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Visual Diagnosis

Papilledema From Craniosynostosis in Pycnodysostosis

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A 6-year-old boy (Fig 1) was referred for eye examination because of difficulty in kindergarten. He walked at age 18 months and had slow speech acquisition. The weight was 19.5 kg (8%), height was 108 cm (<5%), and head circumference was 47 cm (<3%). Visual acuity was 20/20 OU. There was bilateral optic disc swelling (Fig 1). B-scan revealed no drusen. On palpation, the lambdoid suture was gaping. A skeletal survey revealed an abnormally dense skull, straightening of the mandibular angle, bony resorption of distal phalanges, deformity of the distal femur, spool-shaped vertebra, and dental abnormalities. Computed tomography of the head revealed not only diastasis of the lambdoid suture but also synostosis of the coronal and metopic sutures (Fig 2). The optic canals were normal. A magnetic resonance venogram revealed no dural sinus obstruction. A lumbar puncture yielded an opening pressure of 280 mm water.

The radiological studies suggested the diagnosis of pycnodysostosis. Genetic analysis was performed by polymerase chain reaction and direct sequencing of the entire coding region of the cathepsin K (*CTSK*) gene. Two heterozygous mutations were detected: c.436G>C (p. Gly146Arg) and c.721C>T (p. Arg241 Stop).

Pycnodysostosis is a rare autosomal recessive skeletal disorder caused by a mutation in *CTSK*, gene that codes for a lysosomal proteinase required for bone remodeling by osteoclasts.[1] Craniosynostosis is an unusual manifestation, and papilledema has been reported only once previously.[2,3] This is the first report to document papilledema with fundus photography in a patient with craniosynostosis caused by pycnodysostosis.

There have been 33 different mutations of *CTSK* reported in 159 pcynodysostosis patients, with compound heterozygous mutations in 24% and homozygous mutations in 75%.[4] The three most common mutations are: p. Arg241 stop (c.721C>T) in exon 6, c.436G>C (p. Gly146Arg) in exon 5, and p. Ala277Val/Glu (c.830C>T, c830C>A) in exon 7. These single base substitutions account for about 50% of cases of pycnodysostosis. Our

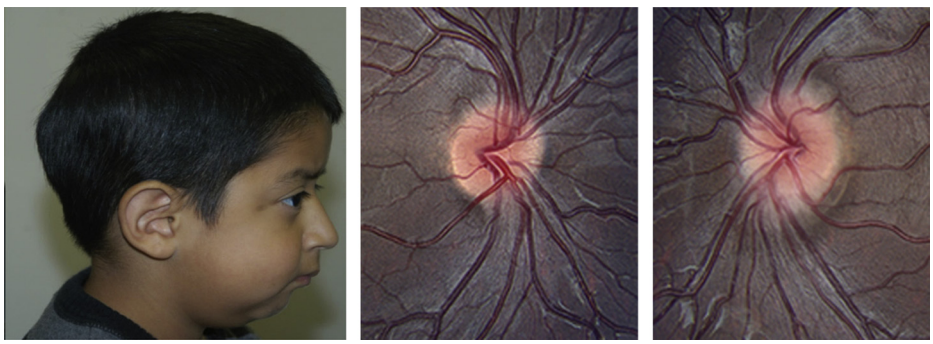

FIGURE 1.
Child with recessed jaw, full cheeks, and cranial deformity. Fundi revealed mild papilledema, more pronounced in the left eye. (The color version of this figure is available in the online edition.)

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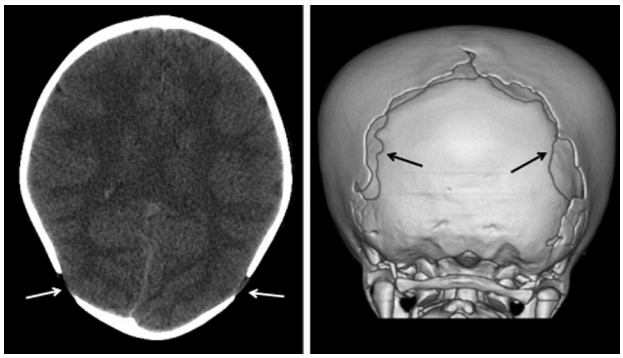

FIGURE 2.
(Left) Axial CT image showing open lambdoid suture (arrows). (Right) Three-dimensional rear view showing the extent of diastasis of the lambdoid suture (arrows).

patient had the first two mutations, a nonsense mutation in exon 6 and a missense mutation in exon 5. Both these mutations have been reported among the seven patients described in the literature with craniosynostosis, but other mutations also have been encountered.[2,3] *CTSK* mutations in pycnodysostosis seem to be indistinguishable phenotypically, and there is no evidence that certain mutations are associated with craniosynostosis and hence, a greater likelihood of papilledema.

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