Clinical and surgical approach to retinoschisis

Shreya Swaminathan and Matthew R. Starr

Purpose of review
To summarize the recent literature on the clinical and surgical management of retinoschisis.

Recent findings
Novel analyses of the existing imaging modalities, including ultra wide-field imaging, near-infrared imaging, blue light reflectance, and color Doppler ultrasound, can be adjuncts to existing diagnostic tools such as ocular coherence tomography (OCT) and clinical examination to differentiate between rhegmatogenous retinal detachment (RRD) and retinoschisis.

Summary
Degenerative retinoschisis can be challenging to differentiate from a RRD through clinical examination. Although ocular coherence tomography (OCT) is the typical approach to diagnosing retinoschisis, there have been many promising diagnostic developments to better prognosticate and differentiate between similar entities. Given the difficulty in managing these cases, medical and surgical management are typically at the discretion of the treating physician.

Keywords
ocular coherence tomography, pars plana vitrectomy, retinal detachment, retinoschisis, scleral buckle

INTRODUCTION

Retinoschisis is a condition characterized by horizontal splitting of the retinal layers. There are various forms of retinoschisis including degenerative (also known as senile or acquired), x-linked juvenile, and secondary (associated with other disease entities such as epiretinal membranes, myopic maculoschisis etc.). In this review, we will mainly discuss the evaluation, clinical characteristics, and management of degenerative retinoschisis.

DEGENERATIVE, X-LINKED, AND SECONDARY RETINOSCHISIS

Degenerative retinoschisis is a condition characterized by the elevation of the inner layer of the peripheral retina, typically at the outer plexiform layer and adjacent nuclear layer. Split layers may be connected by septae composed of remnants of glial cells, axons, and dendrites [1▪]. The overall prevalence is about 3.9–7.1%, which increases with age. Although treatment is not required, affected eyes may progress to schisis-related retinal detachments, which may lead to worse visual prognosis than rhegmatogenous retinal detachment (RRD) [2▪]. Most cases are asymptomatic, however, monitoring for progression or retinal detachment is recommended [1▪].

X-linked juvenile retinoschisis (XLRS) is a bilateral, progressive condition caused by mutations to the retinoschisis (*RS1*) gene, leading to the splitting of retinal layers. Although this condition mainly affects male individuals, some female individuals may exhibit the condition due to skewed X-inactivation [3▪]. The prevalence of XLRS ranges from 1 in 5000 to 1 in 20 000. XLRS can manifest with varying degrees of progressive central vision loss, caused by radial streaks originating from foveal schisis and the splitting of inner retinal layers of the peripheral retina. Electroretinogram recordings have also noted defects in signal transmission from photoreceptors to bipolar cells, characterized by a reduction in b-wave amplitude. However, variability may be noted with different genotypes of XLRS [4▪].

Secondary retinoschisis can be caused by a variety of different conditions, impacting the organization of the retinal layers through different mechanisms. Vascular conditions such as proliferative diabetic retinopathy, retinopathy of prematurity or sickle cell retinopathy can lead to vitreoretinal traction leading to macular schisis [5]. Oncological malignancies such as malignant melanoma and choroidal hemangioma

Department of Ophthalmology, Mayo Clinic Minnesota, Rochester, Minnesota, USA

Correspondence to Matthew R. Starr, MD, 200 1st St SW, Rochester, MN 55905, USA. E-mail: Starr.Matthew2@mayo.edu

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KEY POINTS

- Although retinoschisis can be hard to differentiate from rhegmatogenous retinal detachment through clinical evaluation, the two entities should be differentiated to ensure prompt and appropriate treatment. Current research efforts have been directed towards improving diagnostic modalities to differentiate between the two entities.
- OCT is the traditional diagnostic tool used; however, recent research has focused on other diagnostic tools including ultra wide-field imaging, near-infrared imaging, blue light reflectance, and color Doppler ultrasound.
- Degenerative retinoschisis can result in two types of retinal detachments: schisis detachments and progressive retinal detachments.
- The management of schisis detachment ranges from observation to surgical repair. However, progressive retinal detachments must be repaired surgically.
- Although repair may result in anatomic success, the rate of re-detachment is much higher than in traditional RRD repair.

can lead to cystic degeneration of the retina that can form a retinoschisis cavity. Intraretinal hemorrhage from blunt trauma, shaken baby syndrome, and aplastic anemia or intraretinal exudation in conditions such as Coats' disease can also cause the retina to split. Rarely, inflammatory conditions such as chronic uveitis or pars planitis can contribute to the splitting of the retinal layers, typically seen in the macula [5]. It is important to note that retinoschisis may also occur as a rare complication of retinal surgery [6▪].

Stellate nonhereditary idiopathic foveomacular retinoschisis (SNIFR) is a disorder characterized by splitting at the level of the henle fiber layer, resulting in schisis confined to the outer retina. Notably, this condition is not associated with genetic, structural, inflammatory, or other identifiable causes. In contrast, XLRS presents earlier in life and has a distinct genetic pattern. Degenerative retinoschisis also differs from SNIFR as it is typically confined to the peripheral retina and rarely extends to involve the fovea. Differentiating SNIFR from other entities in clinically important, as patients with SNIFR are minimally symptomatic, maintain preserved visual acuity, and are generally managed conservatively with observation [7▪]. A more severe variant, known as central anomalous retinoschisis with midPEriphEral traction (CARPET), involves central neurosensory detachment and the formation of an outer lamellar macular hole. This leads to significant peripheral vitreoretinal traction. In contrast to typical SNIFR, CARPET may be associated with profound vision loss and progressive maculopathy, often necessitating surgical intervention to relieve vitreoretinal traction [8▪].

EVALUATION

Degenerative retinoschisis may resemble RRD on clinical examination. It is critical to perform a scleral depressed peripheral exam of the affected eye(s) and the contralateral eye. This may help identify any full thickness retinal breaks and differentiate the two conditions. Retinoschisis is typically bilateral, with no full thickness retinal breaks; however, retinoschisis may present with outer retinal breaks. Degenerative retinoschisis may present with microcystoid degeneration resulting in a smooth, transparent elevation of the inner retina. Retinal or iris neovascularization secondary to ischemia may also be noted [9▪]. White particles on the inner retina are indicative of degenerated Muller cell footplates, serving as a useful marker in identifying retinoschisis [10▪]. In contrast, during retinal detachment (RD), Muller cells may not only become reactive, contributing to fibrosis and inflammation, but also develop a white dot appearance [11,12]. The white dots associated with RRDs have been proposed as a sort of bread crumb trail leading to the occult break, while white dots associated with retinoschisis tend to be more diffuse and devoid of any occult retinal breaks. When laser photocoagulation is applied to the retina under a retinoschisis cavity, there will be a faint retinal whitening. However, in cases of RRD, there is typically no reaction. Additionally, the scotoma noted in retinoschisis is absolute, whereas in RRD, it is relative [13]. A thorough history and ocular examination can minimize the risk of missing secondary causes of retinoschisis.

Spectral-domain ocular coherence tomography (SD-OCT) is a useful tool for diagnosing degenerative retinoschisis, with a sensitivity of 94.6% in identifying schisis-associated cavities [2▪]. However, OCT may be limited by media opacity and an inability to visualize peripheral lesions. Newer developments that offer detailed cross-sectional imaging of the periphery, such as wide-field OCT, may be useful to detect peripheral schisis [14▪]. In a study comparing patients with macula-on RRD and peripheral retinoschisis by Patel *et al.*, central choroidal thickness (CCT) was used to differentiate the two entities. A thick CCT was significantly associated with peripheral retinoschisis and a thin CCT was associated with macula-on RRD, suggesting that CCT measurements may help differentiate between these two similar retinal pathologies [15▪]. Cases affected by media

opacity may be able to be diagnostically clarified by B-scan ultrasound and ultrasound biomicroscopy [9▪]. Near-infrared imaging, an imaging modality commonly performed during the first step of SD-OCT, has been proposed to distinguish RRD from retinoschisis as the protein accumulation in intraretinal fluid creates a unique scatter of the light [16].

Degenerative retinoschisis tends to appear iso-autofluorescent on autofluorescent imaging, while retinal detachments are often hypoautofluorescent. Recent studies have highlighted the use of ultra-widefield pseudocolor and green separated images in their evaluation of patients with degenerative retinoschisis. A study by Orr *et al.* [1▪] describes a novel reticular pattern of the neurosensory retina noted on the green separated image of eyes with retinoschisis, but not pseudocolor imaging. Shorter wavelengths of ultra-widefield imaging have been shown to better visualize the elevation and cystic spaces from retinoschisis [17▪].

Blue light reflectance is another novel method to differentiate between RRD and retinoschisis, particularly in cases of early disease or minimal retinal pigment epithelium (RPE) pigmentation. Retinoschisis presents with multiple hyporeflectant oval or elliptical lesions over the elevated area of the inner retinal layer, creating a 'honeycomb' pattern. This pattern is caused by the irregular composition of the inner retinal layer as some retinal reflectance is preserved from portions of the inner retinal layer staying attached. In contrast, outer layer breaks appear as well defined hyporeflectant areas, irrespective of RPE pigmentation. Retinal tears can be identified easily by the hyporeflectance associated with the absence of reflective tissue with this method allowing for retinoschisis to be differentiated from RRD [18▪].

A prospective study by Paris *et al.* investigated the use of color Doppler ultrasound (CDUS) and contrast-enhanced ultrasound (CEUS) as an adjunct to OCT and ultrawide field imaging. Their results highlighted features specific to RD and retinoschisis on both CDUS and CEUS. CDUS depicted a lack of Doppler flow in retinoschisis, higher and longer cavities in acute RD, and thicker membranes in acute and chronic RD. In cases of acute RD, CEUS shows florid microbubble contrast enhancement. CDUS and CEUS may serve as additional diagnostic tools when visualization with OCT is limited [2▪].

RETINAL DETACHMENTS SECONDARY TO RETINOSCHISIS

The majority of degenerative retinoschisis cases without RD are asymptomatic. Retinoschisis is more likely to lead to tears of the inner retina than the outer retina. Tears of the outer retina decrease the risk of RRD, whereas the risk of RRD increases with tears in both the outer and inner retinal layers. Degenerative retinoschisis causes 0.05–2.5% of RRDs [19▪]. RRDs associated with degenerative retinoschisis include schisis detachments and progressive rhegmatogenous retinal detachments. Although both types of detachment tend to progress slowly, visually threatening symptoms, especially in cases of posterior extension, may necessitate intervention [15▪].

In schisis detachments, subretinal fluid from an outer retinal break forms in the absence of an inner retinal hole. Schisis-related detachments often do not progress over time [10▪]. Qureshi *et al.* details a case where the schisis cavity collapsed from outer retinal break formation, which allowed for schisis fluid movement to the subretinal space where it can be absorbed by the retinal pigment epithelium pump. Although the schisis cavity had collapsed, the superonasal scotoma persisted. Pump failure in this case may have led to schisis detachment [20▪].

Progressive RRD occurs when liquified vitreous enters the subretinal space in the presence of both inner and outer retinal breaks. These detachments are also rare with incidence ranging from 0.05 to 2.2% [21]. They tend to present more acutely and similarly to typical RRDs, although they have higher surgical failure rates, with reattachment rates ranging from 57 to 92% [10▪,21].

MANAGEMENT OF DEGENERATIVE RETINOSCHISIS

It is important to differentiate between retinoschisis and schisis-related retinal detachment as the management of both conditions differ. Although schisis cavities can enlarge, retinoschisis is rarely prophylactically treated as thermal laser does not prevent enlargement and can lead to changes in vision [22▪▪]. Surgical intervention may be indicated in macula involving schisis detachments and progressive RRDs. The management of asymptomatic schisis detachments is often controversial. Considering these detachments typically remain asymptomatic and are nonprogressive, observation is often the preferred management modality initially and intervention can then be considered if significant progression is noted. Feo *et al.* presented a photo essay of a 60-year-old man with an incidental finding of schisis detachment noted on widefield color fundus and peripheral OCT. This patient remained asymptomatic despite the pathology noted on examination and the decision was made to observe his schisis detachment [23▪]. In contrast, progressive RRDs typically always necessitate intervention.

Laser retinopexy may be employed in cases of schisis detachments that progress toward the posterior pole, but do not encroach the macula. This is typically done when patients are asymptomatic. Outer retinal breaks towards the posterior pole may be present in cases of schisis detachments involving the macula. When the retina is detached around an outer retinal hole, subretinal fluid may prevent adequate laser retinopexy [10▪]. Due to the risk of macular extension, cryoretinopexy may be challenging. Placing a radial element can lead to postoperative macular distortion and visual distortions. To avoid posterior-radial elements, some studies have suggested external drainage, cryoretinopexy, and long-acting gas tamponade with appropriate postoperative positioning for more posterior detachments. Encircling scleral buckles with cryoretinopexy and gas tamponade have been reported to achieve good anatomic success when the outer retinal breaks are anterior to the equator. In the early postoperative phase, there may be increased fluid shifts, which is self-resolving. PPV may also help relieve any posterior vitreous traction. Schisis cavities may re-open while the previous area of detachment remains attached. Therefore, some studies have proposed the complete removal of the inner retina affected by schisis [10▪]. The treatment of schisis detachments typically leads to favorable anatomical outcomes with no improvement in vision. In a study by Xue *et al.* detailing 55 cases of schisis detachments, the primary re-attachment rate in patients that underwent surgical intervention was 70% and the secondary re-attachment rate was 87%, which is inferior to the repair rate in typical RRD repair [24].

The role of laser photocoagulation for progressive rhegmatogenous schisis RDs is controversial. Okun *et al.* describes how laser photocoagulation may cause collapse of the entire schisis cavity. Although the exact mechanism is unknown, this may be due to the heat produced by photocoagulation causing alterations in the consistency of schisis fluid or decrease in schisis fluid resorption due to damage to the RPE and choriocapillaris [25]. Laser treatment of schisis may come with its own risks. Sometimes, barricade lasers are used posterior to the lesion's borders to prevent progression and to demarcate the area [10▪]. However, laser may not always be helpful, as in Okun's study, one eye progressed despite being treated with laser barricade [25].

In cases of progressive RRDs, either a scleral buckle or PPV is typically done to repair the retinal detachment. Similarly, for schisis detachments, management of the schisis cavity during RRD repair is controversial. Some authors advocate for shelving the inner layers of the schisis cavity, others perform panretinal photocoagulation throughout the bed of the laser, and others simply repair the RRD. Laser photocoagulation has been reported to have mixed results. Although some studies have noted no complications or progression of the schisis cavity after photocoagulation has been applied, other studies have noted that photocoagulation applied to macula-threatening schisis can lead to collapse of the schisis cavity. Photocoagulation is not recommended in cases of fovea-threatening schisis, and surgical intervention is typically favored. Ness *et al.* summarizes two studies where vitrectomy with drainage of a fovea-threatening schisis cavity with an inner layer retinotomy led to improved visual acuity [26]. When the vitreous cannot be sufficiently separated from the inner retinal flap during vitrectomy, an encircling scleral buckle may be placed or the schisis cavity may be unroofed. A study by Garneau *et al.* [27] showed no major difference in anatomical success rate between eyes that underwent PPV with scleral buckle and eyes that underwent PPV alone ($P=0.92$). These results are supported by a similar study by Beatson *et al.* that depicted similar reattachment rates for repair of schisis-related detachments with PPV alone (66%) and PPV with scleral buckle (75%) [28]. Although there have been several studies that have compared outcomes with different surgical techniques, it is important to note that these studies have been conducted in small sample sizes [24]. There is no evidence to suggest a superior technique when handling the schisis cavity.

CONCLUSION

Degenerative retinoschisis is a typically asymptomatic condition that may lead to complications including RRD. Although schisis itself may not require intervention, RRD secondary to schisis may require repair depending on whether it is a macula involving schisis detachment or a progressive RRD. Many new diagnostic tools have been proposed to help differentiate between RRD and retinoschisis. However, validation in larger cohorts and in clinical settings needs to occur before these tools are implemented in practice.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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