Ocular Sonographic and Magnetic Resonance Imaging Features of Osteoporosis Pseudoglioma Syndrome

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ABSTRACT

Osteoporosis pseudoglioma syndrome is a rare autosomal recessive disorder, characterised by early-onset osteoporosis and congenital- or juvenile-onset blindness. The combination of multiple osteoporotic fractures and blindness suggests a clinical diagnosis of osteoporosis pseudoglioma syndrome. The main ocular manifestations include microphthalmia, anterior segment anomalies, cataract, vitreoretinal dysplasia, and retrolental mass. This report describes the ocular sonographic and magnetic resonance imaging features of a 23-year-old Chinese woman who was confirmed to have osteoporosis pseudoglioma syndrome by genetic testing. This case report illustrates how to differentiate this rare clinical entity from retinoblastoma. This report also shows how to differentiate osteoporosis pseudoglioma syndrome from Norrie disease, which shares many of the ocular features. As in this patient, the early onset of osteoporosis and subsequent fractures pose a diagnostic challenge for osteoporosis pseudoglioma syndrome. Studies have shown that many such patients have been erroneously diagnosed with osteogenesis imperfecta.

Key Words: Eye manifestations; Magnetic resonance imaging; Norrie disease (pseudoglioma) protein, human; Osteoporosis; Ultrasound

INTRODUCTION

Osteoporosis pseudoglioma (OPPG) syndrome is a rare heritable entity that features severe osteoporosis and variable ophthalmic findings that may lead to congenital or juvenile blindness. The estimated incidence is 1 in 2 million and the carrier frequency is 1 in 700. The combination of multiple osteoporotic fractures and blindness suggest a clinical diagnosis of OPPG syndrome. The main ocular manifestations include microphthalmia, anterior segment anomalies, cataract, vitreoretinal dysplasia, and retrolental mass.

The diagnosis is confirmed by genetic testing. The OPPG locus has been mapped to 11q12-13. Currently, intermittent intravenous bisphosphonate is the only effective and safe method for the prevention of progressive vertebral deformity in patients with OPPG. Reduction in bone pain and improved mobility have been reported following bisphosphonate therapy.

CASE REPORT

A 23-year-old Chinese woman, who was blind in her right eye since the age of 8 years, was referred with stress fracture of her left femoral shaft. Bone densitometry revealed that she was osteoporotic and, even after pamidronate therapy, her bone mineral density was 0.675 g/cm², -1.8 standard deviations for her age group. Osteogenesis imperfecta was initially diagnosed. Subsequent genetic testing confirmed that she had OPPG. Two of her siblings were blind, and had low bone density and a history of multiple fractures in their childhood; they were also genetically confirmed to have OPPG. Her parents were apparently healthy.

Ultrasound of her eyes showed a microphthalmic right eye with evidence of phthisis bulbi (Figure 1a). The contour of her right eye was irregular, with areas of focal retractions. The right lens was densely echogenic (Figure 1b), compatible with cataract. Heterogeneous soft tissue lesions with foci of calcification were noted at the retrolental region (Figure 1c). Her right retina was echogenic with foci of dystrophic calcification. Her left eye was not so severely affected. Echogenic soft tissue stranding and septa were noted at the posterior segment of the left eye (Figure 1d), possibly due to...
vitreous dysplasia and previous haemorrhage. No abnormal Doppler signal was detected to suggest the occurrence of persistent foetal vasculature in the posterior segments of either eye.

Axial 3T T2-weighted fast spin echo sequence (FSE) [Figure 2a] and coronal T2-weighted FSE (Figure 2b) of the orbits demonstrated a hypointense retrolental mass within the vitreous chamber of the right globe due
to vitreoretinal dysplasia and haemosiderin deposition from previous vitreous haemorrhage. The left eye appeared relatively spared.

X-ray of her lumbar-sacral spine, taken when the patient was 12 years old, showed osteoporosis, ‘picture framing’, biconcave vertebrae, and compression deformities of the vertebral bodies — associated diskal ballooning was also detected (Figure 3a). X-ray of her knees showed decreased mineralisation of bones with coarsening of bony trabeculation (Figure 3b).

**DISCUSSION**

The combination of multiple fractures and blindness suggested a clinical diagnosis of the rare OPPG syndrome. Eye features included vitreoretinal dysplasia resulting in retrolental masses. In the past, some eyes have been mistakenly enucleated because of the suspected diagnosis of retinoblastoma. Other ocular manifestations of OPPG include microphthalmia, anterior segment anomalies, and cataract. The absence of other ocular manifestations together with the absence of osteoporosis should differentiate retinoblastoma from OPPG.

Norrie disease, which shares many of the common ocular features with OPPG, is a differential diagnosis. However, up to 30% of patients with Norrie disease will have hearing loss, and the disease is an X-linked recessive disorder.

Persistent foetal vasculature in OPPG has been demonstrated in an infant with bilateral blindness, using colour-Doppler technique. However, this was not detected in the patient described in this report. The exact pathogenesis of OPPG is unclear. It is thought that the ocular involvement in this syndrome is due to regression failure of the primary vitreal vasculature during foetal development.

The early onset of osteoporosis and subsequent fractures could pose a diagnostic challenge for patients with OPPG. Patients with osteogenesis imperfecta have very similar skeletal manifestations and, many patients with OPPG have been misdiagnosed with osteogenesis imperfecta, as was this patient. In 1985, Beighton et al designated the ocular form of osteogenesis imperfecta to this disease entity. The absence of ocular involvement in osteogenesis imperfecta should help distinguish between the 2 conditions.

The osteoporotic process would lead to multiple fractures and bony deformities. The severity and onset of
the osteoporosis is highly variable and a history of trivial injury is often present. The osteopenic process seems to improve with age and may be alleviated by intravenous bisphosphonate therapy, as for this patient.

Other musculoskeletal features include excessive wormian bones, micrognathia, short stature, repressed bridge of the nose, pes planus and/or valgus, kyphosis or kyphoscoliosis, joint hyperextensibility, frequent fractures, tubular deformities, and laxity of ligaments. Other features of this syndrome include cardiac anomalies, ventricular septal defect, and hypotonia. Abnormal blood and urine levels of calcium, phosphorus, alkaline phosphatase, and hydroxyproline might be found in patients with OPPG.

The OPPG locus has been mapped to 11q12-13. The mutations may affect the molecular interactions of the low-density lipoprotein receptor-related protein 5 (LRP5) gene and so lead to the observed phenotypes. Heterozygous carriers of OPPG-causing mutations have reduced bone-mineral density compared with age- and sex-matched controls, and LRP5 mutations have been identified among individuals with idiopathic osteoporosis and/or skeletal fragility.

OPPG is a rare autosomal recessive disorder, characterised by early-onset osteoporosis and congenital or juvenile-onset blindness. This case report not only demonstrates the salient ocular sonographic and magnetic resonance imaging features of this disease entity, but also illustrates how to differentiate from osteogenesis imperfecta, retinoblastoma and Norrie disease.

**REFERENCES**