

Study of vitreoretinal dystrophies in a Mexican population

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Abstract

Background: We undertook this study to demonstrate the incidence of vitreoretinal dystrophies in a Mexican population.

Methods: This was a retrospective, observational, descriptive, transverse study. We analyzed the files of patients treated at the Retina Department of a medical center for state employees (ISSSTE) from January 1991 to December 2006 to obtain the incidence of vitreoretinal dystrophies.

Results: We studied 36,300 patient files. We found an incidence of 0.008% for familial exudative vitreoretinal dystrophy, 0.008% for X-linked juvenile retinoschisis, 0.005% for Wagner disease and 0.005% for Goldmann-Favre disease. We present here a representative case of each type of dystrophy.

Conclusions: Vitreoretinal dystrophies are uncommon diseases and are difficult to diagnose. Even though their incidence is low, the poor evolution to blindness requires identification of early signs in order to offer timely and opportune treatment.

Key words: vitreoretinal dystrophies, Goldman-Favre disease, X-linked juvenile retinoschisis, familial exudative vitreoretinal dystrophy, Wagner-Stickler syndrome.

Resumen

Objetivo: Determinar la incidencia de las variedades de las distrofias vitreoretinianas en población mexicana ya que no existen reportes de la misma en la literatura. Método: estudio retrospectivo, observacional, descriptivo y transversal con revisión de expedientes de pacientes con enfermedades retinianas de 1991 al 2006 para determinar la incidencia de distrofias vitreoretinianas.

Resultados: Fueron analizados 36,300 expedientes del Servicio de Retina revisados de enero de 1991 a diciembre de 2006 en el Centro Médico Nacional 20 de Noviembre, hospital de tercer nivel de referencia nacional de los pacientes derechohabientes del ISSSTE, de los cuales se encontró una incidencia de 0.008% para la distrofia exudativa familiar, 0.008% para la retinosquiasis juvenil ligada al X, 0.005% para la enfermedad de Wagner y 0.005% para la enfermedad de Goldmann-Favre. Presentamos casos representativos de los mismos.

Conclusiones: Las distrofias vitreoretinianas son enfermedades raras, de difícil diagnóstico, pero aunque su incidencia es baja la tórpida evolución hacia la ceguera nos obliga a identificar los signos precoces para un tratamiento más oportuno.

Palabras clave: distrofias vitreoretinianas, retinosquiasis juvenil, vitreoretinopatía exudativa familiar, enfermedad de Goldmann-Favre, síndrome de Wagner-Stickler.

Introduction

Vitreoretinal dystrophies (VRD) comprise a group of hereditary diseases with ocular and occasionally systemic effects, generally

manifested before 15 years of age. Its incidence is low and is referred to as isolated in the literature or by sporadic cases or family groups. Generally they are localized by independent entity and not by the group of vitreoretinal diseases. There are no national reviews that would allow us to determine the grade of incidence and occurrence in the Mexican population in general. The objective of this study is to determine the incidence of vitreoretinal diseases in Mexico, diagnostic difficulties and possible treatment alternatives. For this purpose, medical records were reviewed from the Retinal Department of a third-level care national hospital for state workers (ISSSTE).

VRD constitute a group of pathologies characterized primarily by a change in the retina and secondarily in the vitreous. Retinal changes include separation of schisis, atrophy, formation of holes or migration of the pigmented epithelium of the retina (PER) and may result in blindness.¹ Known varieties are juvenile

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Received for publication: 23-04-2007

Accepted for publication: 09-07-2007

retinoschisis, familial exudative vitreoretinopathy (FEVR), Goldmann-Favre disease and Wagner-Stickler syndrome.

Materials and Methods

A retrospective, observational, descriptive and transverse study was done by reviewing patient records with retinal diseases at a third-level care hospital from January 1, 1991 to December 31, 2006. Diagnosis for vitreoretinal disease was determined integrated with photographic images. Incidence analysis was performed comparing them with the total number of patients examined in the retinal service of Centro Médico Nacional 20 de Noviembre during this time period.

Results

There were 36,300 files reviewed with the following results: three patients from the same family with FEVR (0.008%), two patients with Wagner's disease (0.005%), two patients with Goldmann-Favre disease (0.005%), and three patients with X-linked juvenile retinoschisis (0.008%), of which two were brothers.

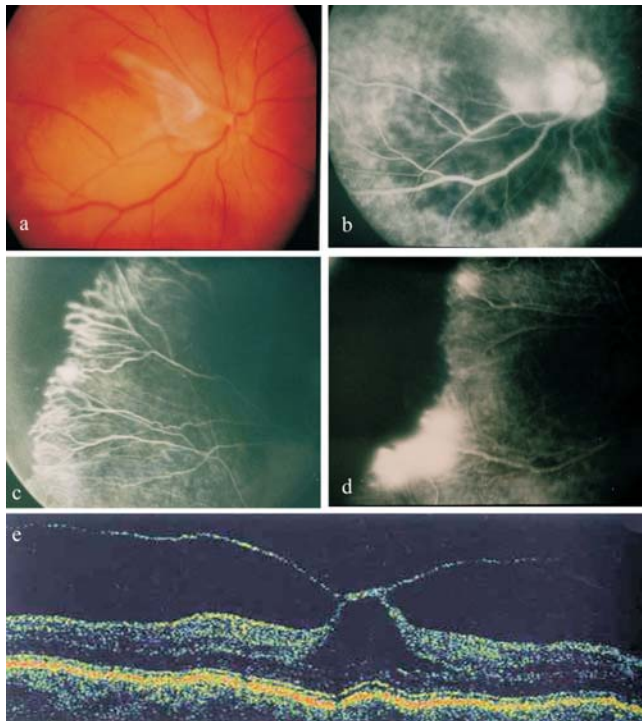


Figure 1. FEVR right eye. (a) Color retinography with peripapillary fibrous tissue. (b,c,d) Fluorangiography (FAR) showing amputated vessels and fan-like filtering arborizations. (e) OCT showing vitreoretinal traction over the macular area and cystic zone below the traction.

Case 1

The patient was a 26-year-old female who was myopic, with photopsias and erythrospias of 2 months evolution. Visual capacity (VC) of the right eye (OD) was 20/50, refraction (Rx): -5.75 spherical equivalent (sph. eq.), CV of left eye (OS) 20/200, Rx: -8.75 sph. eq., intraocular pressure (IOP) of 18 mmHg in both eyes. Fundus of OD demonstrated tractional retinal detachment (RD) with peripapillary fibrotic tissue, pigment anomalies of equator periphery, white zone without pressure and in fluorangiography (FAR) amputated vessels and fan-like filtering venous arborizations in the form of a fan. Optical coherence tomography (OCT) demonstrated vitreoretinal traction in macular area and cystic zone below the traction (Figure 1). Fundus of OS demonstrated peripheral retinal changes similar to retinopathy of prematurity (ROP) and in FAR filtering fan-like venous arborizations (Figure 2) with diagnosis of FEVR.

Case 2

The patient was an 8-year-old child with loss of OD vision and poor vision and hemeralopia of OS. There was articular hyperlaxity, flat nasal bridge, and bilateral hypoacusia. CV of OD showed light perception, Rx: -14.00 sph. eq., CV of OS was 20/60, Rx: -12.00 sph. eq. There was a bilateral central posterior subcapsular cataract that was not dense. OD showed phthisis bulbi secondary to total RD with vitreoretinal proliferation stage C5. OS demonstrated liquified vitreous with abundant lumps and fibrous tracts, lacy degeneration in inferior quadrants and zone of peripheral schisis due to traction on inferior nasal quadrant.

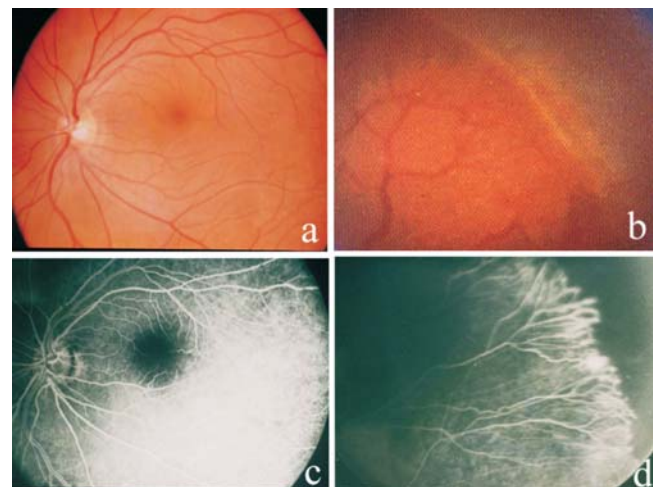


Figure 2. Familial exudative vitreoretinopathy (FEVR) left eye. (a) Color retinography of the posterior pole with minimal changes. (b) Temporal periphery that shows changes similar to retinopathy of prematurity. (c,d) FAR with amputated vessels and fan-like filtering peripheral arborizations.

OCT demonstrated cystic zones at macular level (Figure 3). Diagnosis was Wagner-Stickler syndrome. Phakectomy, pars plana vitrectomy, endophotocoagulation and silicon oil were all done with good evolution.

Case 3

The patient was a 13-year-old female with poor vision and image distortion. CV of OD was 20/70 and Jaeger No. 4, Rx: -3.00 sph. eq. CV of OS was 20/400 and Jaeger No. 10, Rx: -3.00 sph. eq. OD showed incipient posterior subcapsular cataract, syneretic vitreous, macular schisis with inferior RD and chorioretinal degeneration of temporal quadrants. OS showed RD with vitreoretinal proliferation.

Electroretinogram (ERG) demonstrated flat B wave and OCT confirmed macular cysts and vitreoretinal traction (Figure 4). Diagnosis was Goldmann-Favre disease. Retinopexy OD was performed with good results, and phakectomy OS via par plana vitrectomy with injection of silicone oil was done, but visual recuperation was poor.

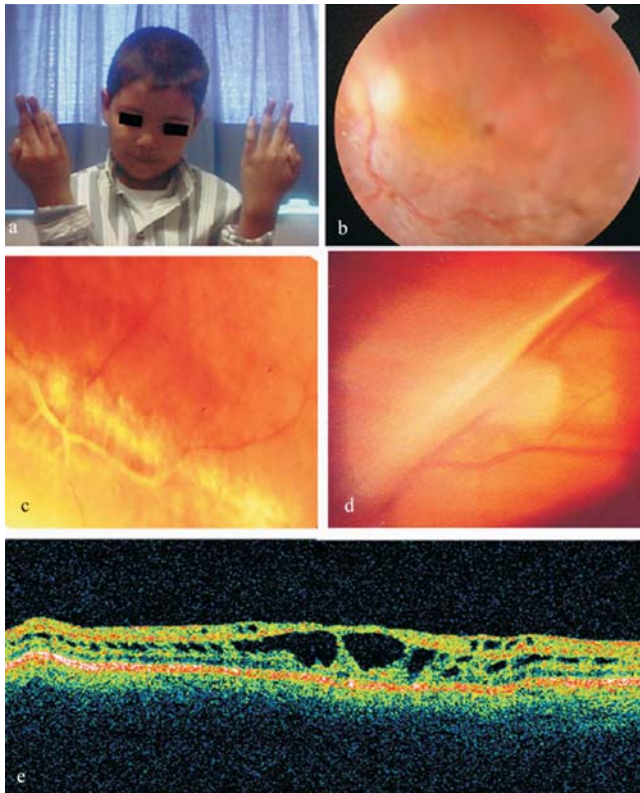


Figure 3. Wagner Stickler. (a) Articular hyperlaxity, hypoplasia of the bride of the nose. (b) Color retinography of the left eye showing liquified vitreous with abundant lumps (c) and degeneration in both inferior quadrants. (d) Fibrous tracts. (e) OCT showing cystic zones at the macular level.

Case 4

The patient was a 10-year-old male with low vision of both eyes. Clinical family history revealed the paternal grandfather was blind and father and brother of patient had poor vision. CV of OD was 20/200 and Jaeger No. 6, Rx: +6.00 sph. eq. CV of OS was 20/200 and Jaeger No. 6, Rx: refractive error +6.00 sph. eq. Both eyes showed macular edema, absence of foveolar reflex and swelling of the foveolar area with central schisis. ERG demonstrated absence of B wave and in OCT there were cystic zones in macular area. Diagnosis of the patient and patient's brother was X-linked juvenile retinoschisis (Figure 5).

The third patient with X-linked juvenile retinoschisis had schisis in the macular area and in the inferior nasal quadrant of the right eye and temporal inferior zone of the left eye (Figure 6).

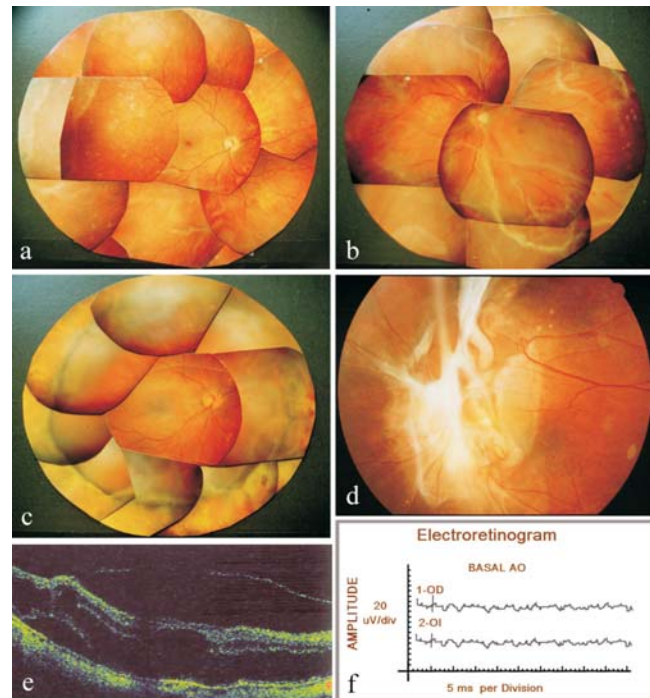


Figure 4. Goldmann Favré. (a) Photographic composition of the retina of the right eye showing syneretic vitreous, macular schisis with inferior retinal detachment and areas of chorioretinal degeneration in temporal quadrants. (b) Photographic composition of the retina of the left eye showing retinal detachment with vitreoretinal proliferation (stage C2). (c) Photographic composition of the surgical results of the right eye. (d) Color retinography showing the evolution of retinal detachment of the left eye. (e) OCT of the pre-surgical right eye that confirmed the presence of macular cysts and vitreoretinal traction. (f) Electroretinogram that shows flat B-wave.

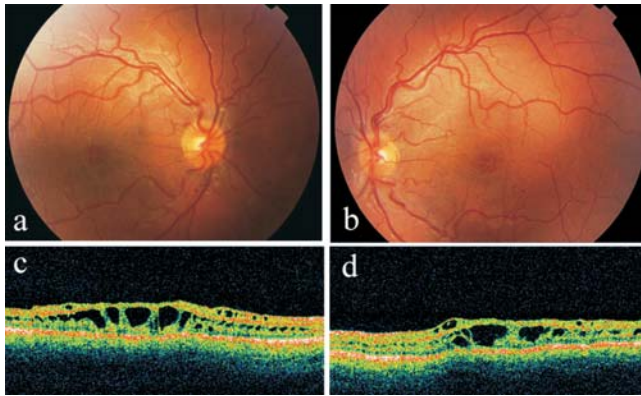


Figure 5. Juvenile retinoschisis, older brother. (a,b) Color retinography of the posterior pole of both eyes showing macular schisis. (c,d) OCT confirming cystic zones in the macular area.

Discussion

Diagnosis of a vitreoretinal dystrophy implies the study of the vitreous and retina. There could be myopia, strabismus, RD, vitreous hemorrhage or PER changes. Dystrophic alterations in vitreo include synchysis (liquified vitreous), and syneresis (collapse of collagen structure). Microscopically, the collapsed vitreous is seen as a “veil”, whereas that which is liquified appears optically empty. Dystrophic changes in the retina include separation of the layers, atrophy, formation of holes and alterations of the PER. Primary change occurs in the retina, and secondarily is accompanied by passive vitreous changes.¹

The following is a review of the most relevant published information of each of the four mentioned vitreoretinal dystrophies, accompanied by a synoptic table with the most relevant findings of the distinctive characteristics of each (Table 1).

Juvenile Retinoschisis

Juvenile retinoschisis was first described in 1898 by Haas and later in 1913 by Pagenstecher. The most common inheritance pattern is X-linked recessive,² although cases with autosomic recessive have been described.³ The gene involved (*RS1*) has been localized on chromosome Xp22 with mutations: Western I, II, III, IV, V and Northern, which produce around 82 different defects in the *RS1* gene.⁴ It is the most common cause of juvenile macular degeneration in males⁵ with a prevalence of 1:5,000 to 1:25,000.⁶ It is generally bilateral. It begins with low central vision and absolute scotomas. In children it may be associated with strabismus and nystagmus.⁷ The most common refraction defect tends to be hypermetropia.⁸ Loss of foveolar reflex is followed by formation of radiated cysts with appearance of a wheel, pigmentary degeneration and cystic macular atrophy. The predominant sign is retinal schisis and its sequelae are more

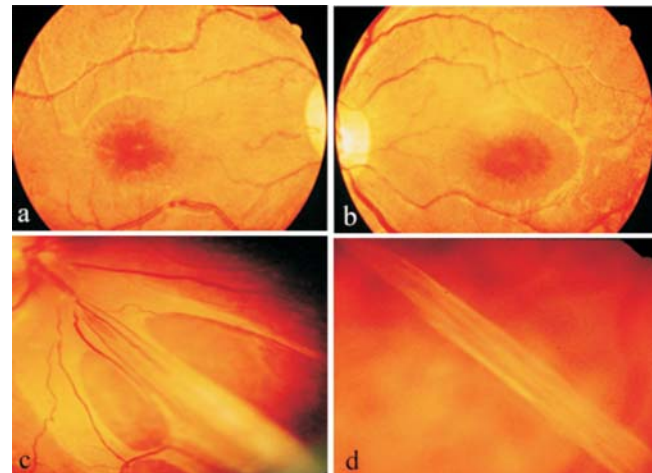


Figure 6. Juvenile retinoschisis, third patient. (a,b) Color retinography of the posterior pole of both eyes showing schisis in the macular area. (c,d) Schisis in the inferior nasal quadrant of the right eye and inferior temporal quadrant of the left eye.

visible in the macula (fovea) in the infero-temporal quadrant. Peripheral changes are seen in autosomic dominant forms. The macula presents a cystoid macular edema, but there is no contrast leak in FAR study. Initially, the internal layer of the schisis is adhered to the vitreous, vessels, internal limiting membrane and layer of nerve fibers. These tissues suffer progressive atrophy as well as gliosis, which resembles perivascular sheath.⁹ The external layer of the schisis suffers apoptosis, gliosis, migration of the pigment between layers and formation of a hole. Rhegmatogenous RD is present in 4 to 22% of the patients.¹⁰ Vitreal detachment could improve schisis on releasing the traction. Adhesions towards the retinal vessels cause vitreous hemorrhage.⁹ The causes for schisis are diverse:¹¹ vascular origin, vitreous traction due to inadequate growth of the cortical vitreous, anomalies in the development of the vitreous, or cytoplasm defect in Muller cells. It has been mentioned that the photoreceptors are the cells primarily affected on being the producers of retinoschisis that maintain the architecture of the internal layers of the retina.¹² This schisis generally occurs in the “median limiting” membrane (between the internal nuclear layer and external plexiform). Adhesions of the vitreous to the internal capsule of the schisis (glía, fibrous nerve layers and vessels) could progress and produce traction, especially if there is vitreous hemorrhage. For the site of schisis, deep retinal capillaries can be interrupted, appearing in angiography with fluorescence as areas of no perfusion. Atrophy of the internal layers is the result of chronic ischemia and decapitation of the glial cells, generating holes and perivascular gliosis. External layers could become atrophied or be invaded by proliferations of EPR.⁹ In ERG, selective absence of B wave is characteristic. The nature of the peak latency and amplitude of B wave suggest damage to Muller

Table 1. Characteristic findings of the vitreoretinal dystrophies

Disease	Juvenile retinoschisis	Familial exudative vitreoretinopathy	Goldmann-Favre disease	Wagner syndrome	Stickler syndrome
Genetic mutation	Cr Xp22 Gene: RS1	Cr 11q Gene: FZD4 and LRP5	Cr 15q22.32 Gene: NR2E3	Cr 5q13-1 Gene: WGN1	Cr 12q13.11-q13.2 Gene: COL2A1
Age at onset	< 10 years	Children (poor prognosis) Adults	< 15 years	< 10 years	< 10 years
Sex	Only male	Both	Both	Both	Both
Cataract	No	Late complication	Posterior subcapsular	Subcapsular posterior	Pre-senile
Nyctalopia	No	No	Yes	No	No
Adaptation to darkness	Abnormal	Normal	Normal	Abnormal	Normal
Vitreol syneresis	++	Secondary to chronic vascular exudation	++	++	++
Macular retinoschisis	++++		++	++	No
Peripheral retinoschisis	Infero-temporal	Occasional	++	++	
Perivascular retinal degeneration	No	Yes	+++	No	++
Peripheral chorioretinal degeneration	No	Cystoid	++++	Lacy and target zones without prission	*
Retinal detachment	Can be rhegmatogenous or tractional	Tractional or exudative. Total/partial	Tractional	Rare, ordinary type	Common, complicated type. Rhegmatogenous
Refraction	Hypermetropia	Emetropia or severe myopia	Emetropia or mild myopia	Mild myopia	High congenital myopia
ERG	Diagnostic method: Absence of B wave	Diagnostic method: 1. Temporal area of non-perfusion, "V" shape 2. Peripheral amputated vessels 3. AV short circuit 4. Peripheral vascular arborization	Altered, undetectable rod response	Normal A wave Abnormal B wave	
FAR	1. Areas of peripheral non-perfusion 2. Late filling of the disc 3. Diffuse intraretinal leak		1. Capillary diffuse leak 2. Areas of non-perfusion	1. Capillary diffuse leak 2. Areas of non-perfusion	1. Capillary diffuse leak 2. Radial retinal perivascular degeneration
Extraocular findings	No	LRP5: decrease of bone density	No	No	Articular hyperlaxity; cleft over the midline; sensorial deafness

*Vitreous degeneration and chorioretinal atrophy was demonstrated in a family with Stickler syndrome (alteration in COL2A1 gene).

ERG = Electroretinogram; FAR = Fluorangiography. Staining intensity: ++, mild; +++, moderate; +++++, intense.

cells. Analysis of the subcomponent of a low frequency in the rheoelectroretinogram (RERG) demonstrates inhibitory neuronal connections weakened in the retina, which is a sign of disease progression.¹³

In FAR study, areas of no perfusion are observed in the extreme periphery. There is no circulation present in the majority of the opacified dendritic vessels in the area of the schisis. There is late filling of the disc, arteries and posterior veins. Diffuse intraretinal leak of fluorescein suggests that the vascular changes can come from the retinoschisis. Progression of the disease is unpredictable and regression occasionally occurs. Surgical indications are rhegmatogenous RD and repetitive vitreous hemorrhages. It has not been shown that photocoagulation is beneficial because it can cause a RD in 14-43% of the cases. With scleral cerclage, although it decreases traction, up to 40% of re-detachments have been reported.⁵ Retinectomy of the internal layer of the schisis theoretically eliminates traction in a more definitive way and can be the technique that has better long-term results.

Familial Exudative Vitreoretinopathy (FEVR)

FEVR was described by Criswick and Schepens in 1969 in full-term newborns who did not receive treatment with oxygen.¹⁴ It is a rare disease. Other factors need to be considered including non-genetic ones in order to explain the variety of characteristics it presents¹⁵ or the associations with other pathologies such as Norrie disease or hereditary retinal vascular tortuosity. It has an autosomal dominant inheritance, although sporadic cases have been reported:¹⁶ autosomal recessives¹⁷ and X-linked recessives¹⁸ (possibly with poor prognosis). The gene responsible for the dominant form is found on the long arm of chromosome 11.¹⁹ Independent mutations have been described in the genes that codify for the pair of receptors Wntm frizzled 4 (FZD4) and lipoprotein of low density related to receptor 5 (LRP5). When both are present, its effects are synergistic. Patients with mutations in LRP5 may also have decrease in bone density and those with mutations in FZD4 may present a less severe disease with an autosomal dominant inheritance pattern.^{15,17,20} Prognosis in infancy is worse. Patients with asymmetric disease may have greater myopia in the eye with more severe changes. Clinical findings include temporal retina traction, macular and papillary, retinal folds, presence of fibrovascular masses, vitreoretinal traction, subretinal exudate, pigmentary anomalies, tractional RD, and similar changes with ROP that should be differentiated from other diseases (e.g., Coats disease, incontinence pigmenti, persistence of primary hyperplastic vitreous and Norrie disease). Primary changes are characterized by areas of “no perfusion” of internal layers of the retina. Vitreous changes are secondary to chronic vascular exudation causing contraction and early detachment of the posterior vitreous.²¹ Areas of no perfusion determine the degree of neovascularization. Three stages have been distinguished: I: areas of no perfusion; II: localized,

tractional exudative RD and neovascularization; and III: total tractional and exudative RD.²² Neovascularization is similar to that found in ROP, whereas subretinal exudate of lipids allows it to be confused with Coats disease. However, in FEVR, exudative RD is combined with a tractional fibrovascular pre-retinal membrane, whereas in Coats disease abnormal intraretinal vessels with vitreous and without alterations predominate.

In the early stages of FEVR, FAR demonstrates a zone of no perfusion in the shape of a “V” in the temporal retina near the ora serrata. Peripheral retinal vasculature demonstrates an important vascular tree, formation of arteriovenous short circuits and pattern of incomplete arteriovenous interdigitation (amputated vessels). Peripheral vasculature is hyperpermeable and exudates below the retina and at the base of the vitreous. Peripheral subretinal fibrosis can be observed, and the collapse of the vitreous induces traction, RD and neovascularization. The vessels of neof ormation tend to exudate and bleed, thereby forming a vicious cycle of vitreous contraction and fibrosis. The no-perfusion zone corresponds to ischemia of the internal layers of the retina and Muller cells, provoking schisis and holes, granulomatous proliferations and vitreous hemorrhage (of low tendency).²³ Vitreous changes of syneresis and sychysis, contraction, partial or complete detachment, opacification and tractional-rhegmatogenous RD appear to be secondary to retinal vasculopathy and is probably is a primary disease of small retinal abnormally permeable vessels. Different from ROP, they tend to present pre-retinal acellular fibrous membranes in the periphery.²¹ The mild form of the disease is most common. The moderate form of FEVR demonstrates blurry vision, floating vitreous bodies, image distortion, flat or elevated neovascularization, and retinal and subretinal exudates. The severe form causes visual loss, macular heterotopia, falciform retinal folds, total RD, atrophy of the iris, neovascular glaucoma and cataracts. Narrow-angle glaucoma has been described by a retrolental process or pupillary blockage.²⁴ Cryotherapy or photocoagulation of the areas of no perfusion, vitrectomy, scleral cerclage and surgical removal of the membrane are included as treatments.^{24,25} Family history investigation should be performed for detection of other cases (Table 1).

Goldmann-Favre Disease

This is a rare disease described by Goldmann in 1957 and by Favre in 1958.²⁶ Ricci suggested the pattern of autonomic recessive inheritance. Mutation of Arg311Gln of the chromosome 15q22.32, called NR2E3 (nuclear receptor subfamily 2, group E, member 3) functions as a regulator of the transcription that interacts with *Crx*. Together they promote and maintain the function of the rods²⁷ that may be responsible for this disease. Patients can have nyctalopia, bilateral atypical pigment changes, and degenerative vitreous changes. There may also be retinoschisis, opaque retinal vessels, diffuse leak of contrast of the capillaries of the retina, and cystoid macular edema.^{28,29} Poor

nocturnal vision corresponds with the retinal area affected. Vision deteriorates on developing schisis, edema or macular atrophy. In FAR there is contrast leak up to areas of no perfusion. The vitreous liquifies and presents with pre-retinal membranes with holes. Vitreous tracts are visualized in an optically empty vitreous. In ERG, the rod response is undetectable, and the response of the cones to a stimulus of long wavelength is found to be reduced.³⁰ If there is a response, it may be the same under conditions of light and darkness. An abnormal response to the stimulus of short-wave length and white light has been described, which has been called "enhanced S cone syndrome". Contrary to retinosis pigmentosa, ERG shows few alterations and spectral ERG is more useful.³¹ OCT shows confluent macular cystoid changes and retinoschisis.³²

Wagner-Stickler Syndrome

This syndrome was first described in 1938 by Wagner in four generations of a family affected with a pattern of autosomal dominant inheritance. Boehringer added 10 new cases in a later analysis. Wagner described a vitreous optically empty with filiform avascular membranes, thin avascular sheathed retinal arteries, and small accumulations of retinal pigmentation in the periphery and around the involved vessels.³³

The term "Wagner-type vitreoretinal degeneration" was coined for a specific type of vitreoretinal alteration or for constituting a sign associated with diseases of the connective tissue complicated by osseous dysplasia, constituting Wagner-Stickler syndrome. The hereditary factor or ocular changes present in Wagner and in Stickler could intermix.³ Wagner syndrome has been associated with alteration of chromosome 5q13-14,³⁴ with liquefaction of the vitreous.³³⁻³⁵ Age may be an important factor because at birth the fundus of the eye may appear normal, but the quantity of the pigment may be increased, showing a mosaic appearance.³⁶ As the child grows, refraction has a tendency to myopia, choroid pigmentation turns gray in the periphery and near the posterior pole. Retinal vessels increase in thickness and become tortuous, the small choroid vessels (choriocapillaries) become atrophied, forming patches around the retinal vessels, particularly in the posterior pole and the papilla with great pigmentary migration. Areas with no pigment accumulation are yellow, and visual acuity remains the same unless the macula is involved at an early stage. The peripheral retina shows evidence of retinoschisis, lacy degeneration with perivascular collections of pigment that extend from the papilla to the equator and later run circumferentially around the globe. The vessels are sheathed, forming a vitreous veil. There may be posterior subcapsular cataract. RD can be observed between 20 and 40 years of age, and there may be associated multiple holes or a large tear. It may occasionally be associated with choroid detachment, iridodonesis, hypotonia, folds in Descemet's membrane and uveitis. There may be glaucoma. If the vision is affected early, there may be nystagmus.

Vitreous membranes are found adhered to the retina in areas of equatorial intraretinal pigmentation, generally grouped around the vessels. PER atrophy may resemble choroid sclerosis. Two types of Wagner syndrome have been identified, one with vitreous changes and another with chorioretinal changes.

In 1965, Stickler described a family of five generations with "hereditary and progressive ophthalmopathy" with an autosomal dominant inheritance pattern, high myopia, "optically empty" vitreous cavity, lacy posterior perivascular radial degeneration, cataract, severe RD, flat aspect of the face and osteoarthritis.^{36,37} As opposed to Stickler syndrome, the prevalence of RD and chorioretinal atrophy in Wagner syndrome appears low.³⁸

Snead and Yates³⁹ proposed the following clinical criteria for diagnosis of Stickler syndrome: congenital abnormality of the vitreous and three of the following findings: 1) myopia beginning before 6 years of age, 2) rhegmatogenous RD or lacy pigmented perivascular degeneration, 3) articular hyperlaxity, 4) neurosensorial deafness or 5) presence of cleft over the midline.

Stickler syndrome is the most common hereditary cause of rhegmatogenous RD in infancy, tends to be bilateral and frequently leads to blindness. Its incidence is 1:10,000 persons, less common than Marfan syndrome.⁴⁰ Mutations have been suggested in the production of type II collagen because it is the major component of cartilage, the vitreous and nucleus pulposus. Type II collagen exists in two forms depending on how exon 2 of gene COL2A1 (which codifies the alpha I chain of the type II collagen localized in chromosome 12q13.11-p13.2) is expressed. One form is of type IIB (short form) is expressed in the cartilage of the adult and the other type IIA (long form) is expressed in the vitreous body of the eye.⁴¹ Due to this tissue-selective expression, there are principal phenotypes: Stickler type I mutation (STL1) is associated with the "type I" vitreous with anterior retrolenticular membranous vitreous and with an optically empty cavity behind, with multiple mutations in the COL2A1.⁴² It is present in 75% and type II (STL2) fibrillar, which is associated with a mutation in the COL11A1 gene (production of type XI collagen).⁴³ A mutation in the COL11A2 gene gives rise to a third systemic phenotype (STL3) without ocular findings. Although 17 mutations have been already described⁴¹ between Wagner's disease and Stickler syndrome, there are not only clinical differences but also genetic differences. Stickler syndrome can also be overlapped with Robin syndrome (palatoschisis, glossoptosis, and micrognathia). In addition to skeletal alterations there may be neurosensory deafness, peripheral neuropathy and occasionally chronic polyarthritis.

It would seem that "perivascular radial retinal degeneration" is the universal manifestation of Stickler syndrome. This pathology has been associated with congenital glaucoma.⁴⁴ Finally, scleral cerclage has been proposed as a preventive measure for tractional RD.⁴⁵

In conclusion, after reviewing the literature in English of the different varieties of vitreoretinal dystrophies, we report the low

frequency of presentation in the retinal department of a target hospital with 0.005-0.008% of the patients with vitreoretinal pathology during a period of 15 years. We reviewed 36,300 charts and diagnosed vitreoretinal dystrophies, and using the characteristics and documented information we prepared a synoptic table that will facilitate diagnosis of the four varieties. On understanding the physiopathology of these dystrophies, we can more accurately choose the therapeutic approach in order to obtain better visual results in these patients, who are generally children or young adults and who will have a productive life with early diagnosis and opportune treatment.

The advance in genetic studies allows us to provide counseling on the possibilities of future transmission, as well as the need for examination of family members. Although in our country the low frequency of these pathologies do not appear to constitute a public health problem, the failure of diagnosis and delay in adequate treatment permits the development of serious clinical pictures which lead to blindness. It is for this reason that we should maintain vigilance and be alert on the clinical signs that could be present to adequately detect them.

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