Macular toxicity secondary to long-term use of Pentosan Polysulfate Sodium (Elmiron)

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INTRODUCTION

Pentosan Polysulfate Sodium (PPS) is the only FDA approved oral treatment for bladder pain associated with interstitial cystitis (IC) since 1996. IC is a condition that affects over 1 million people in the US alone with a strong female predilection. Although rare, recent studies have shown macular toxicity due to the prolonged use of PPS. Toxic effects of PPS include blurry vision, prolonged dark adaptation, decrease in contrast sensitivity, subjective color vision defects, and central scotomas. PPS maculopathy is often misdiagnosed as age related macular degeneration (AMD) or pattern dystrophies due to similar looking fundus appearance on fundus examination of paracentral pigment clumps with yellow orange subretinal deposits. This case highlights a patient who was diagnosed with PPS maculopathy secondary to chronic use of PPS for IC.

CASE REPORT

A 67-year-old Caucasian female presented for a new low vision exam. Her chief complaint was blurry distorted vision at distance and near, difficulty seeing specific colors, light to dark adaptation and nausea when using the computer for more than 20 minutes. Medical history was remarkable for asthma, migraines, fibromyalgia, and IC for which the patient was taking PPS since 2010; the total cumulative dose was unknown as she self-discontinued PPS in 2020. Other medications included: Bupivacaine 0.25%, Tizanidine HCL, Fluticasone-Salmeterol, Atenolol, Amitriptyline, Docusate, Estradiol, Aspirin, Hyophen, Probiotics, Bilberry, Vitamin D, Fesoterdine Fumarate, Phenazopyridine, Marshmallow root, Dexilant, and Restasis. Ocular history was remarkable for optic disc anomaly with longstanding decreased vision OD, dry eyes OU, and previously diagnosed (2017) pattern dystrophy OU. Patient family history was remarkable for Glaucoma (father). Allergies: Opioids, shellfish, sulfas, animal dander and IV contrast.

OCT findings commonly show:

Pertinent Findings			
BCVA @ D	OD: 5/160 (20/640) OS: 20/25 OU: 20/25	**BCVA @ N:** .4m/.4M (20/20)	**EOM's:** FULL OU
Trial Frame Refraction	OD: +4.75 -4.00 x055 OS: +4.25 -3.75x056 ADD: +2.50	**Pupils:** ERRLA OU **CF:** FTFC OU	**Contrast tested with MARS:** OD: 0.16 - Profound CS loss OS: 1.28 - Moderate CS loss
Anterior Segment Findings: 1+ Cortical cataract/1+ NS cataract OU			

Posterior Segment Findings		
OD	DFE Findings	OS
PVD	Vitreous	Clear
severe inferior tilt of disc	Optic Nerve	flat, sharp, good color. (-) pallor
difficult to assess due to staphyloma	C/D	.4/.4
central pigment mottling of macula with extensive inferior atrophy, no drusen, CNVM, or hemes	Macula	**pigmentary macular changes with reticular pattern like subretinal yellow lesion, no drusen, CNVM, or hemes**
Normal vessels	Vessels	Normal vessels
peripheral ST operculum like opacity w/o associated tear/detachment	Periphery	pigmentary changes inf & sup temp

- Hyper-reflective nodules at the level of the RPE that colocalize with macular pigment clumps noted on DFE
- RPE lesions that are distinct from typical drusen and subretinal drusenoid deposits and project a shadow to the underlying choroid
- Loss of definition of the interdigitation zone or a merging of interdigitation zone and ellipsoid zone bands in diseased areas.

OCT:
OD blunted foveal reflex with patchy GA, RPE irregularities, (-) fluid. (-) drusen;
OS: blunted foveal reflex with patchy outer retinal loss, RPE irregularities, (-) fluid. (-) drusen
FAF was deferred due to concerns about migraines.

FIGURE 3A & 3B

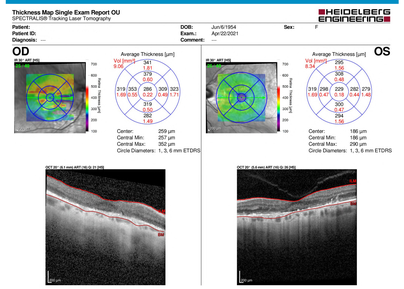


FIGURE 1A & 1B

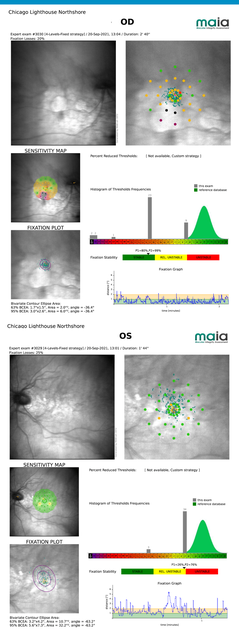


FIGURE 2A

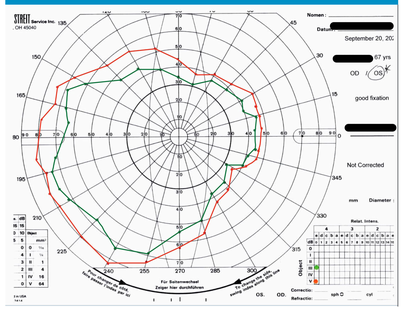


FIGURE 2B

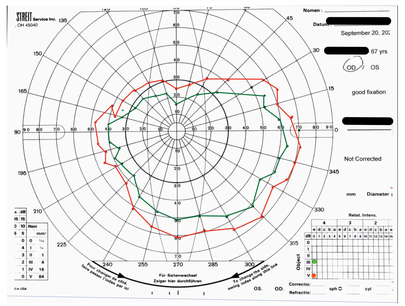
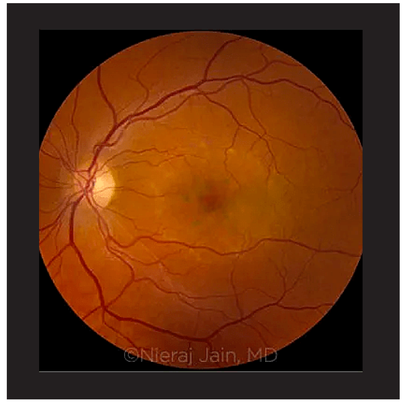


FIGURE 4A



- Funduscopic findings: Paracentral hyperpigmented spots often with interspersed pale-yellow or orange deposits. Patchy para central RPE atrophy. Parafoveal geographic atrophy that ultimately encroaches on the fovea in more advanced cases. Absence of typical macular drusen.

DIFFERENTIAL DIAGNOSIS

1.Pattern Dystrophy
2. Age-related macular degeneration
3. Maternal inherited diabetes and deafness syndrome (MIDD)
4. Pachychoroid disease.

DIAGNOSIS

1. Pentosan Polysulfate Maculopathy (dx in 2020)
2. Optic nerve anomaly - reduced vision OD
3. Bilateral central scotomas
4. Impaired contrast sensitivity

TREATMENT AND MANAGEMENT

1. Discussed the different methods of patching OD when doing near work to relieve discomfort d/t difference in VA/CSF between eyes. Educated patient on cloth patches, taping OD lens, Band-Aids.
2. Continue use of current PAL's.
3. Prescribed 1.5x ruler line reader for enhanced near magnification
4. Patient purchased check book cut out line guide to help with isolating numbers while working.
5. Emailed patient options for anti-glare screen for iPad and computer
6. Continue care with managing providers as directed

DISCUSSION

PPS maculopathy is unique and is strongly associated with chronic PPS exposure and not IC itself. Studies show that PPS exposure emerged as the sole statistically significant predictor of this maculopathy. The mean duration of PPS intake among patients that were affected was 18.3 years, but maculopathy has been shown in patients on PPS in as little as three years. PPS exposed patients were found to have significantly increased risk of being diagnosed with a new macular disease at 7 years. Despite the uncertainty of the mechanism in which PPS maculopathy occurs, PPS maculopathy progresses even after cessation of use may implicate retained toxic compounds, or that the process once began triggers relentlessly progressive retinal degeneration. Multi-modal imaging with color fundus photography, FAF and OCT have been shown to help aid in the diagnosis of PPS.

CONCLUSION

Given the emerging evidence of PPS induced macular toxicity, it is imperative that clinicians are diligent in about acquiring a thorough medication history and specifically question patients about PPS use when maculopathy is present to differentiate between other maculopathies. A baseline spectral domain optical coherence tomography and fundus autofluorescence should be performed on patients when initializing treatment of PPS for IC. Additionally, once PPS induced macular toxicity has been confirmed as the diagnosis, a prompt referral to the prescribing physician should be made to consider alternate therapies for IC. Unfortunately, PPS maculopathy is permanent and can progress despite the discontinuation of the drug.

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