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Retinal detachments in the pediatric population

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Abstract:

In this review, we present a concise summary of the more commonly seen types of retinal detachments (RDs) that one can encounter in pediatric patients. A spectrum of diseases from rhegmatogenous RD in Stickler syndrome, Marfan syndrome, and choroidal coloboma to exudative RD in Coats disease, to tractional RD in persistent fetal vasculature, and combined RDs in familial exudative vitreoretinopathy are described with the management pearls for each.

Keywords:

Pediatric, retinal detachment, scleral buckling, vitrectomy, vitreoretinal surgery

Introduction

Retinal detachments (RDs) in the pediatric population span a variety of congenital and acquired conditions with some not commonly seen in adults. In this review, we describe and illustrate the more commonly encountered types of rhegmatogenous RDs (RRDs), tractional RDs, and exudative RDs and highlight important pearls in the diagnosis and management of each.

Rhegmatogenous Retinal Detachments

Epidemiology and clinical presentation

The incidence of RRD in children is low. The causes of RRD can be divided into traumatic and nontraumatic. Nontraumatic causes include (i) myopia; (ii) hereditary congenital anomalies (more common examples include Stickler syndrome, Marfan syndrome, and X-linked retinoschisis); (iii) nonhereditary developmental anomalies, e.g., choroidal coloboma, cicatricial retinopathy of prematurity (ROP); and (iv) previous intraocular surgery.[1-6]

Delayed diagnosis is a significant feature of pediatric RRDs. Compared to adults, children with nontraumatic RRDs usually present at a later stage and with RD of undetermined duration. At presentation, these detachments are usually macula-involving or have proliferative vitreoretinopathy (PVR). The incidence of PVR at presentation has been reported in various studies to range from 40% to 45%.[2,6,7] Occasionally, a child may present late with sensory strabismus as a result of an undiagnosed chronic RD. Bilateral involvement has also been reported to be more common in pediatric nontraumatic RRDs, with a range of 15%–22%.[2,3]

Conversely, traumatic RRDs usually present acutely and with a known duration. In a large series of 127 eyes, Soheilian *et al*.[2] reported a statistically significant higher male-to-female ratio in traumatic RRDs (9.8:1) but no significant difference in nontraumatic cases.[2] In a retrospective case series of 88 eyes in patients aged 0–16 years by Lee *et al*.,[8] 53% of RRDs were related to trauma and 44% of retinal breaks were retinal dialyses. Retinal dialysis is most often located in the inferotemporal quadrant, which may become symptomatic years after the trauma. In this series, 76%

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of the idiopathic RDs were due to dialyses. Previous series have reported similar findings,[9,10] suggesting that "spontaneous" dialyses are a separate clinical entity in the pediatric age group. It has been postulated that the temporal retina is the last area of the retina to vascularize; therefore, retinal dialyses may occur in children with a congenital predisposition.[11] If vitreous hemorrhage or cataract is absent, treatment of choice is usually a circumferential segmental scleral buckle.[12] It is recommended that the width of the buckle should extend from the ora serrata anteriorly to the posterior edge of the dialysis.[13] Anatomical reattachment was reported in 67%–88% of cases, with low rates of PVR.[14,15]

The reported overall anatomic success rate of surgical repair of pediatric RRDs ranges from 74.9% to 80%.[2,3] Performing a pneumatic retinopexy (PR) may be considered in some older children with RRD. Advantages of PR in this patient population would be reduced risks of cataract and change in refractive status compared to a vitrectomy or scleral buckle, respectively. However, careful patient selection and counseling of patients and parents on the importance of compliance to posturing are essential in achieving success with one procedure. Warder *et al*.[16] reported a retrospective, non-interventional, comparative case series of PR done in 27 eyes, in 26 patients ranging from 9 to 18 years of age, and found an overall anatomical success rate of 63% with a single procedure. A subgroup analysis of patients receiving PR for standard indications (retinal breaks within 2 clock hours, breaks within superior 8 clock hours, and absence of PVR or other traction) demonstrated an increased success rate of 88% with a single procedure. These results reiterate the importance of careful patient selection for PR in the pediatric population.

Rhegmatogenous retinal detachments associated with congenital developmental anomalies

Epidemiology and clinical presentation

The reported incidence of congenital developmental anomalies as a cause of pediatric RRD ranges from 12% to 56%.[2,3,7,17,18] In studies done in East Asian countries, e.g., Taiwan, the incidence reported is lower at 12%–17% as there is a higher incidence of myopia and associated RRD in East Asian populations.[3,6]

In a retrospective case series of 127 eyes, Soheilian *et al*.[2] reported that congenital developmental anomalies comprise 52.5% of RRDs in children below the age of 10 years, with an overall incidence of 39.3%. Hereditary vitreoretinopathies comprise the majority with Stickler syndrome being the most common.[2,18] Hereditary vitreoretinopathies are a group of disorders characterized by abnormally appearing vitreous gel associated with peripheral retinal changes. Alterations in the structure of the vitreous with abnormal vitreoretinal adhesions can predispose to RRD in these eyes. In many of these syndromes, systemic abnormalities affecting the joints and skeletal system are also present.

Stickler syndrome

Stickler *et al*.[19] described a pedigree combining ocular, facial, palatal, and skeletal changes in 1965. Prominent features of this disorder include generalized arthropathy, cleft palate, flat face, hearing loss, and spondyloepiphyseal dysplasia. Abnormalities of the vitreous gel structure are pathognomonic of this disorder. The inheritance is usually in an autosomal dominant pattern, but it can also occur sporadically.

Type I Stickler syndrome has a membranous vitreous phenotype with a well-defined retrolenticular fibrillar condensation separated from a larger and more posterior empty vitreous space (Type I vitreous). This type is most common and is associated with gene mutations for synthesis of collagen Type II (*COL2A1*).[20,21] The less common Type II Stickler syndrome has a beaded vitreous phenotype (Type 2 vitreous) and is associated with mutation in the *COL11A1* gene which codes for Type XI collagen. Type III Stickler syndrome has no ocular findings and is caused by mutation in the *COL11A2* gene.

Nonocular features

Facial features of the patients with Stickler syndrome include abnormal nasal, maxillary, and mandibular bony development. Patients usually have an underdeveloped nasal bone with a saddle nose. Other skeletal abnormalities include epiphyseal dysplasia, lax joints, and early-onset progressive arthritis.[19,20,22,23] Neurosensory hearing loss also affects most patients over time.[23,24]

Ocular features

Ocular abnormalities in Stickler syndrome involve both the anterior and posterior segment. Early-onset cataract is common, with a characteristic lamellar wedge-shaped lens opacity occurring symmetrically in both eyes, reflecting the embryologic abnormality in this syndrome.[23,25] Patients are usually highly myopic with peripheral retinal thinning and retinal breaks, including giant retinal tears. In Type I Stickler syndrome, the vitreous gel is typically optically empty with the presence of a fibrillar retrolenticular membrane extending to the pars plana and the peripheral retina. In Type II Stickler syndrome, vitreous changes present are beaded condensations in the retrolenticular space, with peripheral lattice degeneration and perivascular pigmentation.

RRD is the most serious ocular complication of Stickler syndrome and may occur early in life. Eight percent of affected children have RRD between the ages of 0 and 9 years and 26% between the ages of 10 and 19 years.[23,26]

The incidence of RRD varies between different reports and ranges between 10% and 73%.[23,25,27-29] There is a propensity for giant retinal tear formation [Figure 1], but a spectrum of retinal breaks may be seen.[18,29,30]

A detailed examination of both eyes is mandatory in patients with Stickler syndrome, with the need to consider prophylactic treatment of high-risk peripheral retinal pathology in the fellow eye. Fellow eye examination may reveal lattice degeneration, pigmentary retinopathy, retinal holes, or RD. Bilateral RDs are common and range from 39% to 51%.[18,27,29,31]

Ang *et al*., 2008[27] did a large retrospective study on 204 Type I Stickler syndrome patients and concluded that prophylactic treatment in the eyes unaffected by RD (either unilateral or bilateral 360° cryotherapy applied to the post-oral retina) reduced the risk of developing a retinal detachment. They published a statistically significant difference in the incidence of RD in patients with Type I Stickler syndrome without prophylaxis (73%, 81 of 111) versus failure of prophylaxis in patients with bilateral cryotherapy (5 of 62 [8%]) and patients with unilateral cryotherapy (3 of 31 [10%]). However, this approach is unconventional and based on one study. We prefer to carry out prophylactic treatment only to high-risk lesions such as lattice degeneration.

Finally, screening the family members of Stickler syndrome patients is also an important strategy to identify other affected members for prophylaxis or early treatment.

Marfan syndrome

Marfan syndrome is an autosomal dominant disorder that involves the ocular, cardiovascular, and musculoskeletal systems. The genetic defect is found on the long arm of chromosome 15, known as fibrillin 1 gene. The pathogenesis lies in the defect in production of fibrillin, a glycoprotein that is an essential component of the microfibril assembly in the extracellular matrix. Microfibrils are essential in the deposition of elastin, which is present in the lens, zonules, and joint capsule.[1,32] Fibrillin is also found in ocular structures such as the lamina cribrosa, sclera, choroid, and Bruch's membrane.[33] The revised Ghent nosology is most widely used to diagnose this syndrome.[34]

Nonocular features

The cardiovascular manifestations include aortic dilatation and dissecting aneurysms. Mitral valve prolapse affects 60%–70% of patients.[35] Musculoskeletal features include tall stature (>95th percentile by age/race/sex), joint laxity, hyperextensible joints, arachnodactyly or long fingers, dolichostenomelia or long limbs, scoliosis, pectus deformities of the anterior chest wall, congenital contractures of the digits and elbows, and generalized osteopenia.[36]

Ocular features

Nontraumatic ectopia lentis [Figure 2] is the most common ocular presentation in Marfan syndrome and is seen in 50%–80% of patients.[37,38] The subluxation is usually towards the superotemporal meridian. Patients usually have poorly dilating pupils and iris transillumination defects. Axial myopia is common, and Maumenee[37] found that 21% of eyes had myopia of 7 diopters or more.

Retinal detachment occurs in 5%–11% of these Marfan patients and increases to 8%–38% in those who have ectopia lentis or who have undergone cataract surgery.[37-39] Most develop RD at a young age.[37] In a large series, it has been reported that 70% of 160 patients with RD were below the age of 20 years. Bilateral RD is common and may reach 70%.[40,41]

Due to the high incidence of bilaterality, careful evaluation and monitoring of the fellow eye is

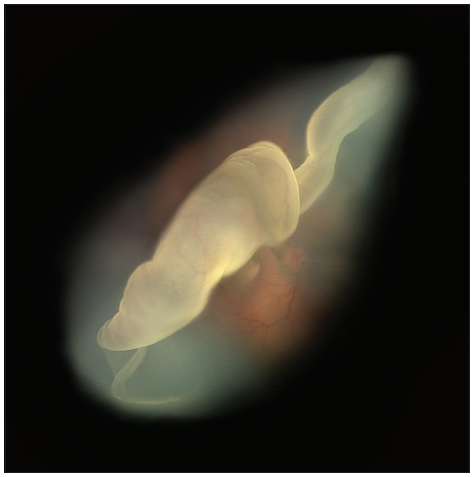

Figure 1: Giant retinal tear in a patient with Stickler syndrome

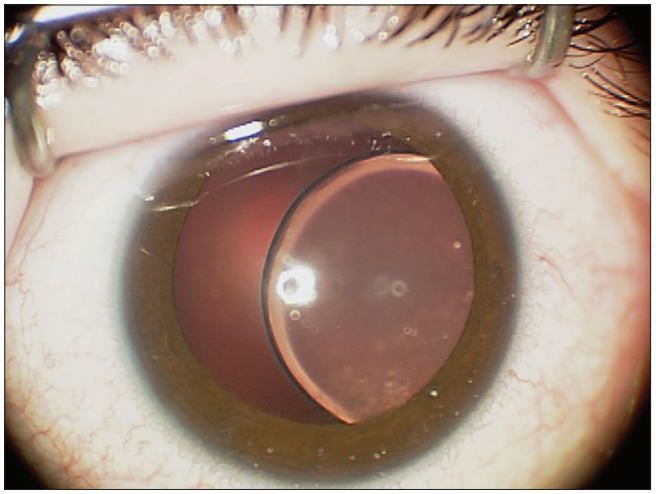

Figure 2: Ectopia lentis in a patient with Marfan syndrome

recommended and prophylactic treatment may be justified.[41] Patients with Marfan syndrome tend to have more complex RD including giant retinal tears. The main difference between patients with Marfan syndrome versus Stickler syndrome is that the congenital vitreous anomaly seen in Stickler syndrome is absent. The pathogenesis of RD in Marfan syndrome is related to posterior vitreous detachment. The incidence of detachment is related to the level of myopia, and these patients have vitreous degenerative changes similar to that found in myopic eyes.[37,42] Lens subluxation and lens extraction are also risk factors for developing RD.[38]

Retinal detachments in Marfan syndrome can be a surgical challenge. Special considerations include a poorly dilating pupil and subluxed lens that can sometimes limit visualization and assessment of the retina. In small pupils, iris retractors may be of benefit. In eyes with minimal lens subluxation and well-dilated pupils, the RD can be successfully repaired using standard scleral buckling techniques. However, complex RDs with severe lens subluxation are better managed with pars plana lensectomy, vitrectomy, and endotamponade using long-acting gas or silicone oil, with or without scleral buckling. With current advanced surgical techniques, visualization, and illumination systems, the anatomic success rates reported for repair of RDs in Marfan syndrome are comparable with non-Marfan eyes at 75%–86%.[40,41]

Choroidal coloboma

Coloboma of the choroid is a rare condition occurring in only 0.14% of the general population[43] [Figure 3]. The prevalence of RRDs in this group of eyes has been reported to be 23%–40%.[44,45]

A choroidal coloboma is caused by incomplete closure of the embryonic fissure at the 7th week of gestation. It may also be associated with colobomas of the eyelid and iris. Histologically, the choroidal coloboma area is deficient in the normal choroid, retinal pigment epithelium (RPE), and retina. The retina splits into two layers near the margin of the coloboma; the inner neuroblastic layer shows central continuation of the intercalary membrane (ICM) to the coloboma, whereas the outer neuroblastic layer turns back, becomes disorganized, and fuses with the RPE. The retina gradually thins into the ICM, with a high chance of breaks in the ICM developing along the edge of the coloboma or towards the center.[46,47] Retinal breaks within such abnormal tissue are hard to identify because of the lack of contrast. With the use of optical coherence tomography, RRDs in colobomatous eyes have been found to be most commonly caused by a combination of a break in the ICM with the presence of communication between the sub-ICM space and the subretinal space[46-48] [Figure 4].

Repair of these coloboma-associated RDs remains a surgical challenge to date, especially if the optic nerve is involved and if there are associated ocular anomalies such as microphthalmia, cataract, or lens coloboma.[49] In retinal detachments occurring in a colobomatous eye that do not involve the area of the coloboma, surgical repair principles are the same. Several operative techniques of coloboma-associated RD have been described.

Previously, Wang and Hilton[49] advised buckling the margin of the coloboma with two radial buckles. Patnaik and Kalsi[50] reported success in a patient in which they buckled the entire coloboma. However, with the advent of small gauge pars plana vitrectomy, most coloboma-related RDs are now repaired via the intraocular approach. The identification of breaks in the ICM is easier with intraocular visualization during pars plana vitrectomy.[51] Direct closure of the breaks with cyanoacrylate glue has been described.[52] However, in most cases, direct closure is not possible. Glue is not effective in a split or atrophied ICM as only the inner layer of the schisis will be sealed and progressive atrophy may enlarge the hole as the ICM contracts. The best approach, therefore, would be to isolate the coloboma from the rest of the retina.[48]

The same principles of retinal detachment repair apply. Both meticulous removal of vitreous attachments and incision of the ICM to weaken it are important steps to relieve traction on the break within the ICM. Laser retinopexy can then be applied around the coloboma margin to create a border of chorioretinal adhesion. It is difficult to create chorioretinal adhesion directly around holes in the ICM as the choroid and RPE are usually absent. After creating a circumferential barrier of chorioretinal adhesion, endotamponade with gas[53] is preferred as silicone oil[51,54] has the potential risk of getting into the subretinal space through the colobomatous defect.

In eyes where the coloboma involves the optic nerve, peripapillary endolaser photocoagulation through the papillomacular bundle may result in laser-induced retinal nerve fiber layer damage, leading to poor visual improvement even with retinal reattachment.[55] In these eyes, underlying amblyopia also limits functional recovery. McDonald *et al*.[55] suggested that postoperative laser treatment through the papillomacular bundle may be preferable. However, this is not easily performed in the clinic, and recurrent RD can occur.

Exudative Retinal Detachments

Coats disease

Epidemiology and clinical presentation

Coats disease is an idiopathic retinal vascular disorder, characterized by retinal telangiectasia and aneurysms

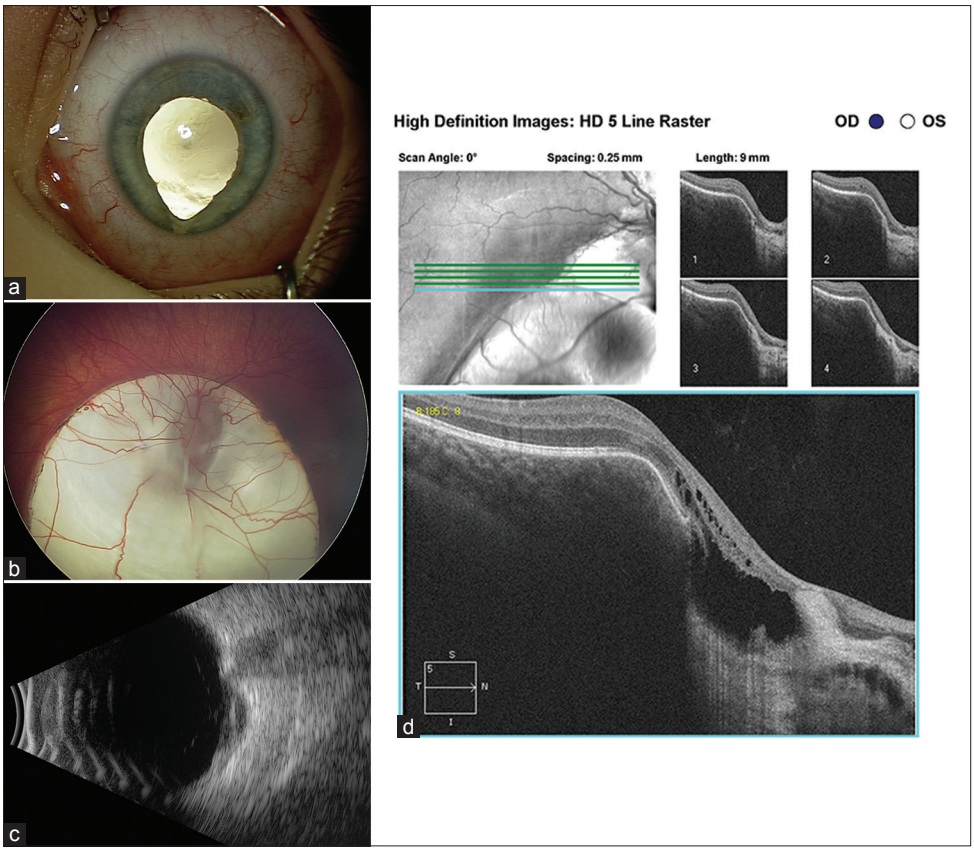

Figure 3: (a) Iris coloboma with inferior key-hole defect, (b) retinochoroidal coloboma involving the optic disc, (c) choroidal coloboma on B-scan ultrasound is seen as an excavation, (d) optical coherence tomography scan through the edge of the choroidal coloboma demonstrating schisis with intraretinal fluid

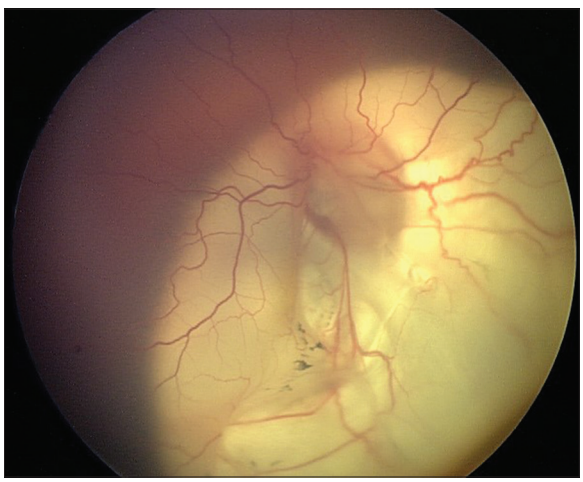

Figure 4: Choroidal coloboma involving the optic disc with retinal detachment

that can progress to intraretinal and subretinal exudation, with later development of exudative RD.

This disease was first described by Coats in 1908,[56] a curator of the Royal London Ophthalmic Hospital. Dr. Coats observed that the disorder had a slow and insidious onset and occurred most frequently in one eye of otherwise healthy boys. The main findings were raised patches of flocculent, yellow-white exudates, usually in the posterior pole, and always beneath retinal vessels. Telangiectatic and aneurysmal changes seen in the retinal vessels were often described as "light-bulb telangiectasia."[57,58] Microscopically, vascular anomalies, retinal hemorrhage, cystic retinal degeneration, and subretinal accumulations of fibrous tissue were seen. The disease was seldom quiescent and progressed slowly to exudative RD, cataract, glaucoma, and phthisis bulbi. Although largely thought to be idiopathic, there have been more recent findings that demonstrate a relationship between Coats disease and NDP gene mutations, associated with Norrin deficiency.[59]

In a population-based study in the United Kingdom, Morris *et al*.[60] estimated the population incidence to be 0.09/100,000. All cases were unilateral and 85% were male. A large retrospective consecutive case series of 150 patients in the USA conducted by Shields *et al*.[61] found that Coats disease was diagnosed at a median age of 5 years (range, 1 month to 63 years), occurred mainly in males (76%, 114 of 150), and was unilateral in 95% (142 of 150 patients). There was no predilection for race or laterality. The most common referral diagnoses were Coats disease in 64 cases (41%) and retinoblastoma in 43 (27%). The first symptom or sign was decreased visual acuity in 68 cases (34%), strabismus in 37 (23%),

and leukocoria in 31 (20%). Thirteen patients (8%) were asymptomatic. Visual acuity at presentation was poor in most, ranging from 20/200 to no light perception in 121 eyes (76%). The anterior segment was normal in 142 eyes (90%).

Posterior segment findings in patients with Coats disease include retinal telangiectasia, intraretinal exudation, exudative RD, retinal macrocysts, retinal hemorrhage, vasoproliferative tumor, optic disc, and retinal neovascularization.[62] Shields *et al*.[62] further classified Coats disease into five stages [Table 1 and Figure 5].

The variability of symptoms in Coats disease means that the clinical presentation can be similar to several other ophthalmic conditions. The most important lesion to be ruled out is retinoblastoma as it is the most common primary intraocular malignancy in children and can be fatal when left untreated. Coats disease misdiagnosed as retinoblastoma has also been reported to be the most common cause of wrongful enucleation.[61]

Other common differential diagnoses that should be considered include familial exudative vitreoretinopathy (FEVR), hemangioblastoma von Hippel, pars planitis, and incontinentia pigmenti, which are more often bilateral, as well as ocular toxocariasis and persistent fetal vasculature (PFV), which tend to be unilateral.[63]

Diagnostic modalities

In majority of cases, it is possible to reach a diagnosis clinically; however, in some, ancillary investigations may be useful, including fundus fluorescein angiography (FFA), B-scan ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI).

FFA plays an important role in both diagnosis and monitoring of disease progression. Retinal telangiectasias cause early hyperfluorescence with leakage and exudation causes blocked fluorescence. Aneurysmal dilatations will be visible as "light bulb" telangiectasia. Areas of retinal ischemia will show hypofluorescence or capillary dropout[61,64] [Figure 6].

Table 1: Shields classification of Coats disease

Stage 1	Retinal telangiectasia only
Stage 2	Telangiectasia and exudation
-2A	-Extrafoveal exudation
-2B	-Foveal exudation
Stage 3	Exudative RD
-3A	-Subtotal RD
-3B	-Total RD
Stage 4	Total RD and glaucoma
Stage 5	Advanced end-stage disease

RD=Retinal detachment

B-scan ultrasonography can be useful as a diagnostic tool in eyes with a poor view of the retina. Typical features of Coats disease on ultrasound are subretinal opacities due to cholesterolosis present from the exudates, as well as retinal detachment.[65] Most critically, it can be used to rule out retinoblastoma, which is typically seen as a hyperechoic tumor with an irregular outline, and often with calcium deposits, which are seen as highly reflective foci within the tumor [Figure 7].

A CT scan of the orbits is also useful to rule out retinoblastoma as it can visualize solid tumors and calcifications. However, this modality of screening is controversial in children due to the radiation exposure, and not all patients with retinoblastoma present with calcified tumors. It should be noted that there have been reports of a submacular calcified nodule forming in up to 20% of eyes with advanced Coats disease.[66]

An MRI scan of the orbits is very useful in the diagnosis of advanced Coats disease but may have less use during the initial stages. MRI is superior to CT in ruling out retinoblastoma as the difference between subretinal exudation and a solid mass is clearer on MRI.[67] Specifically, the exudate in Coats disease is hyperintense, on both T1-weighted and T2-weighted MRI, whereas in retinoblastoma, a T1-weighted image will show a hyperintense mass, but T2-weighted image shows a hypointense mass.[68]

Figure 5: (a and b) Coats disease Stage 2 – retinal telangiectasia and exudation

Management

The main treatment goal in Coats disease is to preserve vision and the globe, by eradication of all abnormal vasculature and areas of non-perfusion to reduce further exudation and retard the progression of the disease.

Patients with Stage 1 disease are usually observed. In Stage 2 disease, the aim is to directly ablate the retinal telangiectasias and aneurysms by laser or cryopexy to reduce further exudation and induce resorption of exudates.[69] Favorable outcomes are more likely in early stages where 1–2 retinal quadrants are involved and in cases where treatment can be applied over areas of vascular, rather than exudative changes.[70] Multiple laser photocoagulation treatments are often needed to contain the vascular activity completely,[62,69] and recurrences may be seen over a decade after successful treatment.[62] A population-based prospective study performed across the United Kingdom in 2010[71] showed that up to 92% of patients with Coats disease are managed with laser photocoagulation, with cryotherapy being used mainly as a second-line or as an adjunctive treatment.

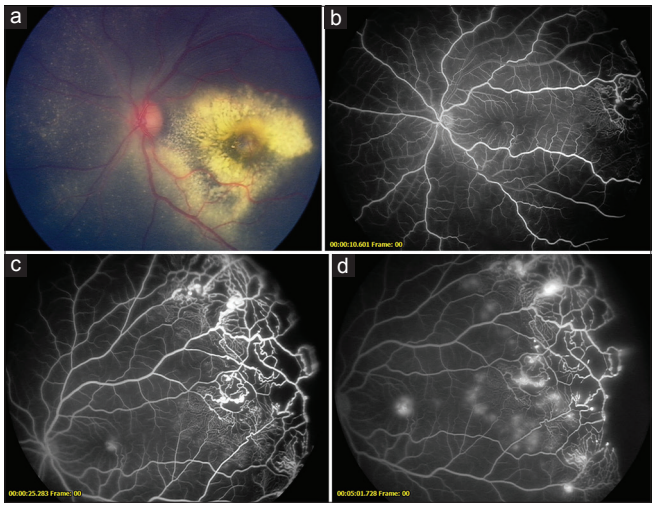

Figure 6: (a) Coats disease stage 2 – Fundus photograph of extensive posterior pole exudates. Fundus fluorescein angiography of early (b), mid (c), and late (d) phases showing retinal light bulb telangiectasia, leakage, and retinal ischemia/capillary fallout

In patients with more advanced disease (Stage 3 and 4), no gold standard treatment currently exists. If the retinal detachment is shallow, laser photocoagulation and/or cryotherapy may be performed alone. Laser photocoagulation is applied directly to the telangiectatic vessels in areas with little or no subretinal fluid (SRF). Cryotherapy is occasionally added, using a double freeze-thaw method, where the lesion is too thick for laser treatment, or the detachment is shallow enough to allow approximation of the cryoprobe to the telangiectasia using scleral indentation.[62] Cryotherapy applied to more than two quadrants can increase the exudative process (ablatio fugax); therefore, it is advisable not to apply cryotherapy to more than two quadrants in one treatment session.[62] Other complications of cryotherapy include posterior subcapsular cataract and proliferative vitreoretinopathy.

In eyes with more extensive retinal detachment in which laser or cryotherapy alone would be ineffective, surgical repair of the RD may be combined with laser photocoagulation or cryotherapy. Initial reattachment of the retina to the RPE may be achieved via external drainage of SRF. Ablation of abnormal telangiectatic vessels can then be carried out once SRF is drained.[69,72]

Adam *et al*.[73] recommended a surgical approach of "less is more" in patients with extensive exudative RD. They treated patients with minimally invasive surgery that involved establishment of a pars plana vitreous infusion line of balanced salt solution, external drainage of SRF

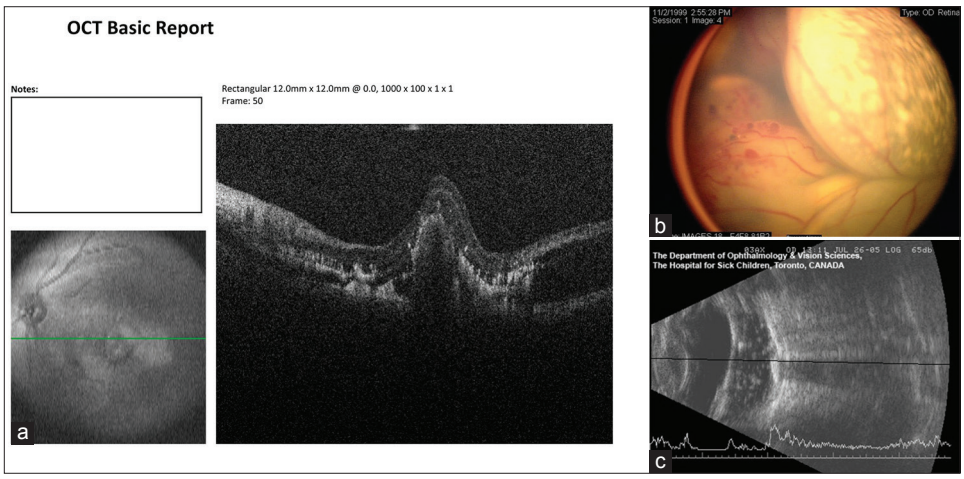

Figure 7: (a) Coats Stage 3A – optical coherence tomography through the posterior pole demonstrating subretinal exudates with partial exudative detachment, (b) Coats Stage 3B – total exudative retinal detachment, (c) exudative retinal detachment seen on B-scan ultrasound with hard exudates appearing as hyperechoic densities within the detachment

via a posterior sclerotomy, and cryopexy of retinal telangiectasia with a double freeze-thaw technique. This approach was first described by Harris in 1970[57] and has since been reported in several other papers with the addition of a vitreous infusion to the procedure as described.[62,74] Several authors have reported more invasive techniques, including vitrectomy, posterior retinotomy, use of intraocular silicone oil or gas, and scleral buckling in advanced Coats disease.[69,75,76] However, in their experience, Adam *et al*.[73] found that these more complex and invasive techniques did not enhance anatomical and functional outcomes in patients presenting with advanced disease and poor vision.

Despite treatment to ablate the vascular anomalies and induce resorption of SRF, Stage 3 disease often progresses to Stages 4 and 5. In advanced end-stage Coats disease (Stage 5), the aim of treatment is to maximize useful vision, ensure comfort, and preserve cosmesis. Macular damage from ischemia or significant exudation is often irreversible at this stage, and visual potential is severely limited. In patients with a painless eye, observation is usually recommended. Often, patients develop rubeosis iridis and neovascular glaucoma, leading to a painful blind eye.[57] In these cases, transscleral diode cyclophotocoagulation may be carried out, and occasionally, evisceration or enucleation is necessary.

Recently, intravitreal triamcinolone and anti-vascular endothelial growth factor (VEGF) agents have also been used as adjuvant therapy to improve anatomic and visual outcomes. Othman *et al*.[77] demonstrated an improvement in visual acuity as well as resorption of SRF and macular exudates in 15 consecutive patients treated with intravitreal triamcinolone in combination with laser photocoagulation and/or cryotherapy. However, the use of intravitreal triamcinolone has been restricted largely due to the common side effects of cataract formation and glaucoma.

The role of VEGF in the pathogenesis of Coats disease and the development of vascular abnormalities were noted in 2007 by Sun *et al*.,[78] who observed elevated VEGF levels in a young male with Stage 4 Coats disease. Kase *et al*.[79] later hypothesized that VEGF could have a role in the pathogenesis and progression of the disease not only by inducing vascular abnormalities but also by contributing to exudation.

In early disease, anti-VEGF treatment alone has been described with good results.[80] However, in more advanced stages of the disease, anti-VEGF treatment alone has transient efficacy.[81] Combination therapy with laser photocoagulation and/or cryotherapy has been described in patients with early (Stages 1 and 2) as well as advanced (Stages 3 and 4) Coats disease with treatment success. As an adjunctive treatment, it seems to reduce macular edema and exudates, improve or even stabilize visual acuity, and enhance the regression of abnormally dilated vessels.

Lin *et al*.[82] administered intravitreal bevacizumab followed by cryotherapy of vascular abnormalities in a patient aged 6 months and with Stage 3B Coats disease. This resulted in resolution of the exudative RD and subsequent partial resolution of the exudation at 1 year. Another group reported the combined use of intravitreal bevacizumab with laser photocoagulation in two patients aged 2 and 7 years with Stage 4 disease. This resulted in reduced exudation and posterior pole retinal reattachment at 6 months.[83]

Stanga *et al*.[84] recently published a retrospective case review of eight eyes in eight children with advanced Coats disease presenting with total or subtotal RD. All eyes initially underwent transscleral drainage of exudative SRF followed by 1–2 intravitreal injections of bevacizumab and laser photocoagulation. Patients were followed for up to 60 months. In all eyes, subretinal fluid was completely eliminated after surgical drainage and intravitreal bevacizumab, with resolution of subretinal exudates and total retinal reattachment after laser treatment. They suggested that this therapeutic approach is successful in treating patients with advanced exudative detachment in Coats disease without the need for vitrectomy.

The benefits of anti-VEGF therapy, however, must be weighed against the possible risks and its limited effect. Ramasubramanian and Shields[85] advised caution with the use of bevacizumab after the development of vitreoretinal fibrosis in four of the eight patients treated with cryotherapy and intravitreal bevacizumab injection, with three eyes progressing to tractional RD.

Tractional Retinal Detachments

Persistent fetal vasculature

Clinical presentation

Persistent fetal vasculature (PFV) is a term used to describe a set of congenital vascular malformations in which different components of the intraocular fetal vasculature persist after birth. Most are sporadic but can be inherited as an autosomal dominant or recessive trait.[86] These variants include persistent pupillary membrane, iridohyaloid vessels, Mittendorf dot, the vasa hyaloidea propria, muscae volitantes, the hyaloid artery, Bergmeister papilla, congenital nonattachment of the retina, macular hypoplasia and dysplasia, optic nerve hypoplasia and dysplasia, and malformations in the shape and size of the cornea and globe.[87]

These PFV malformations may be divided into three categories: anterior, posterior, or both based on the anatomical location of the vascular malformations. In anterior PFV, the most common features include retrolental fibrovascular membrane, elongated ciliary processes, cataract, and microphthalmia. In posterior PFV, clinical features include vitreous membrane and stalk, retinal fold, congenital nonattachment of the retina, hypoplastic optic nerve and macula, and microphthalmia[87] [Figure 8].

Congenital non-attachment of the retina associated with PFV has also been called congenital retinal septum,[88] ablatio falciformis congenita,[89] or posterior persistent hyperplastic primary vitreous as it is most commonly known.[90,91] This is a specific type of tractional retinal detachment that is present at birth, after which it may or may not be progressive.[90] Spontaneous reattachment is rare. Histological studies have shown that it is caused by traction from persistent components of the fetal intraocular vasculature and possibly by neuroectodermal components of the primary vitreous.[92]

The primary pathogenesis is adhesion to and lack of separation of the primary vitreous and its blood vessels from a portion of the inner layer of the developing optic cup. The secondary vitreous is unable to form, and traction from adherent persistent fetal vasculature then causes RD.[87]

Primary malformations of the macula in posterior PFV include hypoplasia and dysplasia with failure of development of the foveal pit.[93,94] Secondary degenerative events may also cause macular dysfunction, including cyst and hole formation, pigmentary changes, and schisis.[89,95] Traction from posterior components of the primary vitreous is a common cause. Occasionally, the macula may be normal [Figure 9].

Primary malformations of the optic nerve head include hypoplasia and dysplasia, of which the pathogenesis is still unclear.[94,96] Secondary changes include mild-to-marked tractional deformations.

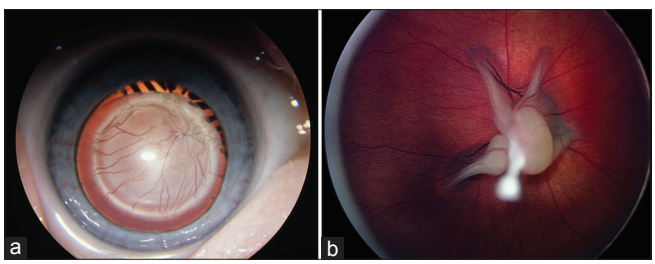

Figure 8: (a) Anterior persistent fetal vasculature showing retrolental fibrovascular membrane and elongated ciliary processes, (b) Posterior persistent fetal vasculature

Bilateral PFV or congenital non-attachment of the retina can also occur in association with a systemic disease, e.g., Norrie disease or Walker–Warburg syndrome. In these patients, severe primary undifferentiation of the neurosensory retina is characteristic.[97,98]

Differentials of tractional retinal detachment in infants or children include FEVR, Norrie disease, incontinentia pigmenti, and retinoblastoma. Direct visualization of any component of the fetal vasculature is the best clue to diagnosing an anomaly associated with PFV correctly. PFV is typically unilateral. The implantation of the stalk is usually to the central posterior lens capsule, whereas in FEVR, Norrie disease, and incontinentia pigmenti, there is no stalk but rather a fold that usually runs to the temporal ora serrata. Retinoblastoma eyes are rarely microphthalmic and will have a mass with possible calcifications on ultrasound or CT scan of the orbits.[99]

The natural history of severe forms of PFV is progression of fibrovascular dysplasia, leading to angle closure glaucoma, opacification of the cornea, cataract, intraocular hemorrhage, retinal detachment, and phthisis bulbi.[87,98]

Surgical techniques

Indications for surgery include the presence of amblyogenic media opacity, progressive glaucoma secondary to angle closure, vitreoretinal traction, and RRD or progressive tractional RD. The aim of surgery is to clear any amblyogenic media opacity (cataract, hemorrhage) and relieve posterior vitreoretinal traction.

The decision to operate and preoperative counseling of outcomes should take into consideration a few factors – visual potential determined by the presence of congenital anomalies of the macula and optic nerve, cerebral function, patient age (duration of visual deprivation), and unilaterality or bilaterality.

Visual outcomes are largely dependent on anatomic outcomes and cortical visual development. Factors associated with poorer visual prognosis and lower chance of achieving form vision (defined as counting fingers, fix-and-follow, or better) include the presence of a significant component of posterior PFV, bilaterality, and microphthalmia.[100]

Certain study groups have advocated that earlier surgery can result in improved visual function. Bosjolie and Ferrone[101] suggested that a period of retinal "physical plasticity" extends to at least 13 months of age and advocate for consideration of early vitrectomy in children with tractional RD and posterior PFV. In their study, all 10 patients who had surgery at 13 months of age or younger had

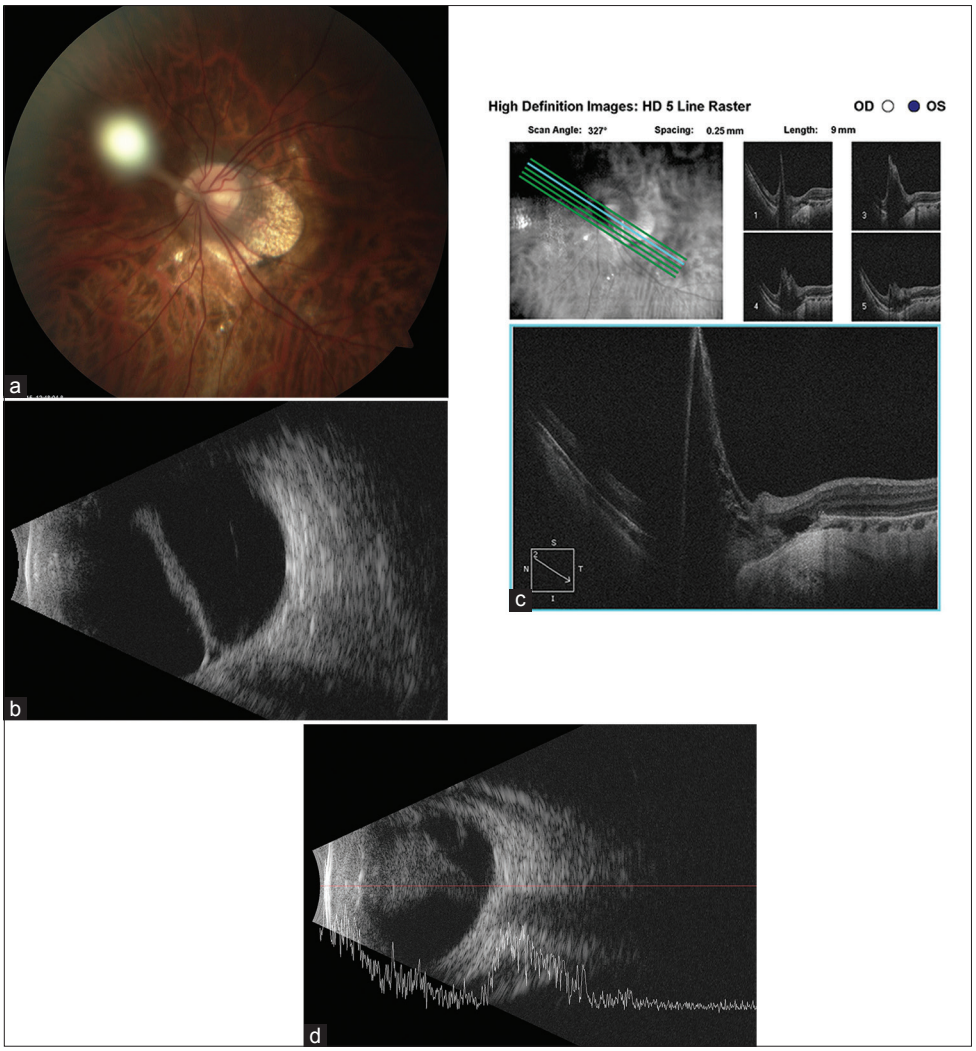

Figure 9: (a) Persistent posterior hyaloidal vessels extending from the disc to the lens, (b) B-scan ultrasound demonstrating the persistent posterior hyaloidal stalk, (c) Optical coherence tomography through the nerve and peripapillary retina showing traction from hyaloidal vessels causing mild tractional retinal detachment, (d) Advanced persistent fetal vasculature with closed funnel tractional retinal detachment

reattachment of the retina with reversal of retinal dragging and decreased retinal folds. Notably, 9 of 10 patients were younger than 6 months of age at the time of surgery. Sixty percent had functional vision of 20/800 or better. This favorable functional visual result may be related to the development of vision after early intervention and early amblyopia treatment.

Vitrectomy with or without lensectomy is the surgery of choice to treat posterior PFV. For vitrectomy, the anterior translimbal approach is preferred by some compared to the posterior pars plicata/pars plana approach. This is an important consideration in microphthalmic eyes as the ora serrata may be anteriorly displaced, the pars plana may be absent, or the anterior retina may insert directly onto the pars plicata or ciliary body.[102,103] In PFV, the peripheral retina and ciliary body may also be dragged anteriorly and centrally, increasing the risk of iatrogenic injury to these structures.[104,105]

Some however advocate the posterior pars plicata approach to vitrectomy and lensectomy.[103,106,107] This approach with earlier transection of the persistent hyaloid stalk may result in reduced disturbance of the cornea and anterior chamber angle, more complete removal of the lens cortex, and reduced anterior traction on the posterior retina. Control of bleeding of the transected fetal vessels is critical, and this can be achieved with intraocular diathermy. Traction on the ciliary body can be relieved with meticulous excision of the retrolental tissue and with radial cuts between the centrally dragged ciliary processes.

In eyes with non-axial lens opacification, Shaikh and Trese[108] recommended dividing the stalk immediately on entry. After division of the stalk with hemostasis, vitreous is then removed with peeling of epiretinal membranes in the posterior pole. The authors believed that manipulation of the stalk by vitrectomy and

diathermy before division can damage the lens capsule with resultant cataract formation.

Regardless of technique, maximum visual rehabilitation requires early surgery (during the critical period of visual development) and aggressive postoperative management of amblyopia.

Rhegmatogenous/Exudative/Tractional Retinal Detachments

Familial exudative vitreoretinopathy

Familial exudative vitreoretinopathy (FEVR) is a hereditary bilateral retinal vascular disorder first described by Criswick and Schepens in 1969.[109] The most common mode of inheritance is autosomal dominant[110] although X-linked recessive and sporadic cases have also been reported.[111] FEVR patients have a mutation in the Norrie disease gene. The mutation results in dysregulation of the Wnt-receptor: β-catenin pathway and has been associated with increased levels of VEGF. This explains the lifelong chronic nature of FEVR, characterized by exacerbation of exudation secondary to upregulated vascular activity.

FEVR is sometimes not recognized as it can resemble other ocular conditions, depending on the patient's age and the stage of the disease. The phenotype of FEVR resembles a forme fruste of ROP, occurring in a larger and often term infant, without a history of low birth weight or oxygen supplementation. The primary abnormality is a cessation of peripheral vascular growth with subsequent abnormal angiogenesis.[112,113] Systemic associations are absent.

The clinical classification is based on five stages [Table 2].[114] Pendergast and Trese[114] divided eyes into groups according to severity of disease and the presence of and extent of RD, and further divided RD into those with a predominantly effusive (exudative) or predominantly tractional component.

Patients usually present with decreased vision in one or both eyes, strabismus, or are asymptomatic and the condition discovered on screening families of known patients. Clinical findings include pseudoexotropia secondary to macular ectopia, posterior subcapsular cataract, neovascular glaucoma, band keratopathy, and a peripheral zone of avascular retina. The peripheral zone of avascular retina is pathognomonic of FEVR.[115,116] This leads to peripheral retinal neovascularization, peripheral retinal traction with temporal dragging, falciform folds, retinal detachment, and lipid exudation[1] [Figure 10].

FEVR tends to be a variably progressive disorder, with detachments often occurring only in the first or

Table 2: Clinical classification of familial exudative vitreoretinopathy

Stage 1: Avascular retinal periphery without extra-retinal vascularization
Stage 2: Avascular retinal periphery with extra-retinal vascularization
Without exudate
With exudate
Stage 3: Retinal detachment: Subtotal, not involving fovea
Primarily exudative
Primarily tractional
Stage 4: Retinal detachment: Subtotal, involving fovea
Primarily exudative
Primarily tractional
Stage 5: Retinal detachment, total
Open funnel
Closed funnel

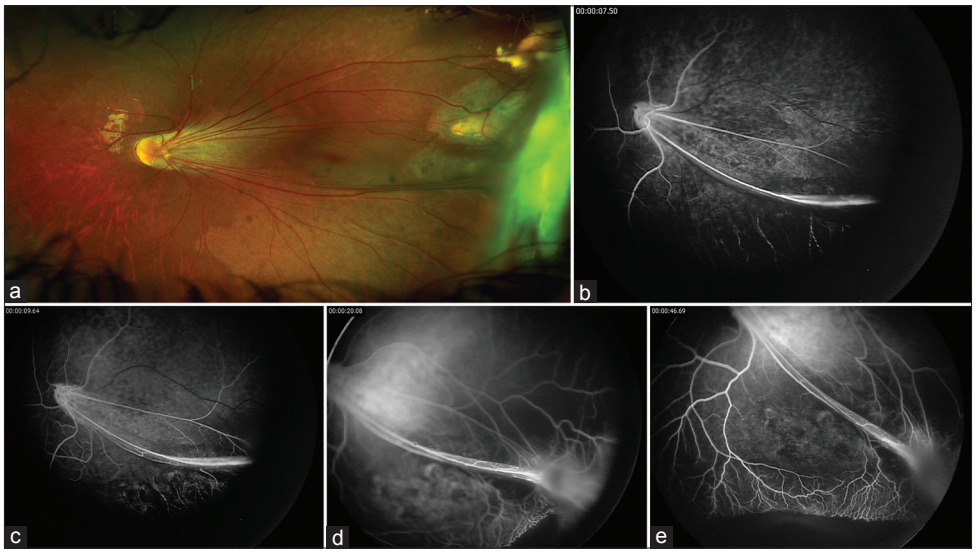

Figure 10: (a) Familial exudative vitreoretinopathy – Wide field photograph showing peripheral exudation and traction with dragged disc, (b-e) Fundus fluorescein angiography of early, mid, and late phases demonstrating disc and peripheral retinal leakage with a zone of avascular peripheral retina

second decade of life. When adulthood is reached, the retinal manifestations may remain stable.[112,117] Besides exudative RD and tractional RD from peripheral neovascular fibrous membranes, RRD may also occur in FEVR and most commonly from atrophic holes.

The management of FEVR is similar to that for ROP. Laser retinopexy or cryopexy is recommended to treat retinal holes to prevent RRD, and to treat the avascular retinal periphery to reduce subretinal and intraretinal exudation, especially secondary exudation at the macula. Laser photocoagulation is the preferred prophylactic modality, and cryotherapy is reserved for patients with hazy media and poorly dilated pupils.[1]

Anti-VEGF therapy may provide a valuable adjunctive treatment for FEVR. One study published successful reduction in exudation with intravitreal injection of pegaptanib sodium (Macugen; 0.3 mg/90 µl) in three children (aged 6–14 years) with persistent vascular activity and increasing exudation, despite aggressive laser photocoagulation and cryotherapy. However, two children developed vitreous hemorrhage due to increased traction and needed pars plana vitrectomy.[118] Another case reported by Tagami *et al*.[119] found rapid regression and accelerated fibrosis of neovascular tissues in a patient with FEVR after a single injection of bevacizumab, with no complications after 4 months of follow-up.

The surgical method of choice (vitrectomy, scleral buckle, or combined) depends on the type of detachment and the severity of PVR.[117] In tractional RD, scleral buckling or vitrectomy is indicated to release vitreoretinal traction. The vitreoretinal adhesions are so strong in the peripheral avascular retina that iatrogenic retinal breaks occur easily in vitrectomy. A bimanual technique with vitreous cutter and forceps is preferred by some in dissecting the vitreous membranes from the retinal surface. Dissection in the peripheral avascular area is difficult and prognosis is poor if dissection is not successful.[114,120] Patients who are symptomatic in the first 3 years of life also usually have poor visual prognosis. Many eyes develop tractional RD despite laser photocoagulation of the peripheral avascular retina. Vitreoretinal surgery can preserve some degree of vision, but amblyopia, reproliferation of tractional membranes, and vitreous hemorrhage may limit long-term visual improvement.[121]

Conclusion

The management of pediatric RD is often complicated, and sound surgical techniques combined with experience are keys to increased success. Compared to adults, surgical treatment usually entails a longer period of postoperative visual rehabilitation and requires close management with pediatric ophthalmologists in the treatment of associated amblyopia. Finally, managing the expectations of anxious parents and pediatric patients can be difficult but essential to ensure continued follow-up to enhance final surgical outcomes.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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