Exudative Vitreoretinopathy 1

**Alternative Names**
- EVR1
- Exudative Vitreoretinopathy, Familial, Autosomal Dominant
- FEVR, Autosomal Dominant
- Criswick-Schepens Syndrome
- Retinopathy of Prematurity
- ROP

**Record Category**
Disease phenotype

**WHO-ICD**
Diseases of the eye and adnexa > Disorders of choroid and retina

**Incidence per 100,000 Live Births**
Unknown

**OMIM Number**
133780

**Mode of Inheritance**
Autosomal dominant; also autosomal recessive and X-linked recessive forms do exist

**Gene Map Locus**
11q14-q21

**Description**
Familial exudative vitreoretinopathy (FEVR) is a rare inherited vitreoretinal dystrophy portrayed by incomplete retinal vessel development. The classic form of FEVR includes large segments of avascular retina within the temporal periphery correlated with arterial venous anastomoses and neovascular proliferations around the ischemic region, a peripheral temporal fibrovascular mass, and a peculiar pattern of retinal vessels. FEVR clinical symptoms might develop to sever complications such as vitreous hemorrhage, exudation of lipids in the retina, macular edema, ectopic macula, retinal detachment, and retracted vitreous leading to a fold in the retina from the optic disk to the temporal edge.

FEVR bears a resemblance to retinopathy of prematurity, however, signs of prematurity or small birth weight were not found in the patient’s history. The severity of FEVR differs from one patient to another, even within the families, varying from frequent minor asymptomatic forms to sever forms with infantile or juvenile onset (until about age 20). FEVR can be surgically treated to help terminate the disorder progression.

**Molecular Genetics**
Numerous categories of transmission were detected including autosomal dominant, autosomal recessive and X-linked recessive. Mutations in the frizzled homolog 4 (Drosophila) gene (FZD4) are implicated in 20% of the autosomal dominant forms of FEVR. FZD4 is located at 11q13-q23. Its product consists of 537 amino acids, and has a molecular weight of 59,881 kDa. Moreover, the autosomal dominant FEVR can also originate due to mutations in the low density lipoprotein receptor-related protein 5 (LRP5) gene. LRP5 is mapped to 11q13.4. The LRP5 protein consists of 1615 amino acids and has a molecular weight of 179,145 kDa. Both FZD4 and LRP5 genes are Wnt receptors where they both underline the significance of Wnt signaling in the vascularization of the eye. Furthermore, X-linked FEVR originates due to mutation in the Norrie disease (NDP) gene located at Xp11.4.

**Epidemiology in the Arab World**

**Kuwait**
Al Essa et al. (1999) conducted a prospective cohort study of 130 preterm infants born at less than 2 Kg weight and/or 36 weeks gestational age in a single hospital in Kuwait to determine the rate and risk factors of ROP in this population. Of these 130 infants, 59 (45%) developed some stage of ROP. Logistic regression analysis identified low birth weight and oxygen therapy to be independently associated with ROP.

Haider et al. (2000) carried out a study on 102 premature newborns of Kuwaiti Arab origin to research the presence of Norrie disease (ND) gene...
and replicate the findings in a diverse population/racial group. Controls constituted 55% (56) of the newborns and they demonstrated normal eyes. Retinopathy of prematurity (ROP) regressed spontaneously throughout stage 1-3 in 34% of cases (35), whereas 11 cases (11%) experienced ROP that progressed to advanced stages. The screened premature newborns presented the R121W mutation of exon 3 in the ND gene; however, 98% of these newborns possessed the genotype (PP) of the second mutation [L108P]. Furthermore, the (LL) genotype was found in only one of the 56 normal infants. Haider et al. (2000) concluded that the Kuwaiti population is genetically homogenous due to the detection of genotype (PP) at codon 108 in nearly all controls and ROP cases. Moreover, no correlation was found among the risk of severe ROP and the presence or absence of missense mutations of the ND gene. Later, Haider et al. (2002) studied the ACE in/del polymorphisms in a group of 74 premature Kuwaiti infants with ROP and compared it to polymorphisms in 107 control premature infants without ROP. The cases could further be divided into two sub-groups; in 53 of the patients, the disease regressed spontaneously, while in 21, the ROP progressed to stages 4 or 5. When the cases were taken as a whole, the incidence of the ID genotype was higher in the controls, while the II genotype was significantly higher in the cases. However, the incidence of the DD genotype was significantly higher in the second sub-group compared to the spontaneously regressing group.

Al-Merjan et al. (2005) presented the causes and incidence rates of disorders leading to blindness and low vision in Kuwait, based on the data collected by the Visual Disability Committee in a 5-year period from 2000 to 2004. Of the 826,083 people (407,871 males) registered with blindness and low vision, 39% were below the age of 20 - years, 32% were between the ages of 21 and 40 - years, while only about 10% were over 60- years of age. Retinopathy of prematurity was found to occur with an overall incidence rate of 0.41 per 100,000 population. The incidence varied between males (0.68) and females (0.14).

Saudi Arabia

Binkhathlan et al. (2008) conducted a retrospective study on retinopathy of prematurity (ROP) in Saudi Arabia in order to evaluate ROP screening criteria in the Kingdom and identify the risk factors of this disorder. ROP was diagnosed in 93 infants, 15% of those patients were in stage 3 of the disease. The mean gestational age (GA) was 30 weeks for ROP patients. Importantly, gestational age at birth was the most significant independent risk factor for developing ROP. National screening for the disorder proved to be 68% sensitive and 55% specific in the context of uncovering ROP cases. These findings prompted Binkhathlan et al. (2008) to suggest widening screening criteria to include 34-week GA infants.

Syria

Alsheikheh et al. (2004) presented six cases of familial exudative vitreoretinopathy disease with various abnormalities of the posterior segment diagnosed in two Syrian families related by first degree of consanguinity. The age of the cases ranged between 3.5 and 13 years, who were found to be systemically healthy, presented with a visual acuity ranging between light perception and 0.4 with bilateral fundus changes. The findings included: papillary, macular, and retinal temporal traction in 11 eyes, a retinal fold in 7 eyes, a fibrovascular mass in 11 eyes, vitreoretinal traction in 5 eyes, subretinal exudation in 2 eyes, pigmentary abnormalities in 2 eyes, temporal or total tractional retinal detachment in 2 eyes, and vitreous hemorrhage in 1 eye. Alsheikheh et al. (2004) concluded that familial exudative vitreoretinopathy is characterized by fundus changes that resemble retinopathy of prematurity and must be differentiated from other diseases (e.g., Coats' disease, incontinentia pigmenti, persistent hyperplastic primary vitreous, and Norrie's disease).

Tunisia

Khairallah et al. (1995) reported the case of a 9 year-old boy with symptomatic exudative vitreoretinopathy featuring retinal neovascularization and minimal vitreous hemorrhage in one eye. He was successfully treated with laser photocoagulation. The mother and her five other children had isolated retinal vascular tortuosity, hence, suggesting the same nosologic frame to these autosomal dominant diseases and the possibility that they represent different expressions of the same genetic disorder.

More recently, Errais et al. (2008) presented what could be considered the first comorbid association of FEVR with hyaloid artery persistence. The case included an 18-year-old Tunisian female and four members of her family (mother, two brothers, and sister) who presented signs of FEVR. Examination of the patient also revealed functional hyaloid artery persistence in her right eye. The two disorders have many common aspects in their pathological process, in particular vascular endothelial growth factor expression.

References


**Related CTGA Records**

Low Density Lipoprotein Receptor-Related Protein 5

**External Links**

http://www.genecards.org/cgi-bin/carddisp.pl?gene=FZD4&search=Familial+exudative+vitreoretinopathy

http://www.genecards.org/cgi-bin/carddisp.pl?gene=LRP5&search=Familial+exudative+vitreoretinopathy


http://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=EN&Expert=891

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