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CASE REPORT

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A case of bilateral stellate nonhereditary idiopathic foveomacular retinoschisis with 14-month follow-up: clinical features, OCT findings and treatment outcome

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Abstract

Background Stellate nonhereditary idiopathic foveomacular retinoschisis (SNIFR) is a relatively recent and rare classification introduced. Currently, there is no reliable treatment for the disease.

Case presentation We discussed an additional case multimodal imaging including Optical coherence tomography (OCT), fluorescein angiography and Optical coherence tomography angiography (OCTA) as well as treatment result. The case was a healthy, non-myopic woman, where foveal cystic changes persisted despite 9 months of topical dorzolamide and an additional 5 months of oral acetazolamide. Genetic testing for Congenital X-linked retinoschisis (CXLR) was negative. ERG results were near normal. Optical coherence tomography showed no vitreomacular traction, while fluorescein angiography ruled out vascular disease.

Conclusions Our findings suggest that bilateral SNIFR can occur in non-myopic females, although this patient did not respond to systemic and topical carbonic anhydrase inhibitors.

Keywords SNIFR, CXLR, OCTA, Diamox, Dorzolamide, Multi modal imaging

Background

Foveoschisis, also known as foveomacular retinoschisis, refers to the separation of retinal layers that affects the central regions, including the macula [1]. A common cause of this condition is Congenital X-linked retinoschisis (CXLR), resulting from a mutation in the RS1 gene. This condition is a hereditary retinal degeneration linked to the X chromosome, marked by the separation of the inner layers of the retina, particularly the nerve fiber layer. It occurs exclusively in males and typically manifests with progressive bilateral retinal involvement at a young age [2]. Additional causes of foveoschisis include glaucoma [3, 4], myopic degeneration [5–8], enhanced S-cone syndrome [9, 10] and vitreomacular traction [11].

Stellate nonhereditary idiopathic foveomacular retinoschisis (SNIFR) is a relatively recent classification introduced by Ober et al., and it differs in several aspects from stellate foveal retinoschisis associated with CXLR. According to the findings of Ober et al., SNIFR primarily affects myopic women without predisposing hereditary background, typically on a unilateral basis, and most patients have a visual acuity of 20/40 or better [12]. The course of the disease is generally benign, and most individuals do

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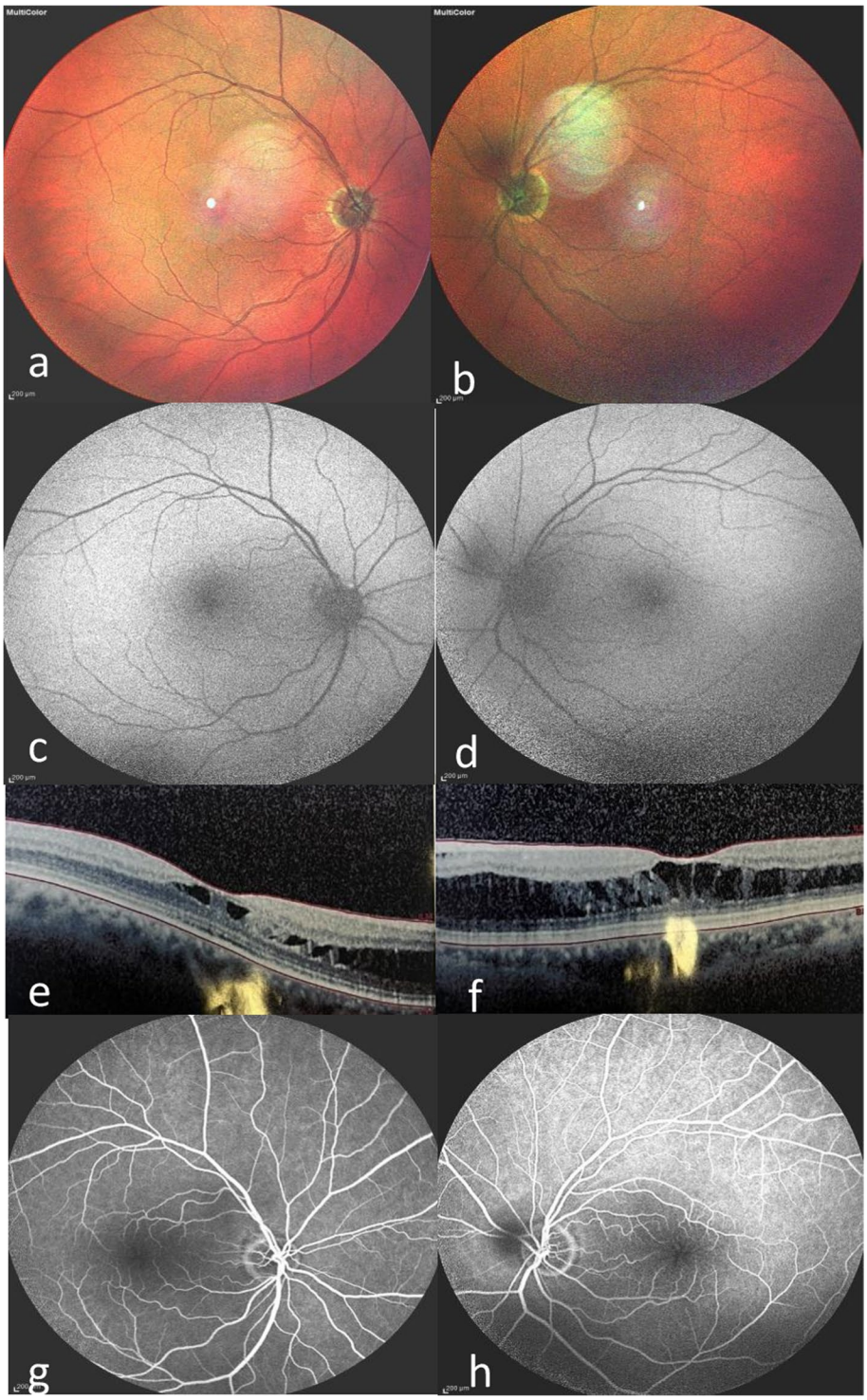

Fig. 1 Angiographically-silent edema in SNIFR. (**a** and **b**) Multicolor fundus photograph showing decreased foveal reflex in both eyes. (**c** and **d**) Fundus autofluorescence (FAF) showing fine radial spoking appearance (hypo and hyper autofluorescence) of the macula in both eyes. (**e** and **f**) The horizontal optical coherence tomography through the fovea revealing intraretinal schisis in the Henle fiber layer. There is no vitreomacular traction or epiretinal membrane. (**g** and **h**) The late-phase fluorescein angiography showing no leakage. Ophthalmic examination revealed a grade 2 cataract, which, limited image quality; nonetheless, multiple attempts were made to obtain acceptable images that illustrate key clinical features of the case

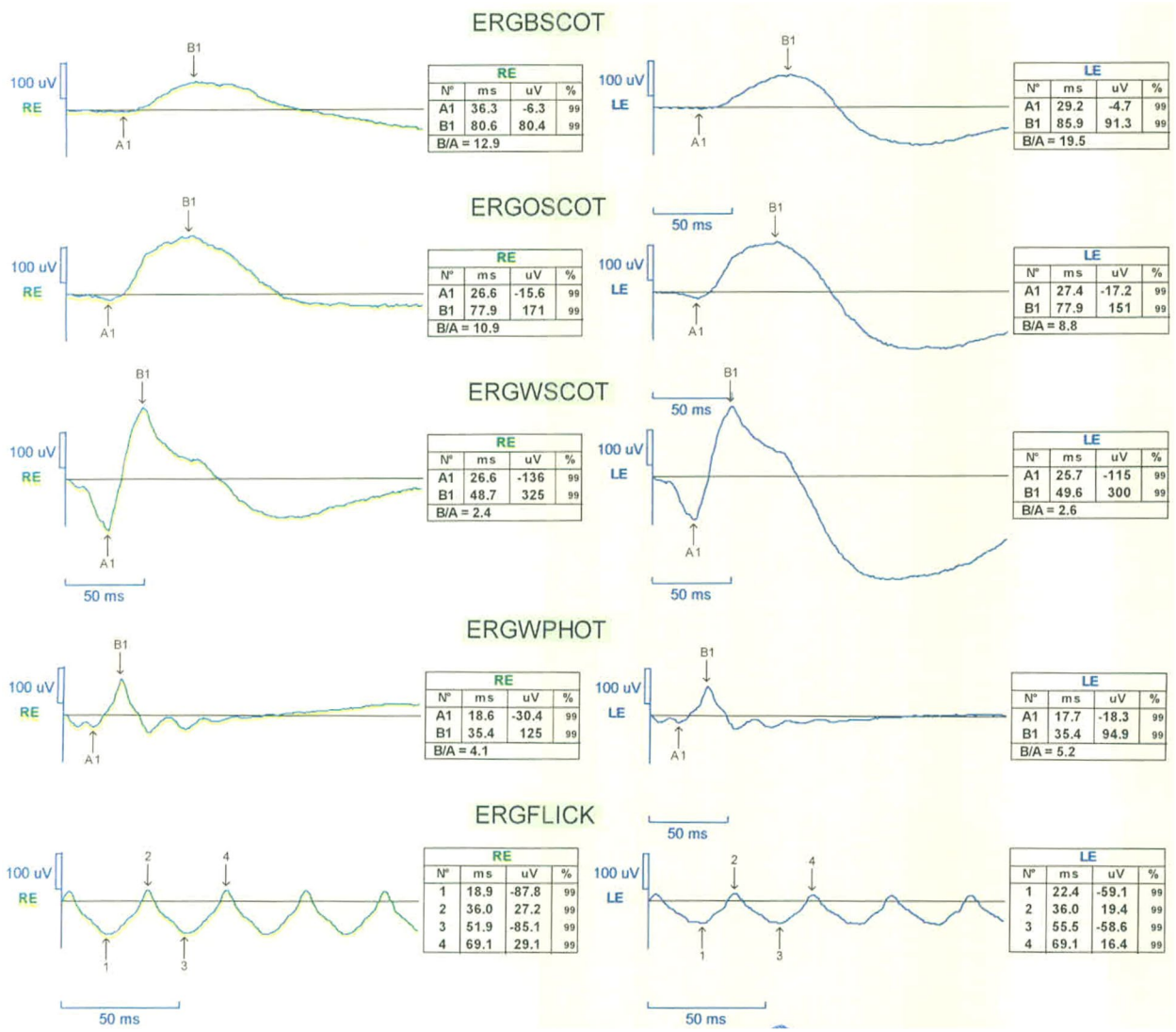

Fig. 2 ERG shows normal photopic and scotopic response

not need significant treatment; however, annual optical coherence tomography (OCT) is advised [1].

Recent case reports [1, 13] have documented instances of bilateral SNIFR in patients without myopia, contrasting with the cases described by Ober et al. In this article, we present an additional case of bilateral SNIFR in a healthy woman who is not myopic. Foveal cystic changes did not resolve despite 9 months of topical dorzolamide and additional 5 months of oral acetazolamide (Diamox).

Case presentation

A 62-year-old woman presented to our outpatient department with gradually progressive vision loss in both eyes. Her medical history was unremarkable, including no history of diabetes, hypertension, or relevant family history. She also denied using medications such as niacin or taxanes. However, ophthalmic examination revealed a grade 2 nuclear cataract, which made imaging challenging; thus, multiple attempts were required to obtain images of acceptable quality.

On examination, her best corrected visual acuity (BCVA) was 20/30 in both eyes (OU) with a minimal refractive error of +0.25 diopter hyperopia bilaterally. Intraocular pressure (IOP) was 14 mmHg in the right eye (OD) and 16 mmHg in the left eye (OS). Anterior segment evaluation via slit-lamp examination revealed no abnormalities. Fundoscopic examination of the optic nerve showed no evidence of optic pits. Fluorescein angiography demonstrated no signs of uveitis, inflammation, or vascular leakage (Fig. 1). Additionally, full-field

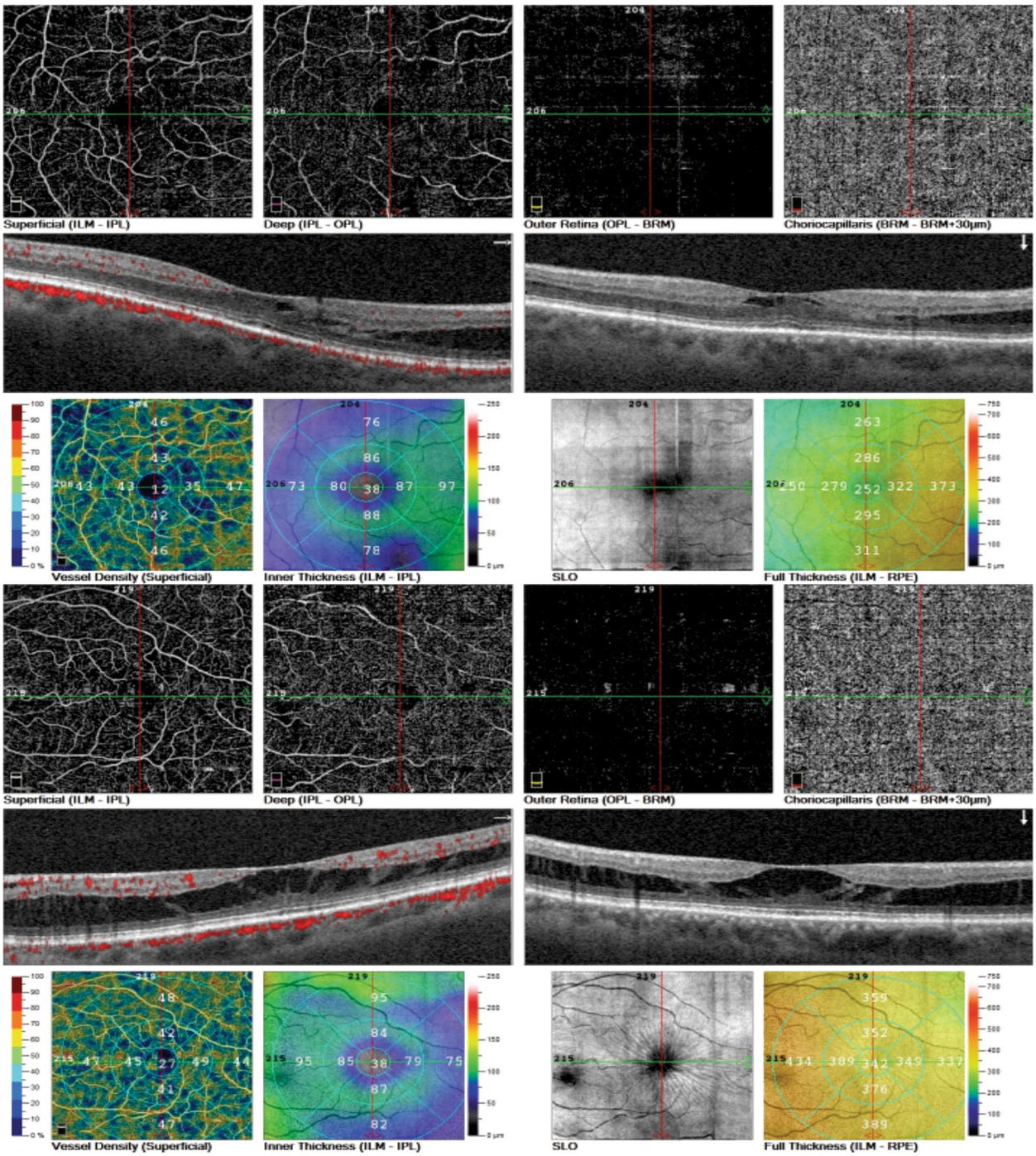

Fig. 3 OCT angiography showed absence of flow signal in the cystic retinal spaces within Henle's fiber layer in both eyes. Please notice the deep capillary plexus defects compatible with cystic spaces area in the b scan image

electroretinography (ERG) was within normal limits (Fig. 2).

Genetic testing was performed to evaluate mutations associated with CXLR. Ideally, a broader genetic panel would have been beneficial to rule out other hereditary macular dystrophies comprehensively; however, the substantial costs associated with such extensive genetic panels, combined with a lack of insurance coverage and the patient's reluctance to incur additional expenses, limited our genetic analysis to this specific evaluation. This

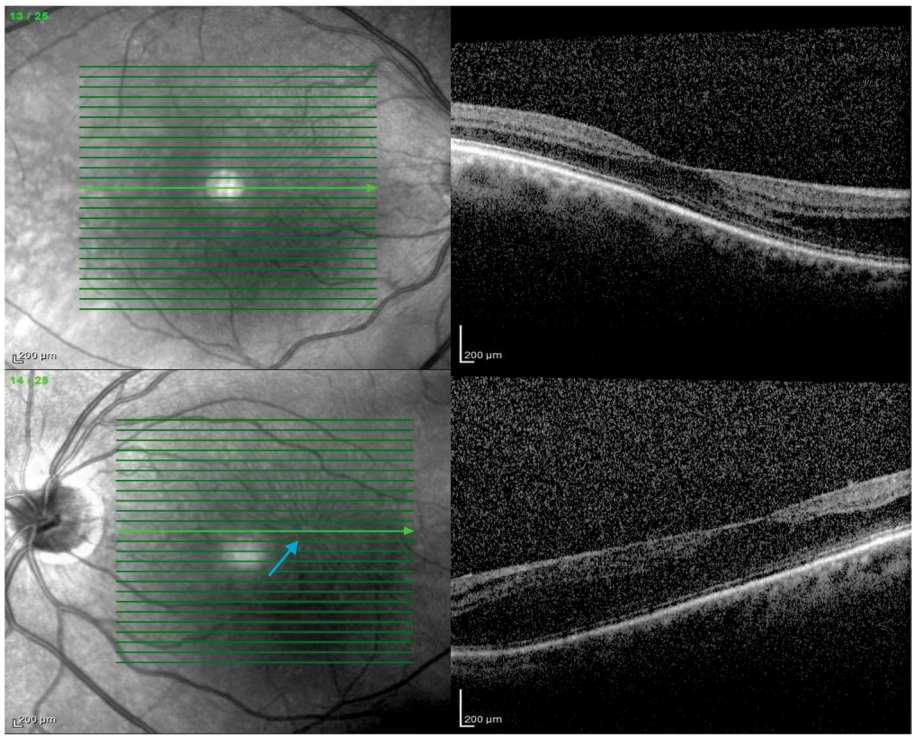

Fig. 4 Showing infrared (IR) fundus image and optical coherence tomography (OCT) of the right (upper row) and left (lower row) eye after 14 months of therapy with no improvement. The blue arrow indicates spoke like appearance in the left eye IR image

represents an acknowledged limitation of our diagnostic approach. Genetic testing for CXLR was negative.

Optical coherence tomography angiography (OCTA) showed an absence of flow signal within the cystic retinal spaces located in Henle's fiber layer in both eyes (Fig. 3). Topical dorzolamide treatment was initiated after discussing the limited probability of visual improvement. After 9 months without significant resolution of the cystic changes, the patient was switched to oral acetazolamide; however, after an additional 5 months, no improvement in foveoschisis was observed (Fig. 4). The patient BCVA in her last follow up visit was 20/40 (mostly due to cataract progression) in her right eye and 20/30 in her left eye.

Discussion

The concept of retinoschisis was first described by Jager in the late nineteenth century [2]. Ober et al. later published a case series involving 17 patients and coined "stellate non-hereditary idiopathic foveomacular retinoschisis" (SNIFR) [12]. SNIFR is marked by a stellate macular reflex on fundoscopy and foveomacular splitting on OCT in eyes without CXLR or other risk factors; it remains a diagnosis of exclusion [14].

CXLR affects young males, is often bilateral and progressive, and splits the inner nuclear layer with bridging vessels on OCTA [2, 15, 16]. SNIFR, by contrast, usually occurs in adult females, is unilateral, involves Henle's fiber layer and lacks vascular flow in the cystic spaces [1, 12, 15]. These anatomical distinctions were investigated by Fragiotta et al. using swept-source optical coherence tomography angiography (SS-OCTA) [15]. The presented patient OCTA showed absence of flow signal in the cystic retinal spaces within Henle's fiber layer in both eyes that was very similar to the OCTA pattern of the case presented by Fragiotta et al. [15].

Enhanced S-cone syndrome can mimic SNIFR on OCT but presents with night blindness, an optically clear vitreous and a pathognomonic ERG [14]. Other causes of a macular star include myopic retinoschisis, optic-disc-pit maculopathy, glaucomatous macular retinoschisis, vitreomacular traction (VMT) and old vascular occlusions. Clinical exam and late-phase fluorescein leakage help separate these conditions from SNIFR [12, 14].

Following Light et al.'s algorithm [14], we first inspected the optic disc margin and cup-to-disc ratio that were normal, with no pits or oedema; OCT showed no membrane or traction, ERG was normal, and RS1 testing was negative. Minimal hyperopia (+ 0.25 D) argued against myopic schisis.

Although most cases are myopic, hyperopic and bilateral presentations—such as ours—have been reported [1, 17].

Table 1 Summary of management strategies, and outcomes in studies of SNIFR

Authors, Year	Patient Demographics (Age, Sex)	Laterality	Clinical Features	Imaging Findings	Treatment Administered	Response to Treatment	Conclusion
Ober et al. 2014 [12]	Mean Age: 61; 16 Female and 1 Male	Predominantly Unilateral	Initial VA: ≥ 20/50; Myopic in 16 eyes	OCT: OPL split	Observation	Relatively preserved visual acuity (≥ 20/40) in all except one eye that developed subfoveal fluid	The First and one of the largest known series of SNIFR patients. Splitting of OPL with relatively preserved vision
Casalino et al. 2016 [25]	Age > 80; 2 Females (3 eyes)	Bilateral (1 case) and Unilateral (1 case)	Initial VA: 72, 66 and 66 ETDRS letters	OCT: OPL split, concomitant n-AMD	Anti-VEGF treatment for n-AMD	Improvement in visual acuity and resolution of n-AMD exudative changes; SNIFR splitting in OPL remained unchanged	SNIFR can coexist with n-AMD. Retinoschisis should be recognized to avoid misinterpreting as intraretinal fluid
Ajlan et al. 2019 [18]	27, Male	Unilateral	Initial VA: 20/40	OCT: IPL/OPL split	Topical Dorzolamide 2% TDS	Visual acuity improved to 20/30 after 6 months. Recurrence upon stopping treatment, with improvement to 20/20 and resolution of IPL/OPL splitting on OCT after restarting for 1 year	First reported case of complete SNIFR resolution with topical dorzolamide
Panos et al. 2020 [26]	67, Female	Unilateral	Initial VA: 20/20	OCT: IPL/OPL split	Observation	Visual acuity 20/20, stable SNIFR on OCT	SNIFR can remain stable without treatment
Nogueira et al. 2021 [27]	67, Female	Unilateral	Initial VA: 20/40 (OD), 20/25 (OS); A grade 2 nuclear cataract (OD)	OCT: HFL/OPL split, VMA (OD); VMT (OS)	Phacoemulsification (OD, 3 months after initial visit), then observation	OD: VMA release and significant improvement of macular schisis at 16 months. Complete resolution of SNIFR at 22 months with posterior hyaloid separation	The resolution of foveoschisis after VMA release suggests that SNIFR might be a result of VMA in individuals with a predisposition to retinal structural weakness
Bloch et al. 2021 [28]	Mean Age: 63.6; 15 Female and 9 Male (28 eyes)	Predominantly Unilateral	Initial VA: 20/20 (Median)	OCT: HFL/OPL split, temporal extension; Attached posterior hyaloid	Observation	Remained stable VA (median 20/20)	This study links SNIFR to incomplete posterior hyaloid detachment, suggesting tractional causes, and associates it with peripheral retinoschisis and extramacular scotomas, despite preserved central vision

Table 1 (continued)

Authors, Year	Patient Demographics (Age, Sex)	Laterality	Clinical Features	Imaging Findings	Treatment Administered	Response to Treatment	Conclusion
Auwera et al. 2022 [17]	51, Female	Bilateral	Initial VA: 20/30	OCT: OPL split	Clear lens extraction with multifocal IOL	Excellent postoperative distance and near vision in both eyes. SNIFR stable at 1-year follow-up	Cataract surgery with multifocal IOL can be performed safely in SNIFR patients with good visual outcomes
Moraes et al. 2022 [24]	46, Female	Unilateral	Severe vision loss; Initial VA: 20/100	OCT: OPL split with outer retinal layer defect	Phacoemulsification; Pars plana vitrectomy, internal limiting membrane (ILM) removal, C3 F8 gas instillation	Progressive recovery of outer retinal layers and improvement of visual acuity during 12-month follow-up	Pars plana vitrectomy with ILM removal and C3 F8 infusion is a safe and feasible treatment with good anatomical and functional outcomes in SNIFR associated with outer retinal layer defect
Liu et al. 2023 [29]	14, Female	Bilateral	Initial VA: 20/66 (OD), 20/100 (OS)	OCT: OPL/HFL split; FFA: Macular split	Vitrectomy (OD)	OD: Retina reattached, vision improved to 20/66;	Vitrectomy can be a beneficial treatment for progressive vision loss in SNIFR cases
Perente et al. 2023 [1]	74, Female	Bilateral	Initial VA: 20/32, +1.25 sphere (OU)	OCT: OPL split, temporal extension, no VMT; FAF: RPE changes, yellowish deposits; FA: Normal	Dorzolamide 2% QID	No positive response; Stable VA and OCT findings	Bilateral SNIFR in a non-myopic female is rare. Annual monitoring suggested for stable cases
Schildroth et al. 2023 [19]	59–63, 3 females	Unilateral (2 cases) and bilateral (1 case)	Initial VA: ranged from 20/20 to 20/60	OCT: OPL split, Peripheral retinoschisis in all; OCTA: Nonvascular retinoschisis cavities	Topical dorzolamide (all cases), Intravitreal bevacizumab (1 case)	No treatment effect observed; One case progressed to foveal involvement	Novel findings include progressive nature in some cases and lack of response to dorzolamide and bevacizumab
Yu et al. 2024 [30]	38, Female	Bilateral	-	OCT: OPL/INL split; FAF/FA/ERG/VF: Normal	topical prednisolone and sub-tenon triamcinolone, Oral acetazolamide, topical ketorolac/brinzolamide	No response to oral and topical treatment; Spontaneous resolution bilaterally	SNIFR can resolve completely and spontaneously without any changes occurring at the vitreoretinal interface

Table 1 (continued)

Authors, Year	Patient Demographics (Age, Sex)	Laterality	Clinical Features	Imaging Findings	Treatment Administered	Response to Treatment	Conclusion
Feo et al. 2025 [31]	Mean age 56, 9 female and 2 male (15 eyes)	Unilateral (7 cases) and bilateral (4 case)	Initial VA: 20/70 (range, 20/250–20/20)	OCT, OCTA: SNIFR contiguous with MPRS, Midperipheral microvasculopathy (7 eyes), CARPET variant (3 eyes)	Observation; Pars plana vitrectomy (1 eye with CARPET)	Spontaneous resolution in 2 eyes. Partial regression in 1 patient. Stable in another. In CARPET variant: schisis resolved and vision improved after vitrectomy in 1 eye	MPRS can progress to SNIFR. SNIFR with MPRS can spontaneously resolve or remain stable. CARPET may respond to vitrectomy

SNIFR Stellate Nonhereditary Idiopathic Foveomacular Retinoschisis, *NS* Not specified, *OCT* optical coherence tomography, *mfPhNR* multifocal photopic negative response, *VMA* vitreomacular adhesion, *VMT* vitreomacular traction, *FAF* fundus autofluorescence, *FA* fluorescein angiography, *ERG* electroretinogram, *VF* visual field, *BCVA* best-corrected visual acuity, *OPL* outer plexiform layer, *IPL* inner plexiform layer, *HFL* Henle fiber layer, *CARPET* Combined Adjacent Retinoschisis, Pigment Epitheliopathy, and Traction, *MPRS* macular/peripheral retinoschisis, *AMD* age-related macular degeneration, *VA* visual acuity, *NS* not specified

SNIFR generally follows a benign, self-limited course; annual clinical visit is sufficient [1, 12]. Carbonic-anhydrase inhibitors give inconsistent results: complete resolution was reported by Ajlan et al. [18], but most studies (including our 14-month trial of topical dorzolamide and oral acetazolamide) show no meaningful change [19]. Anti-VEGF injections [20, 21] and pars plana vitrectomy with ILM peeling [22–24] have not demonstrated clear benefit in non-tractional SNIFR and are not recommended. Phacoemulsification appears safe, with no worsening of schisis in reported cases [17, 24]. An overview of existing literature on SNIFR, including therapeutic approaches, and their effectiveness, is presented in Table 1.

Conclusions

In this paper, we present a case of non-myopic female patient with bilateral SNIFR. This patient did not show any improvement despite systemic and topical carbonic anhydrase inhibitors therapy.

Abbreviations

OCT	Optical coherence tomography
OCTA	Optical coherence tomography angiography
SNIFR	Stellate nonhereditary idiopathic foveomacular retinoschisis
CXLR	Congenital X-linked retinoschisis
ERG	Electroretinogram

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Authors' contributions

All authors participated in research and paper preparation. All authors read and approved the final manuscript.

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Data availability

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

An informed written consent in native language was obtained for participating in this survey. Local research ethics committee (Tabriz Medical University) approval was also obtained.
For this research, the authors employed ChatGPT 4.5 to enhance the clarity and readability of the language. After utilizing this tool, they meticulously examined and adjusted the material as needed, taking complete responsibility for the published work.

Consent for publication

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Competing interests

The authors declare no competing interests.

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