH children followed at the French Reference Center for Rare Diseases of the Calcium and Phosphate Metabolism. The patency of the sutures was noted. The cranial index was calculated and the position of the cerebellar tonsils was analyzed.

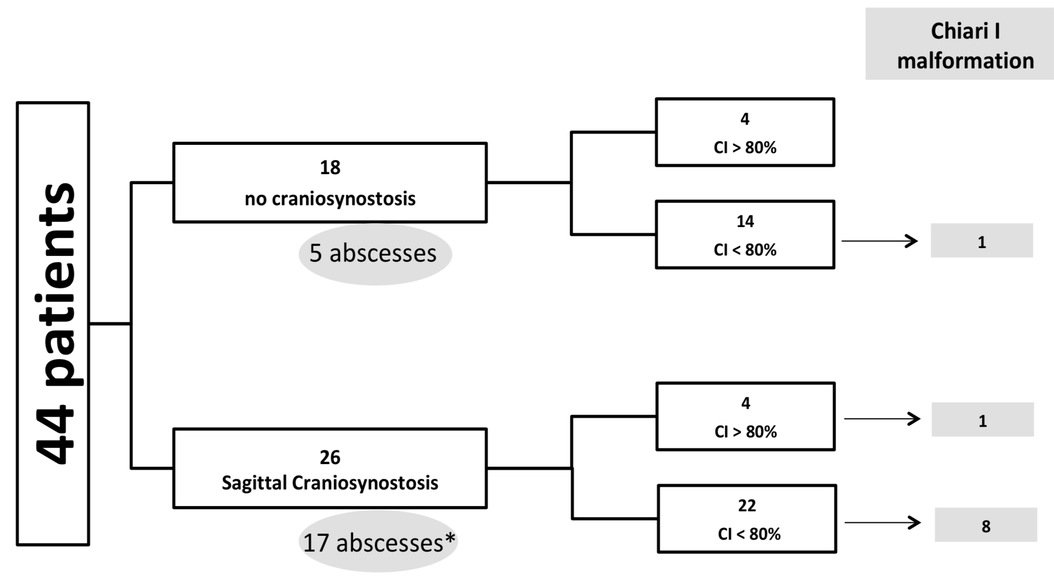
Results

	At diagnosis	N
Boys / girls	15/29	44
Familial / de novo	31/13	44
PHEX mutation yes/no		
all	36/8	44
familial	25/6	31
de novo	11/2	13
ALP (IU/l) mean ± SD (min to max)	560 ± 176 (291 to 1044)	35
Serum phosphate (mmol/l) Mean ± SD (min to max)	0.87 ± 0.18 (0.53 to 1.42)	38
Age (years) mean ± SD (min to max)		
all	2.4 ± 2.1 (0.2 to 10.2)	44
familial	2.2 ± 2.3 (0.2 to 10.2)	31
de novo	3.1 ± 1.4 (1.5 to 6.3)	13
Height (z-score) mean ± SD (min to max)	-1.13 ± 1.25 (-3.6 to 2)	44

Patients' characteristics at XLHR diagnosis

	At CT scanner	N
Age (years) mean ± SD (min to max)	8.7 ± 3.9 (0.4 to 19)	44
Height (z-score) mean ± SD (min to max)	-0.88 ± 1.2 (-3.8 to 1.5)	44
BMI (z-score) mean ± SD (min to max)	0.52 ± 1.1 (-0.77 to 5.1)	43
ALP (IU/l) mean ± SD (min to max)	374 ± 127 (168 to 712)	42
History of dental abscesses yes/no	20/24	44
Leg bowing yes/no	31/13	44

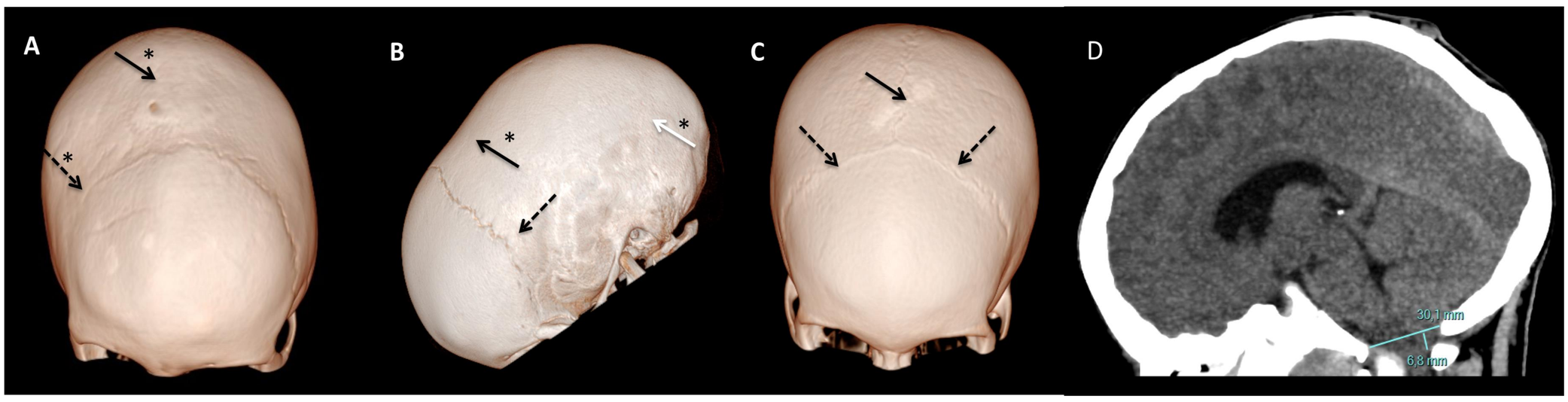
Patients' characteristics at time CT



Study population flow chart. * p=0.035

Chiari I malformation and protrusion of the cerebellar tonsils	> 5 mm N=7	< 5 mm N=3	No protrusion N=29	N/A N=5
Sagittal suture (N)				
Complete fusion	5	2	9	2
Partial fusion	1	1	5	1
Patent	1	0	15	2
Cranial index				
< 75%	4	0	9	3
75-80%	2	3	5	0
>80%	1	0	15	2
Leg deformities (N)				
Yes	6	3	18	2
No	1	0	11	3
Dental abscesses (N)				
Yes	4	1	13	3
No	3	2	16	2
ALP (N)				
< 400 IU/L	4	1	19	3
> 400 IU/L	3	1	10	1
N/A	0	1	0	1

Clinical, biochemical and radiological characteristics of patients with Chiari I malformations



Three dimensional CT skull bone window reconstructions
A. 8-year old XLHR patient. Complete closure of the sagittal and the right coronal sutures. The left coronal suture is patent but narrow.
B. 6-year old XLHR patient. Complete closure of the sagittal and the lambdoid sutures.
C. 12-year old XLHR patient. Patent sagittal and coronal sutures. All very narrow.
D. 8-year old XLHR patient. Head CT sagittal slice parenchyma window showing a 6.8 mm descent of the cerebellar tonsils.
Continuous black arrows: sagittal sutures. Discontinuous black arrows: coronal sutures. Continuous white arrow: lambdoid suture
Asterixes indicate closed sutures

Conclusions

59% of XLH children had a complete or partial fusion of the sagittal suture. 25% of XLH children showed protrusion of the cerebellar tonsils. This study highlights that sagittal suture fusion and Chiari I malformation are two possible complications of XLH.
Because the diagnosis can be underestimated on a purely clinical basis, radiological studies should be considered in XLH children if a proper diagnosis is warranted.