
Familial Hypophosphatemic Rickets Causing Ocular Calcification and Optic Canal Narrowing

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Summary: In a case of familial hypophosphatemic rickets, marked bone thickening caused narrowing of the optic canals, resulting in bilateral optic atrophy. The case also showed metastatic calcification in the walls of both globes.

Index terms: Familial conditions; Orbits, calcification; Optic canal; Metabolic disorder

Familial hypophosphatemic rickets (FHR) is a rare X-linked disorder of renal tubular reabsorption of inorganic phosphate. FHR causes rachitic changes, skeletal deformity, and growth failure if untreated (1). We describe the case of an adolescent boy with FHR who showed calcification in the walls of both globes.

Case Report

The patient is a boy who was first diagnosed with FHR at 1 year 4 months of age, when he presented with bowed legs and rachitic changes. Laboratory values included a decreased serum inorganic phosphate, 2.6 mg/dL (normal, 3.8 to 6.2 mg/dL), elevated alkaline phosphatase, 508 U/L (normal, 150 to 400 U/L), and normal serum calcium, 10.4 mg/dL (normal, 8.0 to 10.5 mg/dL) consistent with FHR. Since diagnosis, he has been treated with a combination of vitamin D and high-dose phosphate with fairly good control of his rickets. He shows growth retardation with a height at the third percentile but has had appropriate gain in height with therapy. Therapy has been complicated by a single episode of secondary hyperparathyroidism caused by phosphate administration at 13 years of age, treated successfully with reduction in phosphate administration. He has a mother, a twin brother, and two younger sisters with FHR.

At 16 years of age, the boy presented with decreased vision bilaterally. Ophthalmologic examination showed visual acuity of 20/25 on the right and 20/40 on the left. Extraocular movements were full. Fundoscopic examination showed bilateral optic atrophy. A computed tomographic scan of the orbit showed marked bone thickening

causing narrowing of the optic canals and superior orbital fissures bilaterally. Calcification was noted in the walls of the globes bilaterally and along the dural margin of the cavernous sinuses (Fig 1). The boy's visual acuity remains stable at 3 years of follow-up.

Discussion

FHR is a rare hereditary disorder of renal tubular reabsorption of inorganic phosphate. It is inherited in an X-linked dominant manner (1, 2). The impairment of phosphate transport is caused by a defect in the renal brush border membrane. Studies in mice suggest that there is also increased renal catabolism of 1,25-dihydroxyvitamin D (1). The disorder is diagnosed when hypophosphatemia is found in association with renal phosphate wasting, elevated serum alkaline phosphatase, normal plasma and urine calcium, and normal or low serum 1,25-dihydroxyvitamin D (2).

FHR causes rachitic changes, skeletal deformity, and linear growth disturbance if untreated. The disease is treated with a combination of inorganic phosphate and vitamin D (3). Vitamin D promotes intestinal phosphate absorption. Phosphate supplementation stimulates bone mineralization and may help maintain serum concentrations of 1,25-dihydroxyvitamin D by decreasing catabolism and increasing renal synthesis (1). Treatment is aimed at normalizing serum phosphate and alkaline phosphatase levels, causing healing of rachitic changes, preventing skeletal deformity, and minimizing growth disturbance (3).

Complications of vitamin D include hypercalcemia, kidney stones, and renal damage. Nephrocalcinosis may be associated with phos-

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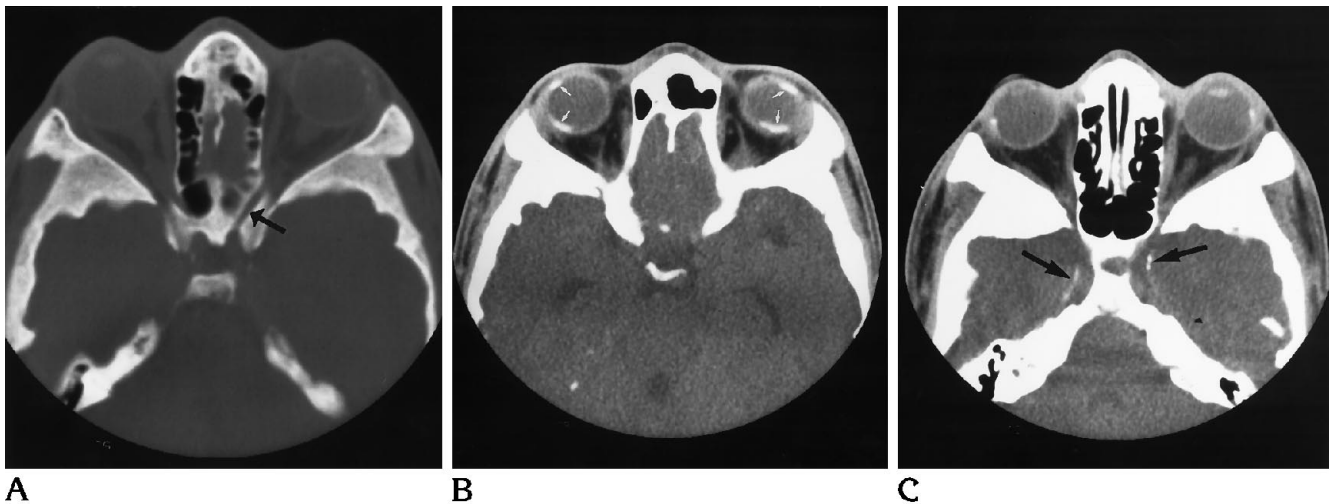


Fig 1. A, Axial nonenhanced computed tomography at bone window settings shows bone sclerosis and expansion causing narrowing of the left optic canal (*arrow*). The right optic canal, seen on a slightly higher image, is also narrow. Also present is slight encroachment on the superior orbital fissures (not shown).

B and C, Axial nonenhanced computed tomography of the orbits shows plaque-like calcification along the margins of the globes (*white arrows*) and cavernous sinuses (*black arrows*).

phate therapy. Phosphate administration may lower serum ionized calcium levels and 1,25-dihydroxyvitamin D concentrations, leading to hyperparathyroidism. Combined administration of vitamin D with phosphate may help maintain higher serum calcium levels and prevent hyperparathyroidism (3).

Soft-tissue calcification may be dystrophic or metastatic. Dystrophic calcification occurs in abnormal tissue because of cell injury or tissue necrosis. Ocular dystrophic calcification may be found in chronic inflammation and infection, tissue hypoxia, trauma, and tumors. The causes of dystrophic calcification are numerous and include retinoblastoma, choroidal osteoma or angioma, cataract, phthisis bulbi, retinal detachment, optic nerve drusen, endophthalmitis, and idiopathic sclerochoroidal calcification. Metastatic calcification occurs in normal tissue and involves calcium deposition caused by abnormal calcium and phosphate metabolism. Ocular metastatic calcification has been shown to be attributable to endocrine causes such as hyperparathyroidism, hypoparathyroidism, pseudohypoparathyroidism, and pseudopseudohypoparathyroidism. Toxic causes include excess calcium phosphate or vitamin D ingestion. Congenital metastatic calcification has been reported in Fanconi syndrome, renal tubular acidosis, and milk-alkali syndrome (4, 5).

Our patient demonstrated calcification in the walls of the globes bilaterally. The calcification seen in this patient is probably metastatic, and the cause may be multifactorial. Metastatic ocular calcification in FHR has been seen infrequently in other hypophosphatemic disorders such as Fanconi syndrome (4). Hyperparathyroidism, excessive ingestion of calcium phosphate, or vitamin D intoxication can also cause metastatic calcification (4, 5). Therefore, it is unclear whether the ocular calcification in this patient is caused by his FHR or is the result of treatment.

Our patient demonstrated bilateral optic atrophy caused by narrowing of the optic canals by bone proliferation. FHR causes deposition of overabundant calcified matrix with decreased trabecular resorption leading to thickening of bones (6). Foraminal compromise has been reported in other causes of bone proliferation such as fibrous dysplasia; when the sphenoid bone is involved, optic canal compromise may result in subsequent optic atrophy (7). Our case shows two interesting findings in FHR: metastatic calcification of the walls of the globes and optic canal compromise caused by bone expansion.

References

1. Tenenhouse HS, Jones G. Abnormal regulation of renal vitamin D catabolism by dietary phosphate in murine X-linked hypophosphatemic rickets. *J Clin Invest* 1990;85:1450-1455

2. Reynolds RD, Lorenc RS, Wieczorek E, Pronicka E. Extremely low serum pyridoxal 5'-phosphate in children with familial hypophosphatemic rickets. *Am J Clin Nutr* 1991;53:698-701
3. Rivkees SA, El-Hajj-Fuleihan G, Brown EM, Crawford JD. Tertiary hyperparathyroidism during high phosphate therapy of familial hypophosphatemic rickets. *J Clin Endocrinol Metab* 1992;75:1514-1518
4. Froula PD, Bartley GB, Garrity JA. The differential diagnosis of orbital calcification as detected on computed tomographic scans. *Mayo Clin Proc* 1993;68:256-261
5. Suzuki J, Takeda M, Sekine N, et al. Bilateral metastatic sclerochoroidal calcification in a patient with hyperparathyroidism. *Ophthalmologica* 1992;205:10-14
6. Steinbach HL, Kolb FO, Crane JT. Unusual roentgen manifestations of osteomalacia. *AJR Am J Roentgenol* 1959;82:875-886
7. Moore AT, Buncic JR, Munro IR. Fibrous dysplasia of the orbit in childhood: clinical features and management. *Ophthalmology* 1985;92:12-20