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Case Report: X-Linked Retinoschisis

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A B S T R A C T
X-linked retinoschisis (XLRS) is a rare inherited vitreoretinal dystrophy caused by mutations in the *RS1* gene located on chromosome Xp22.2. The disorder predominantly affects males and is characterized by splitting of the retinal layers, particularly within the macular region, resulting in progressive visual impairment beginning in childhood. Early diagnosis is essential because patients are at risk of developing serious complications, including vitreous hemorrhage and retinal detachment, which may further compromise visual function. This case report describes the clinical presentation, diagnostic evaluation, and management of a 12-year-old boy diagnosed with XLRS. The patient presented with gradually progressive bilateral visual deterioration and a positive maternal family history of similar ocular disease. Comprehensive ophthalmic examination included best-corrected visual acuity assessment, fundus examination, optical coherence tomography (OCT), and molecular genetic analysis. Fundoscopic evaluation revealed bilateral foveal schisis with characteristic spoke-wheel retinal folds, while OCT demonstrated multilayer schisis cavities involving both the inner and outer retinal layers. Genetic testing confirmed a hemizygous mutation in the *RS1* gene, establishing the diagnosis of XLRS. The patient received conservative management consisting of visual rehabilitation, routine ophthalmic monitoring, and genetic counseling. This case highlights the importance of integrating clinical examination, retinal imaging, and molecular diagnostics for accurate diagnosis. Early recognition and long-term follow-up are crucial for preventing vision-threatening complications and improving patient outcomes. Furthermore, advances in molecular genetics and emerging gene therapy provide promising future therapeutic strategies for individuals affected by XLRS.

INTRODUCTION

X-linked retinoschisis (XLRS) is one of the most common inherited retinal dystrophies affecting young males, with an estimated prevalence ranging from 1:5,000 to 1:25,000 individuals worldwide. The disease follows an X-linked recessive inheritance pattern and results from pathogenic variants in the *RS1* gene, which encodes retinoschisin, a secreted extracellular protein responsible for maintaining retinal cellular adhesion and structural organization. Dysfunction or absence of retinoschisin disrupts retinal integrity, leading to splitting (schisis) of the retinal layers and progressive degeneration of retinal architecture.

The clinical manifestations of XLRS usually become apparent during the first decade of life, although disease severity varies considerably among affected individuals. Patients commonly present with gradually decreasing central vision, reading difficulties, reduced visual acuity, and impaired contrast sensitivity. Fundoscopic examination frequently demonstrates a spoke-wheel pattern at the fovea caused by cystic schisis of the macular retina. Peripheral retinoschisis occurs in approximately half of patients and may predispose them to vitreous hemorrhage, retinal tears, or retinal detachment, which represent major causes of irreversible visual loss.

Recent advances in retinal imaging have significantly improved the diagnosis of XLRS. Optical coherence tomography (OCT) provides high-resolution cross-sectional visualization of retinal layers and is considered the imaging modality of choice for detecting schisis cavities and monitoring disease progression. Electroretinography (ERG) may reveal a characteristic reduction of the b-wave relative to the a-wave, reflecting dysfunction of bipolar cells within the inner retina. However, molecular genetic analysis remains the gold standard for confirming the diagnosis and identifying disease-causing *RS1* mutations.

Although there is currently no definitive cure for XLRS, advances in supportive care, low-vision rehabilitation, and regular ophthalmic surveillance have improved long-term visual outcomes. In addition, gene replacement therapy targeting the *RS1* gene has emerged as a promising therapeutic approach and is currently under clinical investigation. Early identification of affected patients is therefore essential not only for preventing complications but also for facilitating appropriate genetic counseling and future access to novel therapeutic interventions.

This case report describes the clinical presentation, multimodal imaging findings, molecular confirmation, and management of a pediatric patient with genetically confirmed X-linked retinoschisis. The report aims to emphasize the importance of combining comprehensive ophthalmic evaluation with genetic testing for establishing an accurate diagnosis and optimizing long-term patient care.

LITERATURE REVIEW

X-linked retinoschisis (XLRS) is a hereditary vitreoretinal disorder first described by Josef Haas in 1898 and is now recognized as one of the most prevalent inherited retinal diseases affecting males. The disease results from mutations in the *RS1* gene located on chromosome Xp22.2. More than 200

pathogenic variants have been identified, including missense, nonsense, splice-site, insertion, and deletion mutations. These mutations impair the production or secretion of retinoschisin, a protein that plays a fundamental role in maintaining retinal cellular adhesion and synaptic organization.

Retinoschisin is primarily expressed by photoreceptor and bipolar cells and contributes to preserving retinal structural stability. Deficiency of this protein causes separation of retinal layers, particularly at the nerve fiber layer, inner nuclear layer, and outer plexiform layer, leading to the characteristic schisis cavities observed in affected individuals. Progressive structural disruption ultimately results in visual impairment and increased susceptibility to retinal complications.

Clinically, XLRS commonly manifests during early childhood with bilateral reduction in central visual acuity. The severity of visual dysfunction varies depending on the extent of retinal involvement and the occurrence of secondary complications. The classic ophthalmoscopic finding is foveal schisis presenting as a spoke-wheel pattern radiating from the macula. Approximately half of patients also develop peripheral schisis, predominantly involving the inferotemporal retina. Complications such as vitreous hemorrhage, retinal tears, and rhegmatogenous retinal detachment may occur during disease progression and significantly worsen the visual prognosis.

Optical coherence tomography (OCT) has become the primary imaging modality for diagnosing and monitoring XLRS. OCT typically demonstrates hyporeflective intraretinal cystic spaces with vertical septa involving multiple retinal layers. These imaging findings are highly characteristic and allow differentiation of XLRS from cystoid macular edema and other inherited macular dystrophies. Additional diagnostic examinations, including fundus autofluorescence, fluorescein angiography, and electroretinography, may provide complementary information regarding retinal function and structural integrity.

Genetic testing has become an indispensable component of XLRS diagnosis. Identification of pathogenic *RS1* mutations confirms the diagnosis, facilitates genotype-phenotype correlation, enables prenatal diagnosis, and supports genetic counseling for affected families. Because female carriers are often asymptomatic, molecular testing is particularly valuable for identifying carrier status and estimating recurrence risk in future offspring.

Current treatment remains primarily supportive. Visual rehabilitation, refractive correction, amblyopia management when appropriate, and regular ophthalmic surveillance constitute the mainstay of clinical care. Carbonic anhydrase inhibitors, particularly topical dorzolamide and oral acetazolamide, have demonstrated variable success in reducing retinal schisis cavities and improving visual acuity in selected patients. Surgical intervention is reserved for complications such as retinal detachment or persistent vitreous hemorrhage.

Recent developments in molecular medicine have stimulated considerable interest in gene therapy for XLRS. Several experimental studies using adeno-associated viral (AAV) vectors to deliver functional copies of the *RS1* gene have demonstrated encouraging anatomical and functional improvements in

preclinical and early clinical investigations. Although further studies are necessary to establish long-term safety and efficacy, these advances represent a promising therapeutic direction for patients with inherited retinal diseases.

Overall, current evidence emphasizes that early diagnosis through comprehensive ophthalmic examination, multimodal retinal imaging, and molecular genetic confirmation is essential for improving patient management. Long-term monitoring combined with multidisciplinary care involving ophthalmologists, geneticists, and low-vision specialists remains critical for preserving visual function and providing appropriate counseling to affected families.

METHODOLOGHY

This study is a descriptive case report of a 12-year-old boy diagnosed with X-linked retinoschisis. Clinical evaluation included best-corrected visual acuity assessment, slit-lamp examination, fundus photography, and optical coherence tomography (OCT). Genetic testing of the *RS1* gene was performed to confirm the diagnosis. Clinical findings were analyzed and compared with relevant literature.

MANAGEMENT

The patient was informed about the nature of the condition, advised on visual rehabilitation strategies, and scheduled for regular follow-ups to monitor for complications, particularly retinal detachment.

DISCUSSION

X-linked retinoschisis (XLRS) is a hereditary vitreoretinal dystrophy caused by mutations in the *RS1* gene, which encodes retinoschisin, a protein essential for cellular adhesion and structural integrity within the retina. Dysfunction of this protein leads to splitting (schisis) within the retinal layers, most commonly affecting the nerve fiber layer and inner nuclear layer, particularly in the macular region.

Clinically, XLRS typically presents in school-aged boys with bilateral reduction in visual acuity, often ranging from mild to moderate impairment. The hallmark finding is foveal schisis, which appears as a spoke-wheel pattern on fundoscopy. Peripheral schisis may also be present in approximately 50% of cases, increasing the risk of complications such as vitreous hemorrhage and retinal detachment.

Optical coherence tomography (OCT) plays a crucial role in diagnosis by demonstrating hyporeflective cystic spaces within the retinal layers, often with vertical septations. These findings are highly characteristic and can aid in distinguishing XLRS from other macular dystrophies. In this case, OCT confirmed the presence of schisis cavities involving both inner and outer retinal layers, consistent with typical XLRS morphology.

Genetic testing remains the gold standard for definitive diagnosis, particularly in atypical presentations. Identification of a hemizygous mutation in the *RS1* gene not only confirms the diagnosis but also facilitates genetic

counseling for family members, especially female carriers who may be asymptomatic.

Currently, there is no definitive cure for XLRS. Management is primarily supportive and focuses on visual rehabilitation, regular monitoring, and early detection of complications. Carbonic anhydrase inhibitors have shown some benefit in reducing schisis cavities in certain cases. Emerging therapies, including gene therapy targeting *RS1*, are under investigation and hold promise for future treatment.

Early diagnosis and long-term follow-up are essential to optimize visual outcomes and prevent irreversible complications. Multidisciplinary management, including genetic counseling, is strongly recommended to address both clinical and familial aspects of the disease.

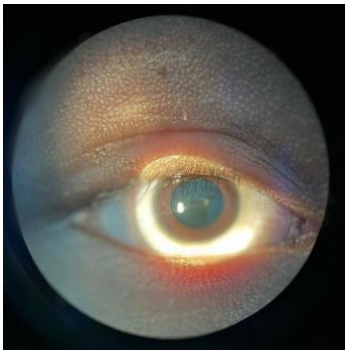

Figure 1: Anterior segment photograph of the eye showing a clear cornea, round pupil, and normal ocular structures.

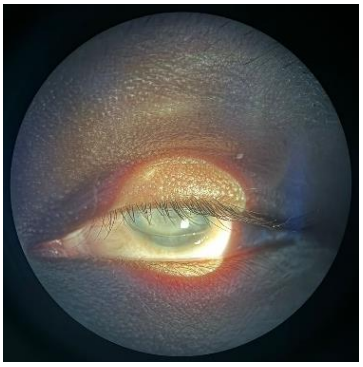

Figure 2: Anterior segment photograph of the eye in a patient with X-linked retinoschisis

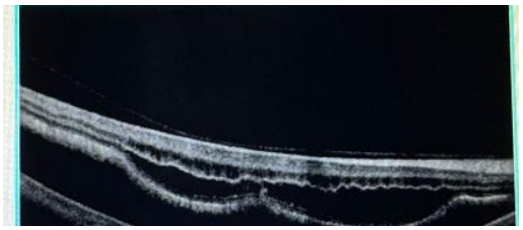

Figure 3: Optical coherence tomography (OCT) of the macula demonstrating schisis-like intraretinal cystic spaces, consistent with X-linked retinoschisis.

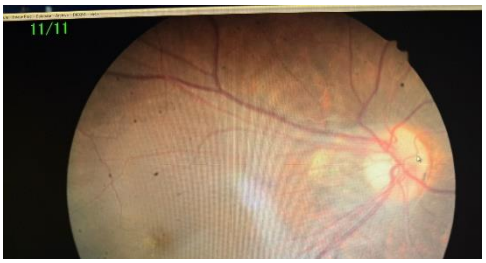

Figure 4: Fundus photograph of the right eye showing radial retinal folds with a spoke-wheel pattern at the macula, characteristic of X-linked retinoschisis.

X-linked retinoschisis (XLRS) is an inherited retinal disorder caused by mutations in the *RS1* gene. The condition predominantly affects males and usually presents during childhood with progressive visual impairment. Characteristic findings include foveal schisis with a spoke-wheel appearance on fundoscopy and schisis cavities on optical coherence tomography (OCT). Genetic testing plays an important role in confirming the diagnosis and facilitating

genetic counseling. Although no definitive treatment is currently available, regular monitoring is essential to detect complications and preserve visual function.

CONCLUSION

This case report highlights the importance of recognizing X-linked retinoschisis (XLRS) as a potential cause of progressive bilateral visual impairment in pediatric male patients. The characteristic clinical findings, together with optical coherence tomography (OCT) and confirmation of an *RS1* gene mutation, enabled an accurate diagnosis and appropriate patient management. Early diagnosis is crucial for initiating visual rehabilitation, providing genetic counseling, and preventing irreversible vision loss through regular surveillance for complications, including vitreous hemorrhage and retinal detachment. Although current treatment remains largely supportive, ongoing advances in molecular genetics and gene therapy may offer disease-modifying strategies in the future. This report underscores the value of combining multimodal retinal imaging with genetic testing to improve diagnostic accuracy and emphasizes the need for long-term multidisciplinary follow-up to optimize visual prognosis and family care.

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