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Two cases of severe Purtscher-like retinopathy demonstrating recurrence and progression to neovascularization and vitreous hemorrhage

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A R T I C L E   I N F O

A B S T R A C T

Purpose: To report the clinical course of two cases with Purtscher-like retinopathy (PLR), associated with peritoneal dialysis (PD), demonstrating disease recurrence and progression to neovascularization and vitreous hemorrhage.

Observations: Case 1 (45-year old woman) experienced acute bilateral vision loss. Medical history included hypertension, end-stage renal failure (ESRF), PD, and obstructive sleep apnea. Visual acuity (VA) was 20/100 OD, 20/80 OS. Fundus findings were pathognomonic for PLR and included white streaks within arterioles. Nine months later, repeat imaging demonstrated disease recurrence and progression, including increased ischemia and new retinal neovascularization. The patient was managed with pan-retinal photocoagulation, sleep apnea treatment, and oral corticosteroids. Four months later, VA remained stable without additional progression.

Case 2 (74-year old woman) experienced acute bilateral vision loss. Medical history included hypertension, ESRF, and PD, complicated by peritonitis. VA was 20/25 OD, 20/32 OS. Fundus findings were pathognomonic for PLR and included white streaks within arterioles. Three months later, further acute vision loss occurred, coinciding with recurrent peritonitis. Repeat imaging revealed disease recurrence and progression, including severely increased retinal ischemia. The PD cather was removed and the patient converted to hemodialysis. Bilateral vitreous hemorrhage later complicated the course.

Conclusions and importance: PLR can occur in association with PD, particularly in acute peritonitis. Contrary to classical descriptions, PLR may take a chronic and progressive course, with increasing ischemia and progression to neovascularization or vitreous hemorrhage. Increased surveillance for complications is recommended and treatment of neovascularization may be required.

1. Introduction

Purtscher's retinopathy is a rare micro-occlusive vasculopathy that occurs following trauma, with the term Purtscher-like retinopathy (PLR) used for similar presentations observed in non-traumatic conditions. Patients present with acute, often bilateral, vision loss of variable severity. Fundoscopic signs include pathognomonic Purtscher flecken, cotton-wool spots, and retinal hemorrhages concentrated primarily in the posterior pole.[1,2] Although the pathogenesis remains uncertain, one prevailing theory involves embolic occlusion of precapillary arterioles by complement-activated leukoaggregates.[3] The disease course is typically described in the literature as self-limited following the initial event, with resolution of acute signs and stabilization of visual acuity occurring within the first few months.[1] Cases are generally not expected to progress to neovascularization or vitreous hemorrhage. Observation along with medical management of any underlying systemic condition is the standard approach, though systemic corticosteroids have been used in certain cases.[1,2]

Here, we report the clinical course of two patients with PLR associated with a combination of vascular and inflammatory risk factors including, in both cases, end-stage renal failure (ESRF) requiring peritoneal dialysis (PD). Both cases took an unusually chronic and severe course, with subsequent appearance of new fundoscopic lesions and worsening of retinal ischemia on angiography. One patient progressed to bilateral retinal neovascularization requiring pan-retinal photocoagulation (PRP), and the other patient developed bilateral vitreous hemorrhages several months after the initial presentation.

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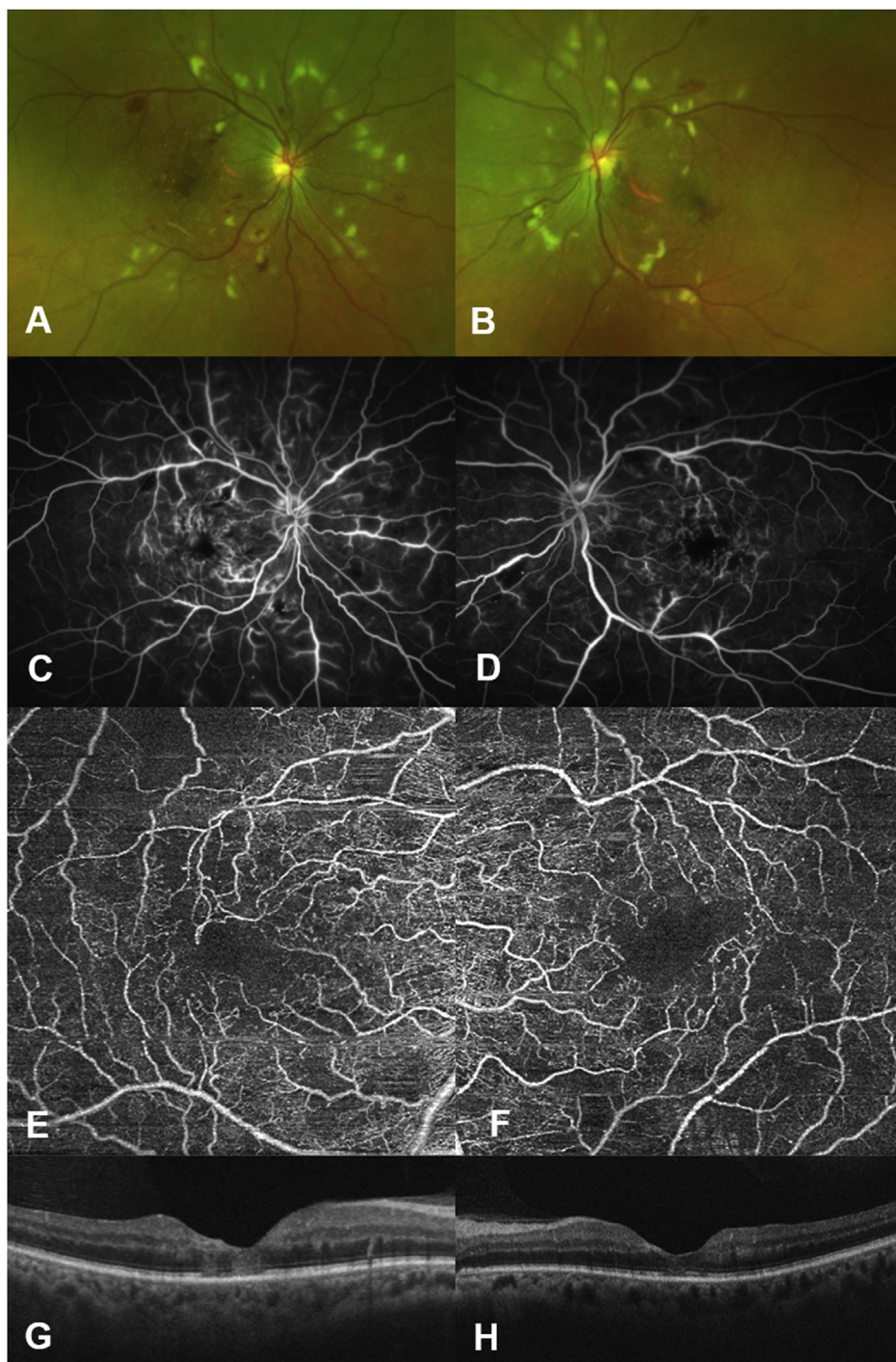 *E-mail address:* tiarnan.keenan@nih.gov (T.D. Keenan).

Fig. 1. Case 1 images at presentation. (**A** and **B**) Fundus photographs of the right and left eyes demonstrate Purtscher flecken, cotton-wool spots, and flame hemorrhages, as well as hyper-reflective lesions in the posterior pole and white streaks within several branch arterioles. (**C** and **D**) Ultra-wide-field fluorescein angiography shows patches of capillary non-perfusion and late perivenous leakage. (**E** and **F**) 6 × 6 mm spectral-domain optical coherence tomography angiography (SD-OCTA) shows areas of capillary non-perfusion in the maculae. (**G** and **H**) SD-OCT reveals patchy partial attenuation of the ellipsoid zone band, hyper-reflective bands in the inner and outer retina, and mildly disrupted inner retinal lamination without frank cystic macular edema.

2. Findings

2.1. Case 1

A 45-year old African American woman was referred for the evaluation of acute painless vision loss in both eyes that had developed three months earlier. There was no history of trauma. Her medical history included hypertension leading to ESRF requiring PD, secondary anemia (receiving erythropoietin injections), secondary hyperparathyroidism, intracranial aneurysm (treated with therapeutic occlusion of the left internal carotid artery 13 years earlier), and previous polyclonal gammopathy (i.e., negative for multiple myeloma). She was taking aspirin 81 mg daily.

Best-corrected visual acuity (BCVA) was 20/100 OD and 20/80 OS. Fundus examination revealed symmetrical findings in both eyes: Purtscher flecken, cotton-wool spots, flame hemorrhages, and multiple scattered tiny white lesions, all concentrated predominantly in the posterior pole, as well as prominent white streaks within some branch arterioles (Fig. 1A and B). Ultra-wide-field fluorescein angiography (UWFA) demonstrated patches of capillary non-perfusion and late perivenous leakage (Fig. 1C and D). Spectral-domain optical coherence tomography angiography (SD-OCTA) showed areas of capillary non-perfusion in the maculae (Fig. 1E and F). SD-OCT revealed patchy partial attenuation of the ellipsoid zone band (including centrally), several hyper-reflective bands in the inner and outer retina, and mildly disrupted inner retinal lamination and thickening without frank cystic
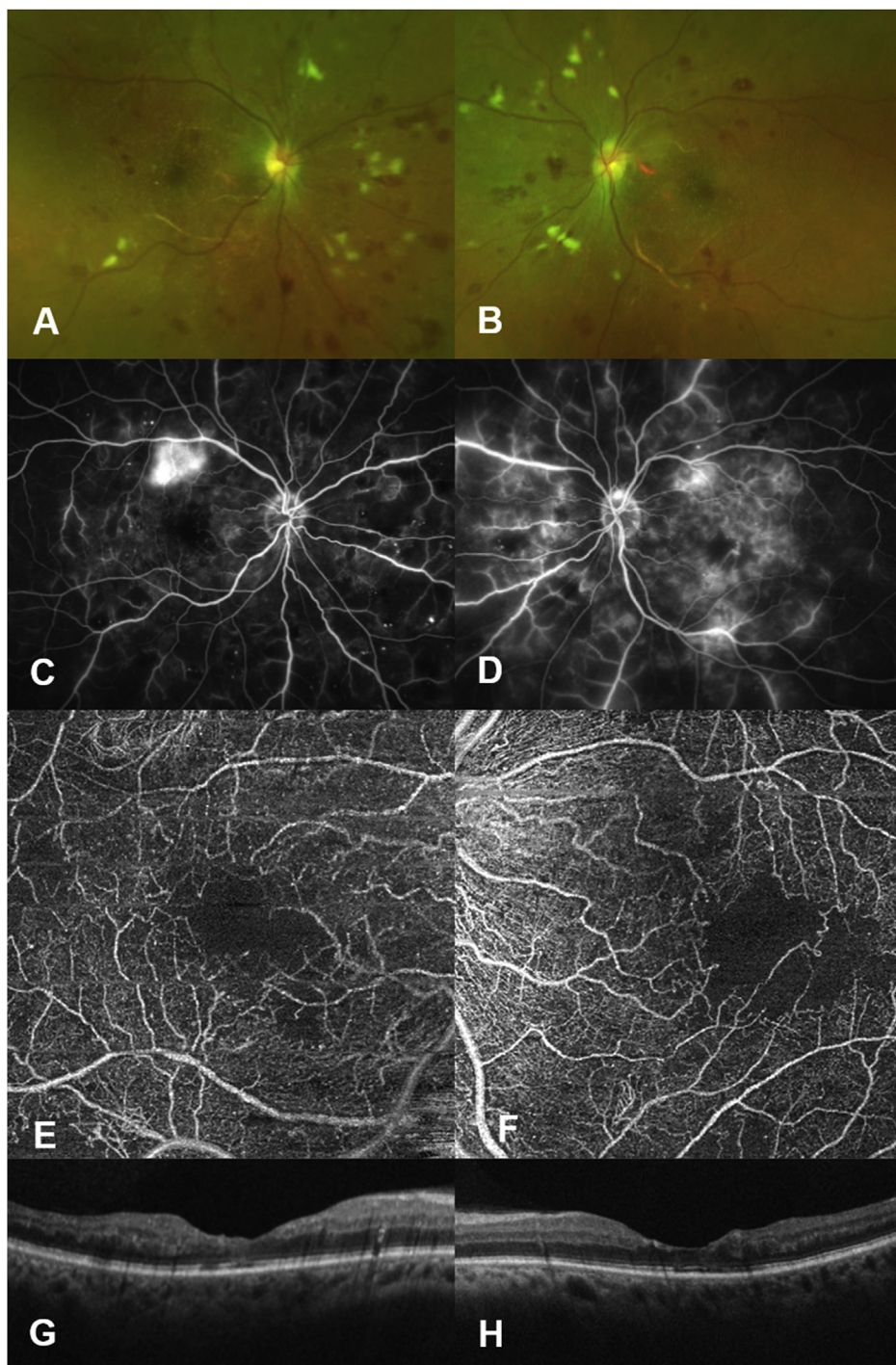
Fig. 2. Case 1 images 6 months after the initial visit. (**A** and **B**) Fundus photographs of the right and left eyes show new hemorrhages and neovascularization along the supertemporal arcades. (**C** and **D**) Ultra-wide-field fluorescein angiography confirms areas of neovascularization and reveals patches of capillary non-perfusion now extending peripherally. (**E** and **F**) 6 × 6 mm spectral-domain optical coherence tomography angiography (SD-OCTA) shows increased areas of capillary non-perfusion in the maculae, and the inferior edge of neovascularization superiorly in the right eye. (**G** and **H**) SD-OCT shows maintained ellipsoid zone attenuation and diffuse macular thinning.

macular edema (Fig. 1G and H).

Laboratory results included low hemoglobin (10.7 g/dL), normal platelet count, elevated erythrocyte sedimentation rate (ESR) (95 mm/hr), and normal lipid profile. Extensive autoimmune, hypercoagulable, and infectious workups were negative, including the absence of systemic lupus erythematosus (SLE) or other rheumatic diseases, except for mildly elevated levels of homocysteine (expected in ESRF) and angiotensin converting enzyme (with normal chest imaging).

Six months later, repeat examination and imaging demonstrated clear evidence of disease recurrence and progression. Although BCVA was relatively stable at 20/100 OD and 20/63 OS, new retinal hemorrhages and cotton wool spots, along with increased vascular attenuation, were present in both eyes (Fig. 2A and B). UWFA revealed increased severity and extent of capillary non-perfusion, as well as new retinal neovascularization originating from the superotemporal arcades in both eyes (Fig. 2C and D), which were also observed on swept-source OCTA (SS-OCTA) (Fig. 3A–F). SD-OCTA demonstrated increased areas of capillary non-perfusion in the maculae (Fig. 2E and F). SD-OCT showed maintained ellipsoid zone attenuation and diffuse macular thinning, compared with previous SD-OCT images (Fig. 2G and H).

Alongside optimization of her underlying systemic conditions, the patient underwent bilateral PRP and received a course of oral prednisone (initiated at 50 mg/day, tapered over two weeks, owing to side effects). In addition, the patient admitted to non-adherence to continuous positive airway pressure treatment for obstructive sleep apnea and restarted treatment immediately. Two months later, BCVA
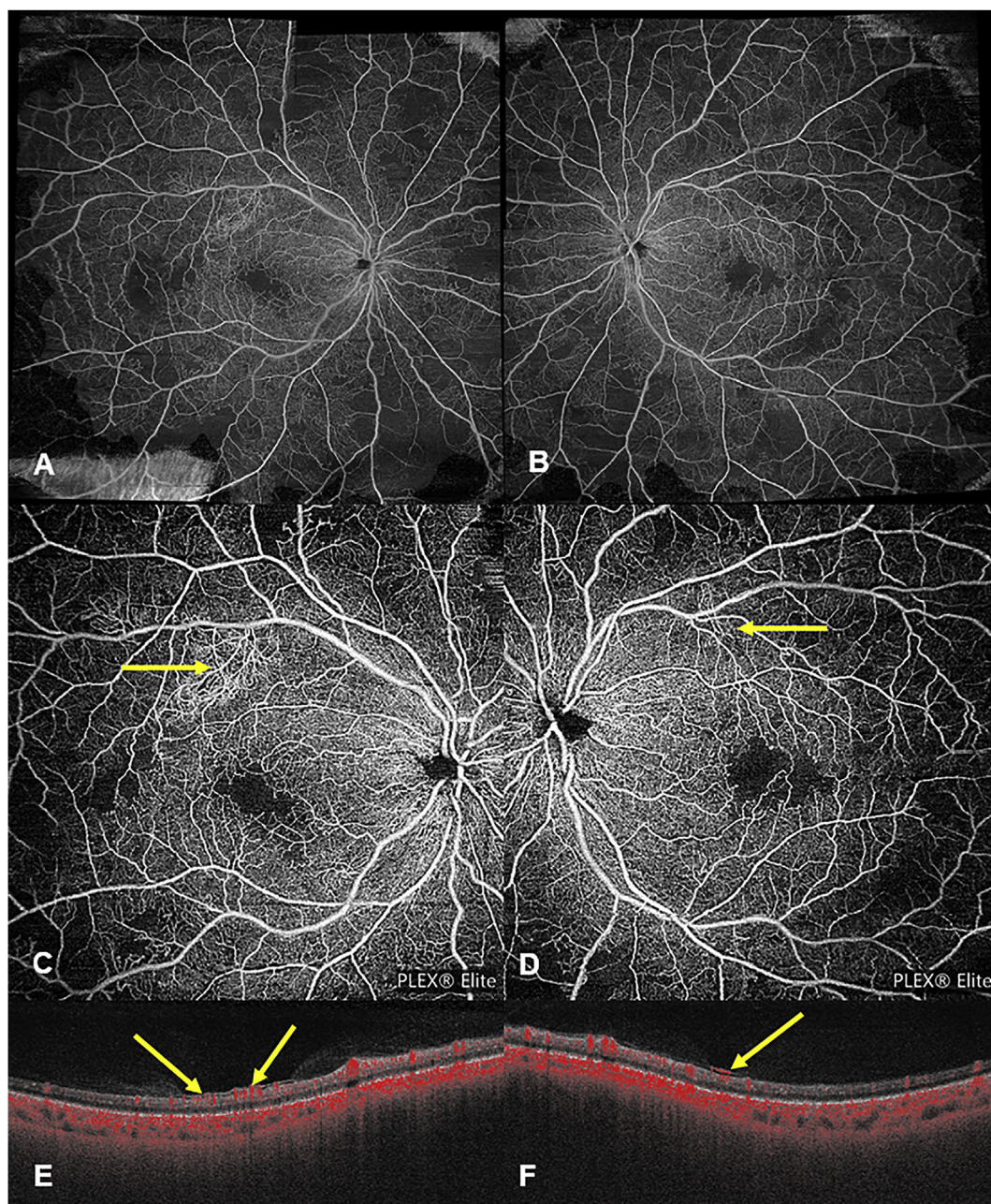
Fig. 3. Case 1 swept-source optical coherence tomography angiography (SS-OCTA) images six months after the initial visit: (**A** and **B**) montage of five 12 × 12 mm SS-OCTA scans shows patches of capillary non-perfusion most pronounced outside the posterior pole; (**C** and **D**) central 12 × 12 mm scans, showing neovascularization along the superotemporal arcades (yellow arrows) in both eyes; (**E** and **F**) corresponding B-scan images showing the neovascular vessels (yellow arrows) in the posterior hyaloid face with positive flow signals (red). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

remained stable at 20/80 OD and 20/63 OS, and no further acute events or disease progression were observed on examination or imaging.

2.2. Case 2

A 74-year old Asian woman was referred for the evaluation of acute, painless vision loss affecting the whole visual field in both eyes that had developed two weeks earlier. There was no history of trauma. Her medical history included hypertension leading to ESRF requiring PD, secondary anemia (receiving erythropoietin injections), gout, and chronic hepatitis B. She was taking aspirin 81 mg daily. Notably, she had been diagnosed with PD-associated peritonitis several days after

the onset of visual symptoms and had commenced intravenous antibiotics.

BCVA was 20/25 OD and 20/32 OS. Fundus examination revealed symmetrical findings in both eyes resembling those seen in Case 1: Purtscher flecken, cotton-wool spots, flame hemorrhages, and scattered tiny white lesions, all concentrated predominantly in the posterior pole, as well as very prominent white streaks within most branch arterioles (Fig. 4, A–D). UWFA showed relatively few patches of capillary non-perfusion, but definite late perivenous leakage in both eyes (Fig. 4E and F), and SD-OCTA also suggested areas of capillary non-perfusion in the maculae (Fig. 4G and H). SD-OCT revealed patchy partial attenuation of the ellipsoid zone band (including centrally OS), scattered intraretinal hyperreflective foci, and mildly disrupted inner retinal lamination and
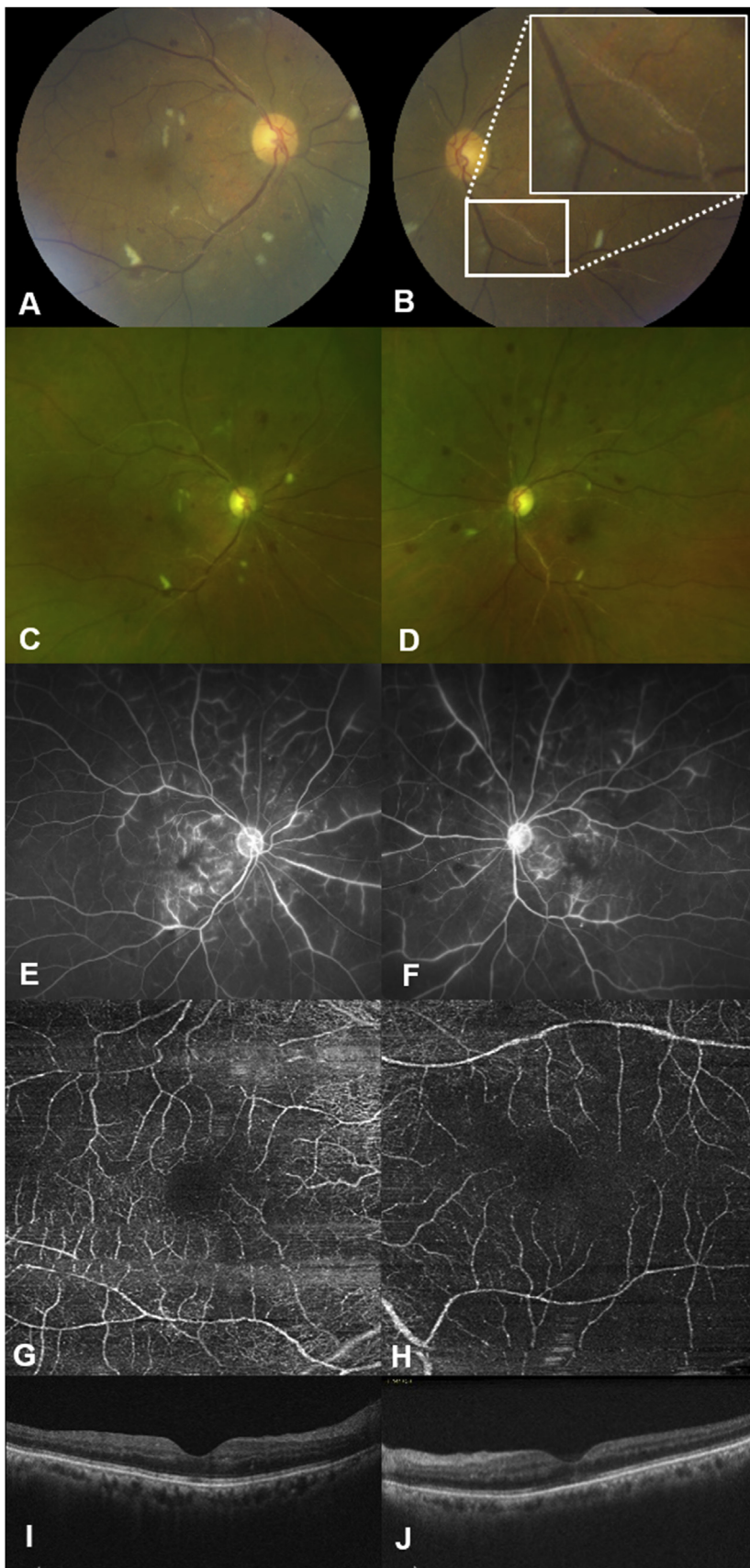
Fig. 4. Case 2 images at presentation. (**A** and **B**) Topcon and (**C** and **D**) Optos fundus photographs of the right and left eyes show Purtscher flecken, cotton-wool spots, flame hemorrhages, and scattered tiny white lesions in the posterior pole, as well as white streaks visible (showcased in **B**) within most branch arterioles. (**E** and **F**) Ultra-wide-field fluorescein angiography shows few patches of capillary non-perfusion with late perivenous leakage. (**G** and **H**) 6 × 6 mm spectral-domain optical coherence tomography angiography (SD-OCTA) shows areas of capillary non-perfusion in the maculae. (**I** and **J**) SD-OCT shows patchy partial attenuation of the ellipsoid band, scattered intraretinal hyperreflective foci, and mildly disrupted inner retinal lamination and thickening without frank cystic macular edema.
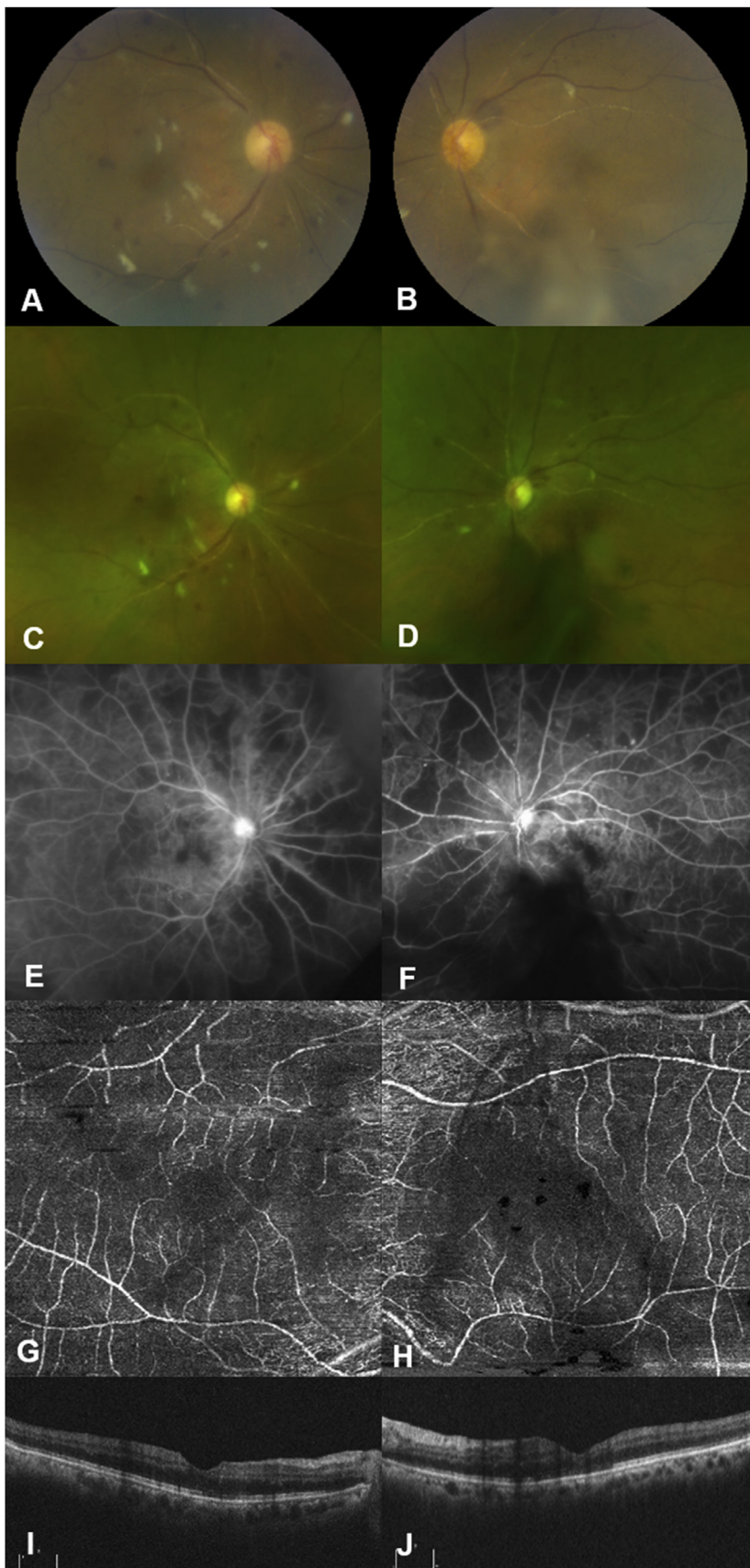
Fig. 5. Case 2 images 3 months after the initial visit. (**A** and **B**) Topcon and (**C** and **D**) Optos fundus photographs of the right and left eyes show new Purtscher flecken, cotton-wool spots, and flame hemorrhages, with increased white streaks in the branch arterioles and apparent obliteration of several vessels. (**E** and **F**) Ultra-wide-field fluorescein angiography reveals severe progression of the capillary non-perfusion, particularly in the mid-periphery and with increased macular involvement. (**G** and **H**) 6 × 6 mm spectral-domain optical coherence tomography angiography (SD-OCTA). (**I** and **J**) SD-OCT shows slightly increased macular thickening but without frank cystic macular edema. (**B**, **D**, **F**, **H**, and **J**) Shadow artifact is visible inferiorly from resolving vitreous hemorrhage in the left eye.

thickening without frank cystic macular edema (Fig. 4I and J).

Laboratory results included low hemoglobin (8.6 g/dL), normal platelet count, elevated ESR (102 mm/hr) and C-reactive protein level (125 mg/L, both consistent with peritonitis), normal lipid profile, and normal serum amylase level. Extensive autoimmune, hypercoagulable, and infectious workups were negative, including the absence of SLE or other rheumatic diseases, except for positive lupus anticoagulant (not unexpected with active infection).

One month later, she had signs and symptoms of left vitreous hemorrhage, possibly related to episodes of vomiting. BCVA was 20/32 OD and counting fingers at two feet OS. The vitreous hemorrhage cleared over two weeks. While repeat UWFA did not demonstrate clear retinal neovascularization in either eye, some increasing hyperfluorescence was present at both optic discs. However, ophthalmoscopy and color fundus photography showed vascular congestion at the left optic disc and, together with SD-OCT imaging of the discs, did not reveal neovascularization.

Three months following the initial visit, the patient described a further gradual deterioration in vision over one week, again affecting the whole visual field in both eyes. Notably, she was diagnosed with a second episode of PD-associated peritonitis during this time, and was treated with intravenous antibiotics, removal of the PD catheter, and initiation of hemodialysis. BCVA was 20/63 OD and 20/125 OS. Fundus examination showed new Purtscher flecken, cotton-wool spots, and flame hemorrhages, with increased vascular attenuation in both eyes (Fig. 5, A–D). UWFA demonstrated severe progression in the extent and severity of capillary non-perfusion, particularly in the mid-periphery and with increased macular involvement (Fig. 5E and F), and SD-OCTA also suggested an increased extent of macular ischemia (Fig. 5G and H). SD-OCT showed slightly increased macular thickening without frank edema (Fig. 5I and J).

Following PD catheter removal and conversion to hemodialysis, the patient achieved remission of peritonitis and further continued optimization of her other systemic conditions. However, over nine months of follow-up elsewhere, she ultimately required bilateral sequential vitrectomy and endolaser treatment for non-clearing vitreous hemorrhage in both eyes, presumed secondary to retinal neovascularization.

3. Discussion

Purtscher's retinopathy and PLR are characterized by acute or subacute vision loss accompanied by patches of retinal whitening and hemorrhage in the posterior pole of patients with trauma or other systemic conditions. Typically, the disease is considered self-limiting following a one-time insult. The retinal appearance generally normalizes within the first few months, as conditions stabilize, with reperfusion of the retina, washout of the inflammatory mediators, and recanalization of the microcirculation. However, more recent reports have emerged of disease progression extending beyond this duration among patients with SLE, Still's disease, and hemolytic uremic syndrome (HUS).[4–7] In these cases, findings have included the development of retinal neovascularization, vitreous hemorrhage, and neovascular glaucoma, as well as progression of retinal ischemia and macular edema. In line with these cases, we discuss two patients without history of SLE, Still's disease, or HUS, who developed severe PLR departing from the classically described disease course.

The reason why certain individuals develop a more chronic and progressive presentation is unclear. However, from these recent reports associating SLE, Still's disease, and HUS with a more protracted course of PLR, it seems likely that ongoing underlying inflammatory and vascular risk factors predisposed these patients to more progressive disease. Indeed, our two patients had several PLR-associated risk factors that presumably contributed to their pathology.

Both patients had ESRF and were, interestingly, undergoing PD. Adult PLR has not previously been related to PD in the literature, to our knowledge. In ESRF patients on hemodialysis, complement activation can occur from the exposure of plasma to hemodialysis membranes, leading to leukocyte aggregation and embolization.[8] In PD, direct complement activation occurs more locally within the peritoneal cavity; however, acute and chronic inflammation can occur systemically following peritonitis, which is a common complication of PD.[9] In addition, both the relative immunosuppression associated with ESRF and the contamination risk propagated by PD catheters predispose to systemic infections, which can then stimulate complement and immunologic activity. This explanation is supported by our case 2 who developed two separate episodes of PLR that coincided temporally with two episodes of peritonitis.

Notably, both our cases had multiple vascular and inflammatory risk factors in addition to ESRF and PD. Given that PLR does not occur in most patients undergoing PD, or even in those complicated by peritonitis, the combination of our patients' risk factors taken together may help explain why they initially developed PLR, and further proceeded to recurrent or progressive disease. In particular, the most relevant factors in case 1 may be obstructive sleep apnea and anemia in an individual with known vasculopathy, while those in case 2 may be anemia and chronic hepatitis. Indeed, obstructive sleep apnea is known to promote chronic systemic inflammation. Additionally, the background of anemia and metabolic imbalances (secondary to ESRF) is known to increase tissue susceptibility to injury during ischemic events.[10] Our cases overall provide additional evidence for the microembolic theory of PLR, with both patients having possessed inflammatory and vascular conditions that may have predisposed them to the formation of complement-induced leukoemboli and the development of variable degrees of occlusive ischemia. Indeed, the very prominent white streaks seen within multiple retinal arterioles of both our patients may represent complement-activated leukoaggregates visible within the arterioles. Of course, it is possible that underlying mechanisms may differ between PLR cases, according to the underlying etiology.

With regards to management, classical descriptions of Purtscher's retinopathy and PLR typically call for conservative management and relatively infrequent surveillance, due to the general expectations against disease recurrence or progression to neovascularization. However, in the context of more recent reports of PLR demonstrating progression in SLE, Still's disease, and HUS, an increased awareness of potential complications is required. In these reports, all patients received at least systemic steroids, anti-VEGF injections, or PRP.[4–7] Our two cases lend strong support to the idea that certain eyes may subsequently develop increasing ischemia and neovascular disease potentially requiring treatment, and increased vigilance is necessary.

4. Conclusions

These cases demonstrate that, contrary to classical descriptions, PLR may take an unusually chronic and progressive course, with the appearance of new retinal lesions, worsening of ischemia, and progression to neovascularization or vitreous hemorrhage. The disease course may strongly depend on both the specific cause and the underlying background of systemic vascular and inflammatory risk factors. This is the first description of adult PLR in association with PD, but additional systemic factors likely contributed to our patients' atypical presentations. Increased surveillance for disease complications is recommended and treatment of neovascular disease may be required.

Patient consent

The patients consented to publication of the cases in writing.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

None of the authors has any financial disclosures.

Acknowledgements

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