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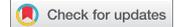


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CASE REPORT



Novel retinal findings in peroxisomal biogenesis disorders

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ABSTRACT

Peroxisomal biogenesis disorders are caused by disruption of long chain fatty acid metabolism due to mutations in PEX genes. Individuals with these disorders often have vision loss due to optic atrophy and pigmentary retinopathy. We report an unusual retinal manifestation of peroxisomal biogenesis disorder.

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KEYWORDS

Chorioretinal fold; epiretinal membrane; peroxisomal biogenesis disorder

A two-year-old female was evaluated because she was not meeting visual developmental milestones. She had hearing loss and speech and motor delays. On examination, she was able to fixate, follow, and maintain fixation bilaterally. She had large angle intermittent exotropia with manifest latent nystagmus. Dilated fundus examination revealed a large chorioretinal fold of the right eye extending from the optic nerve inferotemporally to the ora serrata, with associated fibrosis and involvement of the inferior temporal arcade vessels (Figure 1). In the left eye, she had an epiretinal membrane overlying the fovea (Figure 2), with inferior peripheral pigmentary changes and healthy appearing optic nerves bilaterally.

The patient was referred to genetic pediatric genetics service. Very long chain fatty acid analysis revealed elevated C26:0, C26:1 and pristanic acid levels as well as elevated C24/C22 and C26/C22 ratios consistent with peroxisomal biogenesis disorders. Red blood cell plasmalogen testing revealed mildly decreased C16:0 dimethylacetal (DMA)/C16:0 fatty acid and C18:0 DMA/C18:0 fatty acid levels. Genetic testing of PEX1 exons 13, 15, 18, and 19 revealed compound heterozygous mutations of c.2097 dup T (a frameshift mutation with premature stop codon) and a c.2528 G > A (p.Gly843Asp) missense mutation, confirming her diagnosis. Due to agreement of the biochemical and genetic data, parental testing to assess cis/trans conformation of the alleles was not performed.

She underwent strabismus repair shortly after initial presentation, and had significantly improved tracking post-operatively with excellent alignment. She has required only mild hyperopic refractive correction, which has been stable for the past 4 years. The chorioretinal fold and epiretinal membrane have been stable on annual dilated examinations over the last 7 years.

Her medical course has been complicated by slow weight gain associated with significant oral aversions and swallowing dysfunction, for which she had a g-button placed. She has no

evidence of liver or adrenal dysfunction. She has profound sensorineural hearing loss for which she wears hearing aids. She walks with a walker but can take independent steps. She is able to speak in 3–4 word phrases.

Peroxisomal biogenesis disorders are a group of rare diseases with variable severity, all caused by aberrant function of the peroxisome, an organelle involved in oxidation of very long chain fatty acids. As a group, they are referred to as Zellweger spectrum disorders. Disease-causing mutations in 13 PEX genes have been described, with mutations in PEX1 being most common. The majority of peroxisomal biogenesis disorders are inherited in an autosomal recessive fashion(1).

Children with peroxisomal biogenesis disorders are often noted to have decreased visual tracking in infancy, which may be among the first signs of milder phenotypes. Patients are frequently found to have pigmentary retinopathies (2,3), with case reports of peripheral leopard spotting(4) and flecked pigmentary changes (5,6). A case series of 31 patients with mild disease found retinopathy common to all(7).

ERG testing may reveal extinction of both cone and rod function. Visual evoked potential (VEP) testing may also be extinguished, depending on the severity of the phenotype(3). Optical coherence tomography in one individual able to comply with testing revealed cystoid macular edema, which may also contribute to reduced visual acuity(8). Other ophthalmologic findings of peroxisomal biogenesis disorders include congenital cataracts, corneal clouding and optic nerve atrophy (1,3). Individuals with diagnosed or suspected to have peroxisomal disorders should undergo screening ophthalmic examination and should receive low vision services when appropriate.

Systemic manifestations include hypotonia, feeding difficulties, seizures, sensorineural hearing loss, and hepatic dysfunction. Bony stippling (chondrodysplasia punctata) of long bones may occur. Life span is often reduced in severe disease. Phenotypic severity depends on the number and type of mutations. Some individuals can live into adulthood(1).



Figure 1. Fundus photograph of the right eye, with a large chorioretinal fold of the extending from the optic nerve inferotemporally to the ora serrata, with gliosis in the retinal periphery.



Figure 2. Fundus photograph of the left eye, with a epiretinal membrane overlying the fovea.

Testing for peroxisomal biogenesis disorders includes measurement of plasma very long chain fatty acid levels. Elevation of C24/C22 and C26/C22 are consistent with defective peroxisomal fatty acid metabolism. Genetic testing can confirm the diagnosis, and may be helpful in prenatal diagnosis and family planning decisions. Referral to a geneticist is critical in making the diagnosis, and can also help to coordinate the complex medical care required by these individuals.

Peroxisomal biogenesis disorders should be considered in children or infants who present with retinal abnormalities and multiorgan dysfunction. Our patient exhibited

typical peripheral pigmentary retinopathy and also had unusual findings of a congenital chorioretinal fold and epiretinal membrane. To our knowledge these have not been reported in peroxisomal biogenesis disorder, and represent new ophthalmologic findings in this spectrum of diseases.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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