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Progression of Pentosan Polysulfate Sodium Maculopathy following Discontinuation

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Introduction

Pentosan polysulfate sodium (PPS) is a semisynthetic polysaccharide analog of glycosaminoglycans found in bladder epithelium and oral administration of PPS is commonly used for management of bladder pain caused by interstitial cystitis. PPS was first approved in 1996, and its use has grown since then, given its overall favorable safety profile and efficacy in clinical trials.[1,2] There have been recent reports, however, of PPS-associated maculopathy, resulting in severe visual loss.[3,4,5] We present a case of PPS-associated maculopathy two years after discontinuation of PPS in a woman with a family history of age-related macular degeneration (AMD).

Case Report

A 69-year-old woman with a family history of AMD and a relatively recent diagnosis of bilateral dry AMD herself presented for a second opinion. She had been taking 400 mg of PPS daily for seven years (cumulative dose ~1000g) but had stopped two years prior to presentation to us. Two years prior, visual acuity was 20/30 in the right eye and 20/25 in the left eye. On exam at her visit with us, visual acuity had decreased to 20/50 in the right eye and 20/30 in the left eye. Examination revealed bilateral macular atrophy with surrounding hyper- and hypo-autofluorescent deposits evident on fundus autofluorescence (FAF) (Figure 1). The differential diagnosis included dry AMD, Stargardt-like maculopathy, pattern dystrophy, and PPS maculopathy. The extent of macular atrophy in this almost 70 year old woman, lack of typical drusen, and FAF pattern did not support a diagnosis of AMD. Her clinical presentation was consistent with pentosan polysulfate sodium (PPS) maculopathy. Review of available previous images demonstrated continued progression of the maculopathy after PPS discontinuation (Figures 1A-C). FAF demonstrated atrophy in both eyes 18 months after PPS discontinuation (Figure 1A), as well as its progression over the subsequent six months (Figures 1B-C). Figure 1D shows the progression of the retinal pigment epithelial atrophy from 18 to 24 months.

Genetic testing using the Blueprint Genetics (Helsinki, Finland) My Retina Tracker Panel, a broad next-generation sequencing (NGS)-based panel, was negative for AMD, also ruling out any possibility of pattern dystrophy or Stargardt-like maculopathy. Combined with the lack of typical drusen seen in AMD, her clinical presentation was consistent with PPS maculopathy with evidence of progressive atrophy despite PPS discontinuation two years earlier.

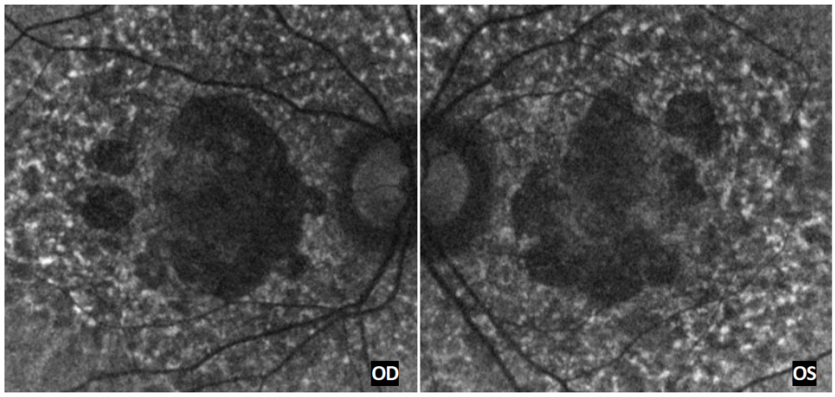

Figure 1A. Fundus autofluorescence images 18 months following PPS discontinuation.

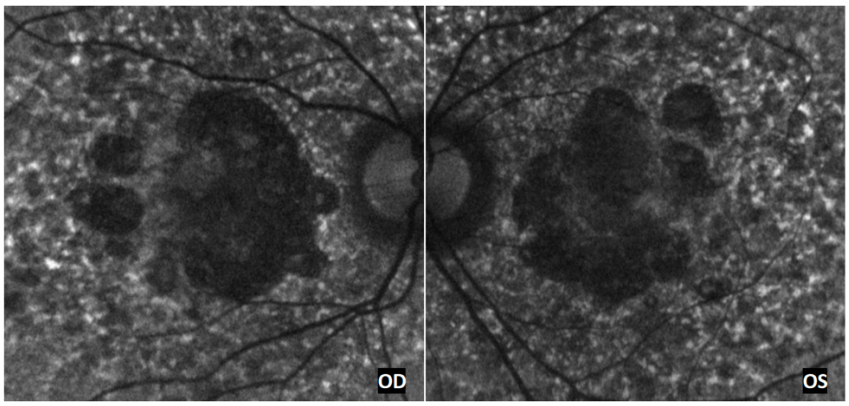

Figure 1B. Fundus autofluorescence images, demonstrating its continued progression over the subsequent 6 months, now 22 months following PPS discontinuation.

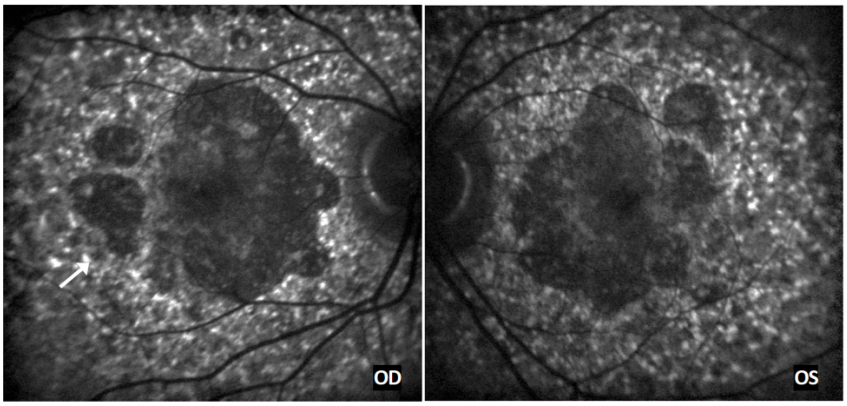

Figure 1C. Fundus autofluorescence images, demonstrating its continued progression over the subsequent 6 months, now 24 months following PPS discontinuation.

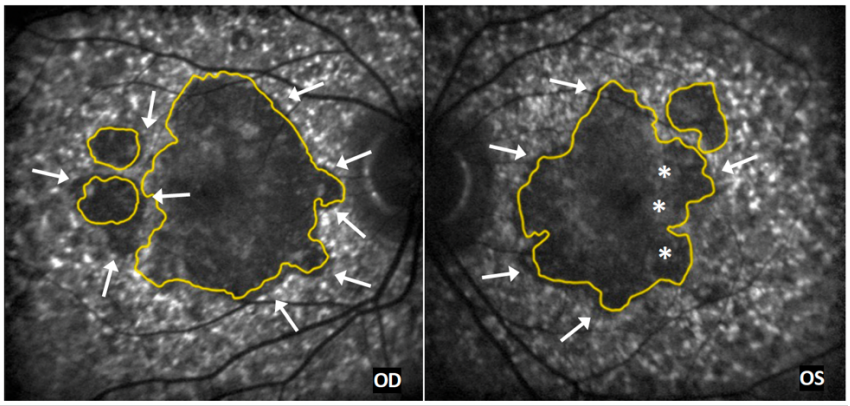

Figure 1D. Areas of progressive atrophy highlighted with arrows and asterisks over the subsequent 6-month period (from months 18 to 24 following PPS discontinuation).

Discussion

We report one of the first known cases of PPS maculopathy in a patient with family history of AMD and demonstrate that PPS maculopathy can continue to progress even after PPS discontinuation. On FAF, characteristic features include bilateral pathology centered on the fovea, paracentral macular hyperpigmented spots, and hypoautofluorescent spots, consistent with prior descriptions of PPS-associated maculopathy on FAF.[4] The lack of typical macular drusen differentiates PPS maculopathy from AMD and in this case, genetic testing confirmed the diagnosis and excluded other potential diagnoses on the differential such as pattern dystrophy and Stargardt-like maculopathy.

The accelerated rate of atrophy over just six months shows the potentially high rate of maculopathy after discontinuation of PPS. Huckfeldt et al. previously reported longitudinal follow-up of PPS maculopathy, even after PPS discontinuation.[6] In our patient, the high dose of PPS prior to discontinuation (400 mg/day for 7 years) may have contributed to the rate of progression of the PPS maculopathy.[7] While the pathophysiology of PPS maculopathy remains poorly understood, biological sex may play a role. In a previous retrospective review, minority females responded to PPS in the same manner as their counterparts but were symptomatic for a longer period of time.[8] In the setting of a family history of AMD, this case highlights the importance of keeping PPS maculopathy in mind when seeing patients taking oral PPS. This case also highlights the value of FAF imaging in establishing a PPS maculopathy diagnosis.

Conclusion

This case demonstrates that PPS maculopathy can masquerade initially as AMD and highlights an approach to distinguish PPS maculopathy from AMD in patients with a history of PPS intake.

References

1. Teichman JM. The role of pentosan polysulfate in treatment approaches for interstitial cystitis. *Rev Urol*. 2002; 4: S21–27.
2. Pearce WA, Hanif AM, Jain N. Re: FDA BRUDAC 2018 Criteria for Interstitial Cystitis/Bladder Pain Syndrome Clinical Trials: Future Direction for Research: J. C. Nickel and R. Moldwin. *J Urology*. 2018; 200: 39–42.
3. Pearce WA, Chen R, and Jain N. (2018). Pigmentary maculopathy associated with chronic exposure to pentosan polysulfate sodium. *Ophthalmology*. 2018; 125(11): 1793–1802.
4. Hanif AM, Shah R, Yan J, et al. Strength of association between pentosan polysulfate and a novel maculopathy. *Ophthalmology*. 2019; 126(10): 1464–1466.
5. Kalbag NS, Maganti N, Lyon AT, Mirza RG. Maculopathy secondary to pentosan polysulfate use: A single-center experience. *Clin Ophthalmol*. 2021; 15: 513–519.
6. Huckfeldt RM and Vavvas DG. Progressive maculopathy after discontinuation of pentosan polysulfate sodium. *Ophthal Surg, Lasers & Imaging Retina*. 2019; 50(10): 656-659.
7. Lindeke-Myers A, Hanif AM, Jain N. Pentosan polysulfate maculopathy. *Surv Ophthalmol.* 2022; 67(1): 83-96.
8. Sant GR. Interstitial cystitis in minority women. *J Assoc Acad Minor Phys*. 1993; 4(3): 89-92.

Statement of Ethics
This case report adheres to patient confidentiality and ethical principles in accordance with the guidelines of the Declaration of Helsinki and relevant local regulations. Written consent was obtained from the patient for the publication of this case report.

Conflict of Interest Statement
The authors declare no conflicts of interest related to this topic.

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Authorship
We attest that all authors contributed significantly to the creation of this manuscript, each having fulfilled the criteria as established by the ICMJE.