Microcornea and bilateral ectopia lentis in an infant: unusual severe ocular presentation of neonatal Marfan syndrome

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We present an unusual case of microcornea, bilateral spontaneous dislocation of lenses, and anomalous optic disks in a 7-week-old girl in whom a systemic diagnosis of Marfan syndrome had not yet been confirmed at presentation. The causes and differential diagnoses of this condition are discussed, and the literature on ocular manifestations of neonatal Marfan syndrome is reviewed.

Neonatal Marfan syndrome is a rare condition that manifests earlier in life and is associated with a worse clinical prognosis than classical Marfan syndrome.[1] We report the case of a 7-week-old infant who presented with bilateral spontaneous lens dislocation, which, especially in infancy, is rare,[2] and in whom an eventual diagnosis of neonatal Marfan syndrome was confirmed by genetic testing.

Case Report

A 7-week-old girl of Asian ethnicity was referred by her family doctor for absent red reflexes. She was the second born of a nonconsanguinous marriage. There was no family history of significant ocular problems. She was identified to have mild cardiac anomalies antenatally, confirmed after birth, including patent foramen ovale and dysplasia of mitral and pulmonary valves, with a mildly dilated aortic root. These anomalies were not significant enough to require treatment, nor did they fit into the diagnosis for Marfan syndrome. She also had arachnodactyly, with contractures of her fingers, toes, and wrists. The constellation of her systemic features prompted a systemic diagnosis of congenital contractural arachnodactyly (Beals syndrome) and genetic testing results were awaited.

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On ophthalmological examination, she did not fix or follow light or a target. Her eyes appeared mildly sunken, and she had downward sloping palpebral fissures. She had bilateral microcorneas, with a horizontal corneal diameter of 9.5 mm in each eye. The anterior chambers were deep, and there was bilateral iridodonesis. The pupils were miotic, sluggishly reacting, and poorly dilating even after 3 days of atropine eye ointment application. Her intraocular pressures were 10 mm Hg in the right eye and 13 mm Hg in the left eye as measured with Icare tonometer (Icare Finland Oy). Both lenses were completely dislocated posteriorly and found freely floating in the midvitreous (see Figure 1). There were no visible lens zonules. The lenses appeared microspherophakic and cataractous. Both lenses prevented a clear visual axis, because they were obscuring the macula.

The patient underwent bilateral sequential pars plana lensectomies with core vitrectomies. A high-arched palate was noted during examination under anesthesia. Intraoperatively her optic disks were found to be large and anomalous—the right disk had an absent nasal neuroretinal rim and the left appeared colobomatous (Figure 2). Postoperative retinoscopy revealed +19.5 D of hypermetropia in both eyes. She was fitted with bilateral aphakic contact lenses of +28 D (contact lens power was obtained after adjusting for vertex distance of 12 mm and overcorrecting by +2.5 D). On follow-up 8 weeks later she could fix and follow faces.

On subsequent cardiology follow-up, she was noted to have a marked dilatation of the aortic root over a period of 10 weeks. On the basis of bilateral ectopia lentis and her cardiac features, she was diagnosed clinically with Marfan syndrome, according to the revised Ghent nosology. Genetic testing was negative for Beals syndrome, but it did reveal a heterozygous pathogenic change in c.3038G>C on exon 24 of the *FBN1* gene, confirming Marfan syndrome.[3] She was started on systemic treatment with losartan and atenolol but died of cardiac complications at the age of 6 months.

Discussion

Neonatal Marfan syndrome—variably termed as *infantile Marfan syndrome*,[4] *congenital Marfan syndrome*, and *severe perinatal Marfan syndrome*—is a rare disorder with very high mortality within the first 1-2 years of age because of severe cardiovascular manifestations.[1,5] In most cases, there is no positive family history, because the condition is usually due to sporadic mutations.[4] The gene defects in neonatal Marfan syndrome tend to cluster around exons 23-32 of *FBN1*, which has been called the "neonatal region."[3]

The systemic features of Marfan syndrome, especially in infancy, resemble those of congenital contractural arachnodactyly, or Beals syndrome.[6] The conditions are genetically distinct but phenotypically similar. Although Marfan

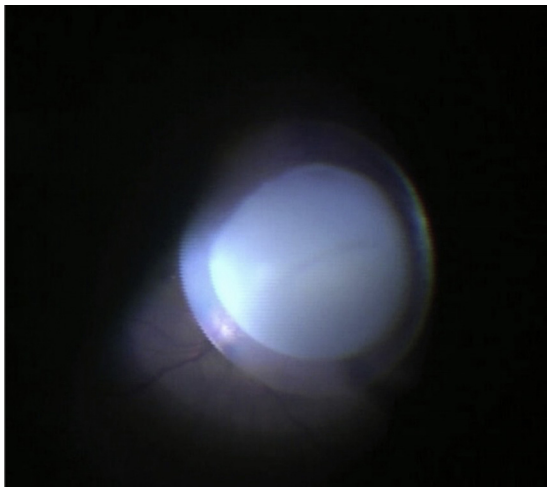

FIG 1. Microspherophakic cataractous lens freely floating in the midvitreous of the right eye (view during pars plana vitrectomy).

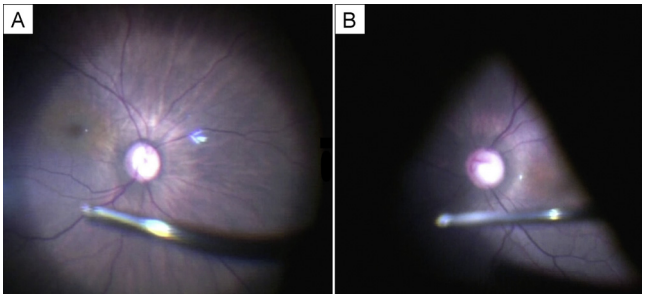

FIG 2. Optic disks (view during pars plana vitrectomy): right optic disk with absent nasal neuroretinal rim (A) and left colobomatous disk (B).

syndrome is caused by mutations affecting the *FBN1* gene on chromosome 15 encoding fibrillin-1, CCA is associated with mutations of *FBN2* on chromosome 5, encoding fibrillin-2. Marfan syndrome is diagnosed based on the revised Ghent nosology.[7] Beals syndrome has overlapping features with Marfan syndrome, including Marfanoid habitus, arachnodactyly, camptodactyly, and kyphoscoliosis. Characteristic features of Beals syndrome that are rare in Marfan syndrome include multiple joint contractures and crumpled ears.[8] However, in infancy, these differences blur, because neonatal Marfan syndrome can present with crumpled ears and joint contractures.[9] Some helpful differentiating features of Beals syndrome are the absence of significant aortic root dilatation and the rarity of ectopia lentis. In our case, the patient's systemic features and the absence of aortic root dilatation initially suggested a diagnosis of Beals syndrome. It was only after ophthalmic examination that Marfan syndrome was considered, especially because she developed significant aortic root dilatation on follow-up. This highlights the importance of ophthalmic evaluation in infants with Marfanoid habitus, because identification of ocular features may help in earlier recognition of the correct systemic diagnosis.

The following ocular findings of neonatal Marfan syndrome have been reported: downward sloping palpebral fissures, blue sclerae, megalocorneas, hypoplastic irides with complete translucency, miosis, spherophakia, ectopia lentis, retinal detachments, and severe myopia.[4,10] Our patient had some of these typical phenotypic features, but she also had distinctive findings not previously reported, although it is possible that they are coincidental. Although ectopia lentis is a well-known feature of Marfan syndrome, spontaneous lens dislocation is commonly observed in adulthood; bilateral complete dislocation of the lenses in an infant has not been reported. Furthermore, there are no previous reports of microcornea associated with Marfan syndrome, as seen in our case. Indeed, megalocornea in neonatal Marfan syndrome has been reported previously.[5] Finally, our patient was also found to have anomalous optic disks, which has not been described as a typical feature of neonatal Marfan syndrome.

Literature Search

PubMed was searched (1970-present) on March 1, 2018, for English-language results using the following terms: *neonatal Marfan syndrome*, *infantile Marfan syndrome*, and *ocular features* AND *Marfan*.

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