An association between subclinical familial exudative vitreoretinopathy and rod-cone dystrophy

 Associação entre vitreorretinopatia exsudativa familiar subclínica e distrofia de cones e bastonetes

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INTRODUCTION
Familial exudative vitreoretinopathy (FEVR) is a retinal vascular pathology that is considered as a vitreoretinal dystrophy. It emerges in the first decade of life and may lead to vision threatening complications at any subsequent time(1). FEVR was first described by Chriswick and Schepens in 6 patients in 1969(2). These patients displayed a pathology resembling retinopathy of prematurity (ROP), but had no history of prematurity or oxygen support at birth. FEVR cases are often overlooked due to its low prevalence, highly asymptomatic clinical course, and diversity of symptoms. Characteristically, it is bilateral but clinical findings may be asymmetric(3). Clinical findings may include macular ectopia, retinal folds, vascular tortuosity, retinal neovascularization, telangiectasia, peripheral retinal ischemia, macular edema, telangiectasia in both eyes, and retinal dragging toward the temporal periphery in both eyes. Full field electroretinography showed that rod responses were almost absent and that cone responses were reduced. Macular optical coherence tomography showed normal structure in both eyes. Vascular changes were attributed to a subclinical form of familial exudative vitreoretinopathy. This was an interesting case due to the association of familial exudative vitreoretinopathy with rod-cone dystrophy.

Keywords: Retinal diseases/genetics; Vitreoretinopathy, proliferative; Electoretinography; Retinal rod photoreceptor cells; Humans; Male; Adult; Case reports

CASE
A 21 year-old Caucasian man presented with a complaint of nyctalopia. Visual acuity in both eyes was 20/20 and anterior segment biomicroscopy results were unremarkable. Fundoscopy revealed peripheral avascular zones, minimal peripheral retinal exudation from the retinal vessels, peripheral retinal telangiectasias and anastomosis in both eyes, and retinal vascular dragging toward the temporal periphery in both eyes. Full field electroretinography showed that rod responses were almost absent and that cone responses were reduced. Macular optical coherence tomography showed normal structure in both eyes. Vascular changes were attributed to a subclinical form of familial exudative vitreoretinopathy. This was an interesting case due to the association of familial exudative vitreoretinopathy with rod-cone dystrophy.

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Figure 1. Fluorescein angiography of both eyes.

Figure 2. Full-field electroretinogram of both eyes.

Figure 3. Dark adaptation curve.

Figure 4. High resolution optical coherence tomography images.

DISCUSSION

In this report, we present a case of FEVR and rod-cone dystrophy. Although the pathogenesis of FEVR is not completely clear, a number of mutations have been defined for specific disease subtypes. Furthermore, the genetic inheritance pattern is varied, and may be autosomal dominant, autosomal recessive, X-linked, or sporadic. However, the autosomal dominant form is most commonly observed, and mutations in at least four genes have been associated with FEVR. Mutations to the frizzled family receptor 4 (FZD4) gene are responsible for the autosomal dominant form, while mutations to the NDP, LRP5, and TSPAN12 genes are responsible for the X-linked, dominant, and recessive forms, respectively. The NDP gene is also responsible for the pathogenesis of incontinentia pigmenti, ROP, and...
Norrie’s disease. As our patient’s father and brother suffered from the same symptoms, autosomal dominant inheritance can be assumed. FEVR is characterized by various combinations of macular dragging, temporal radial retinal folds, peripheral avascularity, retinal neovascularization, vitreous hemorrhage, tractional retinal detachment, and subretinal exudation. As the disease progresses, complications due to ischemia and fibrovascular proliferation threaten vision. Optic nerve atrophy, cataracts, glaucoma, chronic subfoveal exudation, and strip keratopathy may also contribute to vision loss if present.

Retinitis pigmentosa (RP) is a generic term used for a group of hereditary retinal diseases that are characterized by degeneration of photoreceptors and pigment accumulation in the retina. The disease displays genetic heterogeneity, similar to FEVR. Autosomal dominant, autosomal recessive, and X-linked patterns are all possible. Forty-five different gene loci have been reported to be associated with the disease, but in almost half of the cases no specific causative mutation has been found. RP is usually seen as an isolated disease in the retina, but in 20–30% of cases it may present systemic associations. As in FEVR, symptoms may differ but peripheral visual field deficiency, nyctalopia, and central vision loss in the late period are certain. Although rod dysfunction is prominent even in the disease’s early stages, some cases show simultaneous rod and cone dysfunction or dominant cone degeneration. Cataract, vitreous degeneration, retinal vascular attenuation, intraretinal pigmentations, and a waxy appearance of the optic disk head are other possible clinical signs. In our patient, the symptoms of nyctalopia in association with non-recordable rod responses and reduced cone responses, was sufficient to make a clinical diagnosis of rod-cone dystrophy. The typical symptoms and signs of rod cone dystrophy in a patient with typical fundus findings of FEVR makes this patient an interesting case.

Only a few previous studies have presented the electrophysiological features of FEVR and, to our knowledge, an association between FEVR and any hereditary fundus dystrophy, including rod-cone dystrophy, has not been previously reported. Feltman et al. examined six patients in a family with FEVR and found that electroretinographic responses were normal. In addition, Nicholson et al. examined four cases and all electroretinograms were within normal limits, except for one eye of a single patient. In contrast to these findings, Ohkubo et al. reported abnormal ERG findings (a reduction of oscillatory potentials, a and b waves of bright white flash ERG, and scotopic and photopic b waves) in two cases. We speculate that these findings were possibly related to the general retinal destruction due to FEVR. However, in our patient, the complaint of nyctalopia beginning from early childhood, and the very subtle fundus findings in association with the ERG findings, dictates that our patient had both FEVR and rod-cone dystrophy simultaneously.

In conclusion, this case report is possibly the first to report the coexistence of FEVR and rod-cone dystrophy. Genetic analyses and detailed clinical descriptions should be provided in further case reports.

REFERENCES