Exudative maculopathy in presumed X-linked retinoschisis with review of literature

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X-linked retinoschisis (XLRS) is an inheritable juvenile retinal dystrophy.[1] The prevalence ranges from 1:5,000 to 1:20,000, making it one of the most common juvenile-onset retinal degeneration in males involving the macula.[2] The pathognomic feature is foveal schisis (98–100% cases) with some displaying typical bicycle-wheel patterns of radial streaks extending from the fovea. Mild-to-severe central vision loss correlates with foveal schisis. Rarely sudden visual loss results from complications such as vitreous hemorrhage and retinal detachment.[3] We present a rare complication of XLRS, where exudative maculopathy led to sudden irreversible vision loss in a young male. We also present the scant literature about this complication and discuss the basis of the management strategy adopted by us.

An 18-year-old male patient with a history of sub-optimal vision in both eyes (BE) since childhood presented with complaints of recent onset painless vision loss in the right eye (RE). Presenting visual acuity was 20/500 in the RE and 20/50 in the left eye (LE). Large angle sensory exotropia was noted in the RE. BE were unremarkable on anterior segment examination. Fundus examination revealed peripheral retinoschisis with pockmarks and vitreous veils in BE. RE macula revealed a yellowish clump of subretinal exudate with edema, whereas LE showed features of foveal schisis [Fig. 1]. The boy was presumed to have XLRS on the basis of fundus features and multi-modal imaging was suggested to investigate the cause of macular edema in RE.

Optical coherence tomography (OCT) revealed retinoschisis involving multiple layers of macula BE, with predominant involvement of the outer plexiform-inner nuclear layer complex. Additionally, RE had subretinal hyper-reflective material corresponding to the clinical site of exudation with a large central cyst [Fig. 2]. Fundus fluorescein angiography of RE revealed pooling of dye within the area of the cyst, early-moderate leakage nasal to the fovea along with staining in the area of the plaque [Fig. 2]. No new vessels, microaneurysms, or telangiectasia could be detected. OCT angiography (OCTA) ruled out the presence of Choroidal Neovascular Membrane (CNVM) [Fig. 2]. Electroretinogram was more affected in the RE, showing subnormal scotopic b wave amplitude, reduced the "a" wave amplitude, reduction in oscillatory potential, reduction in photopic amplitudes, and absent flicker response at high frequency [Fig. 3].

On leading questions, the family denied a history of ocular disorders, and his brother who was available at the time of the patient interview, refused examination citing fear. The family could not afford a genetic test for the RS1 gene. The patient was thus presumed to have XLRS with exudative maculopathy after a careful review of the literature.[3,4] He was advised topical dorzolamide in BE and also an intravitreal injection of triamcinolone acetonide (2 mg/0.05 mL) for the RE. After 1 month, there was no change in the exudation or the size of the cyst. Although topical therapy was continued, the patient has then advised a trial of intravitreal ziv-aflibercept (2.0 mg/0.05 mL) in the RE. At 2 months of follow-up, visual acuity and OCT of RE did not show any signs of resolution [Fig. 4]. LE and periphery of RE remained stable all this while. At this juncture, maculopathy of RE was considered refractory. The patient was advised to continue topical dorzolamide, informed possibility of complications of vitreous hemorrhage and retinal detachment in BE, and the risk of maculopathy in LE. Regular follow-up, family screening, and genetic testing were also encouraged.

Discussion

The formation of cystic cavities is typical of XLRS; however, exudative maculopathy is rare. Joshi *et al*.[5] proposed that tractional force exerted by the vitreous combined with a defect in retinoschisis promotes schisis cavity formation. Molday *et al*.[1] attributed the same to alteration in intracellular NA+/K + ATPase pumps resulting in fluid accumulation. The fluid that accumulates in the schisis cavity has largely been described as translucent and non-exudative in nature. Greven *et al*.[6] reported a case of bilateral exudative maculopathy in XLRS without preceding hemorrhage into the schisis cavity. Vitreous traction resulting in vascular leakage was proposed as the mechanism for exudation. Rao *et al*.[4] reported the largest series yet of the exudative variant with 11 eyes in 18 patients of XLRS that showed signs of subretinal exudation. Exudation

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corresponded to leakage on Fundus fluorescein angiography (FFA) implicating increased vascular permeability as the possible mechanism. Our patient had similar findings on FFA as described in that series. The older mean age of patients with exudative variant (14.4 years) was reported in the study by Rao *et al*.,[4] with the oldest being 17.6 years, which corresponds to the age of our patient. The occurrence of exudation in such chronic cases with concurrent FFA leakage points toward vascular incompetence as the etiologic agent, not just a resolution of previous intraschisis hemorrhage.

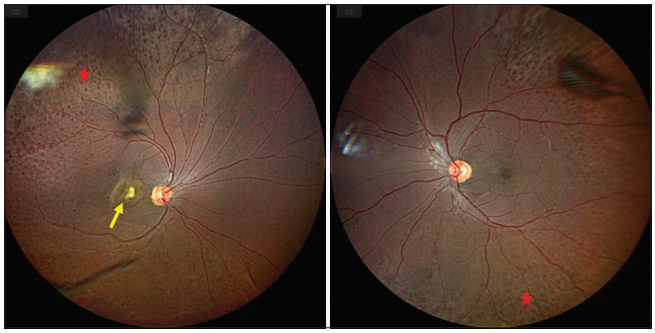

Figure 1: Fundus image showing submacular exudation RE (arrow mark) and foveal schisis LE. Peripheral pigmentary deposits (star mark), vitreous veils noted in BE

SD-OCT in our case shows schisis with predominant involvement of the inner nuclear layer as demonstrated in recent studies. The apparent decrease in flow and irregular foveal avascular zone seen on SS-OCTA imaging is possibly an artifact caused by the displacement of vessels by the schisis. An alternate hypothesis proposed by Han *et al*.[7] is that there is true flow loss in the superficial and deep capillary plexus corresponding to vascular alterations as a factor in the pathogenesis of the disease.

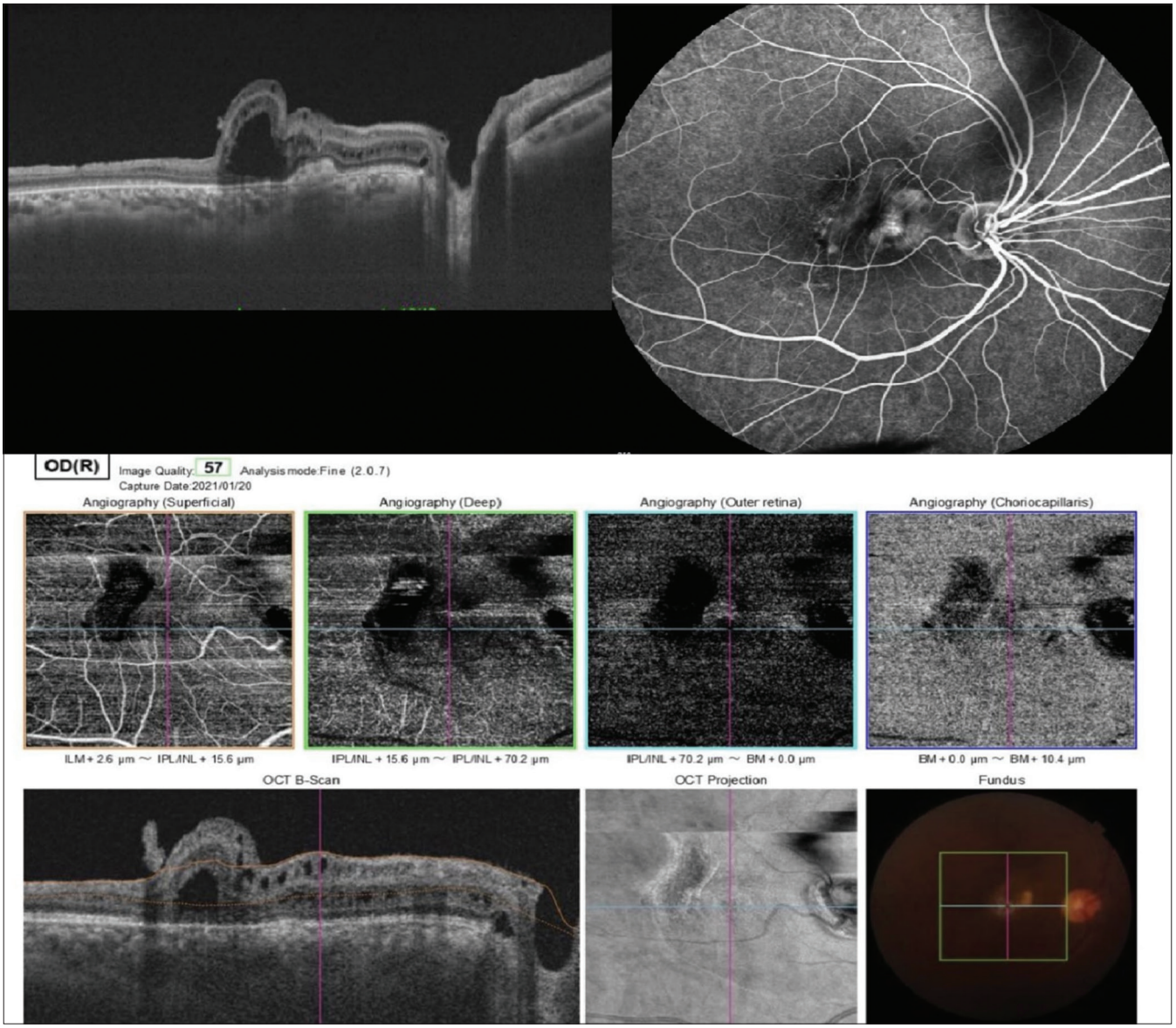

Figure 2: RE OCT shows characteristic schisis with subretinal exudate (arrow mark) and FFA RE shows hyperfluorescence corresponding to the exudation (arrow mark). OCTA confirmed the absence of CNVM

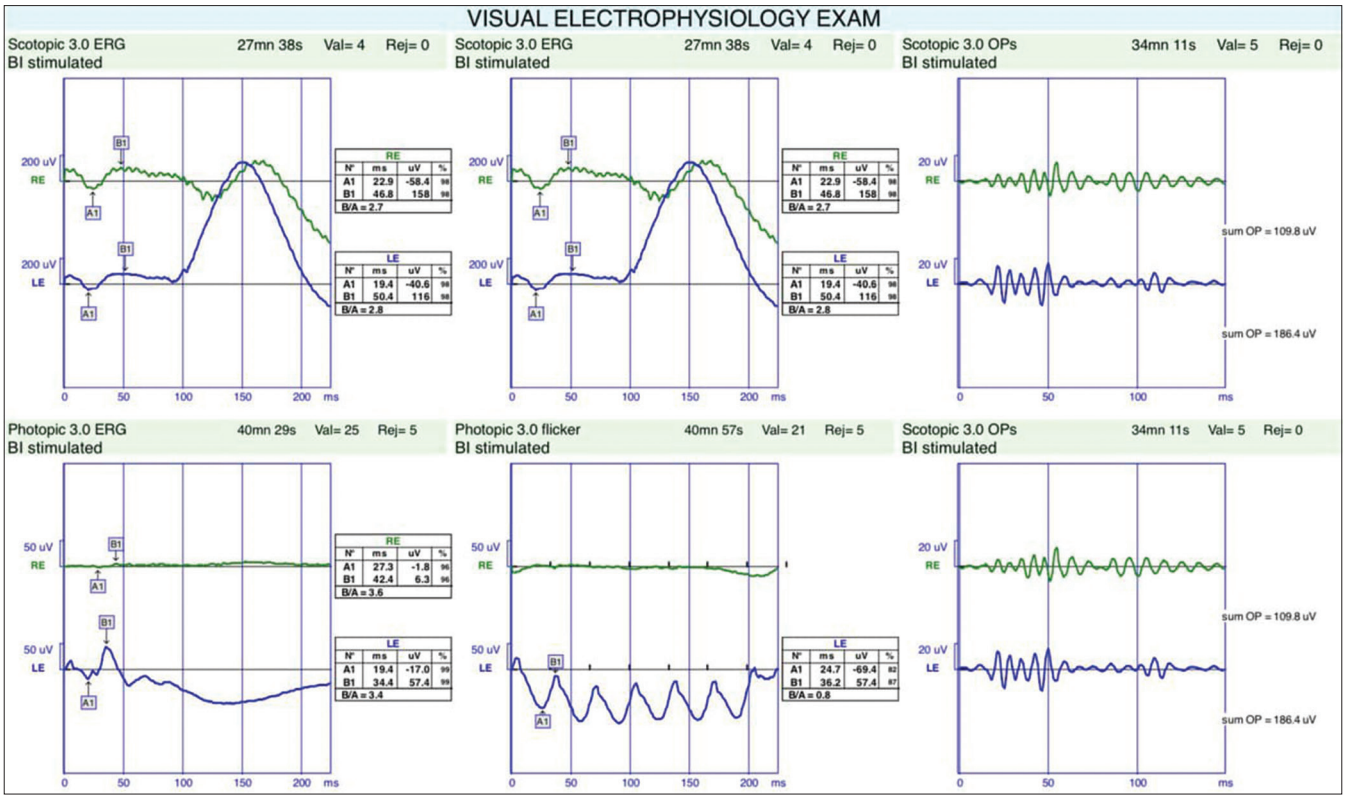

Figure 3: ERG was more affected in the RE, showing subnormal scotopic "b" wave amplitude, reduced the "a" wave amplitude, reduction in oscillatory potential, reduction in photopic amplitudes, and absent flicker response at high frequency

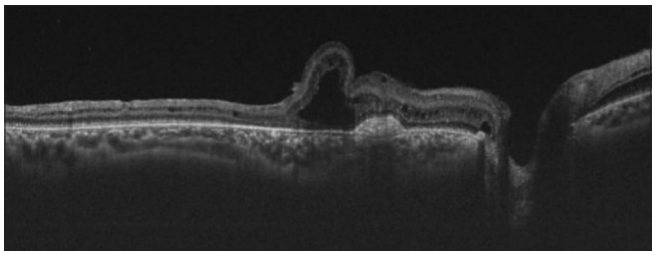

Figure 4: OCT RE at last follow-up showing persistence of foveal schisis and subretinal exudative material

This case report elucidates a rare presentation of XLRS, the exudative variant reiterating the role of chronic vascular permeability in its pathogenesis. However, our patient did not show a response to both intravitreal steroid and anti-VEGF agent indicating a poor prognosis in such eyes. Further research into therapeutic options and longer follow-up are needed to establish the natural course of an exudative variant of XLRS.

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Conflicts of interest

There are no conflicts of interest.

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