A Scleroderma Patient with Sudden Loss of Vision in Both Eyes

Weng-Nga Lao, Man-Lung Yip, Andrew Kui-Man Wong

Abstract: Scleroderma is a multi-systemic disease. Patients with evidence of major internal organ involvement have increased risks of significant morbidity and mortality. Sudden bilateral painless loss of vision is an uncommon presentation of systemic sclerosis. We reported a case of autoimmune painless loss of vision in the form of Purtscher’s like retinopathy in a scleroderma patient with major internal organ involvement.

Keywords: Autoimmune retinopathy, Purtscher's retinopathy, Scleroderma

Case History

A 49- year- old housewife, with history of treated cutaneous tuberculosis, left hemi-thyroidectomy for thyroid colloid nodules and uterine fibroid, presented to us in June 2007 with symmetrical polyarthralgia, Raynaud’s phenomenon, progressive skin thickening over her hands, forearms, legs, trunk, neck and face for six months. She also reported generalized fatigue, shortness of breath on exertion, and occasional acid regurgitation. She did not experience any malar rash, photosensitivity, alopecia, recurrent oral ulcers, sicca symptoms or proximal muscle weakness. Her elder sister has a history of Rheumatoid Arthritis and is on treatment.

Physical examination revealed tightening of skin over her hands, forearms, trunk, legs, neck, and face. Raynaud’s phenomenon was noted over her fingers with skin cracking of the fingertips. However, no digital gangrene or nail fold infarcts were detected. Prominent synovitis was detected over the small joints of her hands. Fine crepitations were heard over her lung bases.

Laboratory investigations revealed a positive anti-nuclear antibody (ANA) at 1:320. Rheumatoid Factor (RF) was negative. Anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody was not elevated. Anti-extractable nuclear antigen (anti-ENA) antibody was negative. Complements C3 and C4 levels were normal. Erythrocyte sedimentation rate (ESR) was elevated at 94 mm/hr. C-reactive protein (CRP) was normal. Lupus anticoagulant was negative. Anti-cardiolipin immunoglobulin G was negative.

Baseline Chest X-Ray was unremarkable. X-Ray of her hands and wrists did not demonstrate any bony erosion. Barium swallow showed mild dilatation at mid-esophagus while the mucosal pattern remained unremarkable. Full lung function test revealed a severe diffusion defect as evidenced by a depressed carbon dioxide diffusion capacity (DLCO) as 44% predicted value, and a restrictive total lung volume at 75% predicted.

High Resolution Computed Tomography (HRCT) of thorax revealed subpleural linear to reticular shadows compatible with pulmonary fibrosis in the right middle lobe, right lower lobe and left lower lobe. There were no ground glass opacities. Electrocardiography (ECG) and echocardiogram did not show any evidence of pulmonary hypertension. A diagnosis of scleroderma with interstitial lung disease was made.

She was given oral diltiazem for relief of Raynaud's phenomenon and oral colchicine for sclerodactyly. Low dose prednisolone 5 mg once daily and cyclosporine A were
commenced for the treatment of small joint arthritis and sclerodactyly.

She was admitted in October, 2007 for fever, productive cough with whitish sputum. Chest X-Ray showed haziness over both lower lobes. She was treated as chest infection with a course of oral antibiotics. Sputum culture was negative.

Her respiratory condition deteriorated again two weeks after discharge, with increasing shortness of breath, cough with whitish sputum, and poor exercise tolerance limited to ground level only. More alarmingly, she reported sudden onset of blurred vision over both eyes in the last few days, with inability in reading newspapers and magazines. She could barely recognize faces and failed to tell the time from the clock hanging over the wall. She would manage to count fingers at one arm’s length.

Chest X-Ray showed reticular shadowing over the middle and lower zones of both lungs. Blood gas revealed type I respiratory failure with hypoxaemia. Blood test showed a borderlinely elevated total white cell count at $10.5 \times 10^9/L$ with lymphopenia $0.4 \times 10^9/L$. Her renal and liver function tests were normal. Both viral and atypical pneumonia titres were not elevated, and her sputum culture was not revealing. HRCT of thorax demonstrated the presence of significantly more extensive pulmonary fibrosis at both lower lobes and right upper lobe, and diffuse areas of ground glass opacities mainly over right lung and the lingular segments.

Bronchoscopy did not reveal any endobronchial lesions. Bronchial aspirate was sent for bacterial culture, Ziel-Neelsen stain for acid-fast-bacilli, polymerase chain reaction (PCR) for *Mycobacterium Tuberculosis*, silver stain for *Pneumocystis carinii pneumoniae* (PCP) and cytology. All were negative. Serum anti-HIV antibody was negative.

First ophthalmological assessment was performed on 4th December 2007, showing a diminished visual acuity (VA) with pinhole of 6/36 in both eyes. The intra-ocular pressure was normal. The anterior chamber was clear. Ophthalmoscopy demonstrated the presence of multiple cotton wool spots, as well as dots and blot haemorrhage mainly restricted to the posterior pole of the retina over both eyes, with slightly more severe changes in the right eye. The optic disk was pink without swelling, and there were no florid retinitis changes (See Figures 1a and 1b). Some small vessels were found to be obliterated on magnified view probably due to complement, lymphocyte or platelet activation. The patient’s blood pressure was well controlled in the range of 110-120/70-75 mmHg at that time. A diagnosis of autoimmune retinopathy, Purtscher’s like Retinopathy related to scleroderma was suggested. The differential diagnoses included opportunistic infections e.g. herpes simplex virus (HSV), Cytomegalovirus (CMV), *Pneumocystis carinii pneumoniae* (PCP), *Mycobacterium Tuberculosis*.

![Retinal Photo of the patient's Right Eye at initial presentation](image1a.png)

(a)

![Retinal Photo of the patient's Left Eye at initial presentation](image1b.png)

(b)
The patient's serum amylase level was normal. Serum CMV pp65 antigen was negative. Serum Toxoplasma polyvalent antibody was not elevated. Venereal Disease Research Laboratory (VDRL) was non-reactive.

In view of the presence of: (1) rapidly progressive interstitial lung disease, and (2) bilateral florid autoimmune retinopathy with risk of progressive visual loss, the patient was given intravenous pulsed Methylprednisolone 500 mg once daily for 3 consecutive days, followed by oral prednisolone 40 mg once daily. Upon the second ophthalmological assessment one week later, an improvement in visual acuity of at least twenty percent was recorded in both eyes. VA with pinhole was 6/18 in the right eye and 6/24 in the left eye. Fundoscopy demonstrated reduced severity of cotton wool spots over the posterior pole of the retina, although scattered dots of retinal haemorrhage were still present. In view of both the subjective and objective improvement of visual acuity after pulsed steroid and a negative screening result for opportunistic infection, the ophthalmologist made a diagnosis of "Purtscher's like Retinopathy", a kind of autoimmune retinopathy related to scleroderma.

Substantial improvement in respiratory symptoms and signs was noted after pulsed steroid. Chest X-Ray shadows diminished after treatment, and the patient successfully weaned off oxygen therapy.

Following treatment with systemic steroid, the patient was given intravenous cyclophosphamide at a dose of 0.5 gm per squared meter body surface area, as aggressive therapy for both scleroderma related interstitial lung disease and autoimmune retinopathy.

The patient's visual acuity continued to improve but became static in the sixth week into her treatment with steroid. Repeat fundoscopy showed decreasing extent of cotton wool spots over bilateral eyes. Figures 2a and 2b showed the residual fundal abnormalities after treatment. Her most recent VA with pinhole at 4 months after pulsed steroid was 6/10 in the right eye and 6/15 in the left eye, corresponding to a percentage loss of visual impairment from 60% at initial presentation to around 12% to 20% after 4 months.

Despite a partial recovery of vision and satisfactory control of interstitial pneumonitis, her renal function deteriorated rapidly 2 weeks after high dose steroid, coupled with accelerated hypertension, consistent with scleroderma renal crisis. Multiple anti-hypertensive drugs were implemented including angiotensin converting enzyme inhibitor (ACEI). One month after admission, her serum creatinine climbed upto 818 umol/L and she subsequently required renal dialytic support. Renal biopsy revealed features of thrombotic microangiopathy, compatible with changes in scleroderma (Figures 3a and 3b). There was no recovery of renal function despite regular dialysis upto the writing of this report.

**Figure 2.** (a) Retinal Photo of the patient's Right Eye at 4 months after pulsed high dose steroid. (b) Retinal Photo of the patient's Left Eye at 4 months after pulsed high dose steroid. Both pictures showed a significant resolution of cotton-wool spots and retinal haemorrhages after treatment.
Discussion

Purtscher’s Retinopathy is a rare condition. It was first described in 1910 by Otmar Purtscher, a Tyrolean ophthalmologist, about a middle aged man sustaining brief loss of consciousness and transient visual loss after a minor head injury. He described the retinal findings in this condition as consisting of cotton wool spots and retinal haemorrhage confining to the posterior pole. Pathogenesis was believed to be embolic occlusion of pre-capillary arterioles. This fundal appearance was subsequently identified in other types of trauma, and various non-traumatic systemic diseases (Table 1). In the latter conditions it was described as Purtscher’s like Retinopathy.

In a prospective observational study about the epidemiology, clinical features and outcome of Purtscher’s retinopathy by Agrawal A. and co-workers, the case definition for Purtscher’s Retinopathy was as follows:

1. An associated contributing illness e.g. acute pancreatitis, long bone fracture, orthopaedic surgery,

Figure 3. (a) Renal Biopsy – Renal arterioles showing hypertensive changes, with marked intimal thickening and medial hypertrophy nearly occluding vascular lumens. (b) Renal Biopsy – Glomerulus showing non-specific increase in mesangial cellularity and matrix, with thickening and wrinkling of capillary basement membrane.

Table 1. Known associations with Purtscher’s Retinopathy and Purtscher’s like Retinopathy:

<table>
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<tr>
<th>Head trauma</th>
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<td>Long bone fractures, orthopaedic surgery</td>
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<td>Acute pancreatitis</td>
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<td>Chest compression</td>
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<td>Chronic renal failure</td>
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<td>Haemolytic uraemic syndrome/Thrombotic thrombocytopenic purpura</td>
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<td>Complicated childbirth</td>
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<td>Connective tissue disorders e.g. systemic lupus erythematosus, dermatomyositis, scleroderma, systemic vasculitides, Adult Still’s disease</td>
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<td>Cryoglobulinaemia</td>
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<td>Weight lifting</td>
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<td>Battered baby syndrome</td>
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<td>Orbital Injection e.g of suspended steroid particles, retrobulbar anaesthesia</td>
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chest compression or crush injury

(2) Multiple areas of polygonal retinal whitening between the retinal arterioles & venules (Purtscher flecken) and/or superficial cotton wool spots in one or both eyes
- Typically restricted to the posterior pole
- Accompanied by minimal, if any, retinal haemorrhage
- No visible emboli in the large retinal vessels
- No direct globe trauma

Patients with Purtscher's Retinopathy and Purtscher's like Retinopathy typically present with sudden painless loss of visual acuity (VA) in one or both eyes, ranging from minimal impairment to hand movements visual acuity only. The symptoms may be delayed by 24 to 48 hours from the onset of the associated systemic illness. Visual loss is usually in the form of scotomata which may be central, paracentral, or arcuate. Peripheral visual function is usually preserved.14

The underlying pathogenesis for Purtscher's Retinopathy and Purtscher's like Retinopathy is most likely embolic occlusion of the pre-capillary arterioles restricted to the posterior retina. The emboli generated by the underlying condition are usually of intermediate-sized. This is in contrast to the occlusion of proximal retinal arteries by large emboli in branch arterial occlusion.14 The emboli in Purtscher's retinopathy and Purtscher's like Retinopathy consist of leukocyte-platelet aggregates and fibrin clots as a result of complement activation in underlying inflammatory disorders. Other possible sources include fat emboli in case of long bone fractures and pancreatitis; amniotic emboli during childbirth and postpartum; air emboli from traumatic chest compression. The mechanism involves activation of the clotting cascade, vascular endothelial damage by oxygen free radicals, platelet activation and aggregation. However, the vascular occlusion is usually transient and of insufficient duration to cause fixed retinal infarct.

The fundal abnormalities of Purtscher's Retinopathy include the followings:14

(1) Purtscher flecken which are multiple, discrete polygonal areas of retinal whitening (Cotton Wool spots) of variable size in the superficial aspect of inner retina, between the arterioles and venules.
(2) Retinal haemorrhages are often minimal, typically flame-shaped, but dots and blots may occur.
(3) Optic disc swelling may or may not be present

(4) Lesions (1) and (2) are typically confined to the posterior pole, within the macula and immediately nasal to the optic disc
(5) Most cases are bilateral

Without treatment, these lesions usually resolve spontaneously within 1 to 3 months, subsequently replaced by mottling of retinal pigment epithelium, temporal disc pallor, and attenuation or sheathing of retinal vessels.

Intravenous Fluorescein Angiography (IVFA) shows areas of choroidal hypofluorescence as masked by retinal whitening and haemorrhage, non-perfusion of the smaller retinal arterioles or capillaries, and late leakage from the retinal vessels in areas of ischemia. In most cases, the fundal appearance and an associated systemic illness, plus supporting evidence from IVFA, will be sufficient to make the diagnosis.

Differential diagnoses for Purtscher's Retinopathy and Purtscher's like Retinopathy include other microangiopathies such as diabetic retinopathy, hypertensive retinopathy, HIV retinopathy, retinopathy related to anaemia, but there are usually more haemorrhages or vascular changes and those conditions can be easily ruled out. Purtscher's Retinopathy and Purtscher's like Retinopathy differ from the other diagnoses in that symptoms and signs are often delayed relatively to the systemic event. Many a time there is no direct globe trauma. Visible retinal emboli are frequently absent. The multi-focal fundal lesions are restricted to the posterior retina. Retinal whitening spares the retina immediately adjacent to the retinal arterioles.

Regarding the visual outcomes of Purtscher's Retinopathy and Purtscher's like Retinopathy, variable visual recovery without specific treatment within the first few weeks of initial insult has been reported. Speculation is that VA remains diminished due to infarction of either the foveal photoreceptors or optic nerve itself. Poor prognostic factors consist of: (1) optic disc swelling, (2) leakage seen on IVFA, (3) choroidal hypoperfusion, (4) involvement of outer retina, (5) retinal capillary non-perfusion, (6) a prior episode of Purtscher's retinopathy, (7) persistence of acute retinal changes more than one month after the initial presentation.

No definite guidelines exist for the treatment of Purtscher's Retinopathy and Purtscher's like Retinopathy. Treatment of
A Scleroderma Patient with Sudden Visual Loss

A precipitating condition is essential. There have been isolated case reports of successful treatment using intravenous pulsed methylprednisolone followed by high dose oral prednisolone.\textsuperscript{14, 16,17} The rationale for steroid therapy is that high dose steroid stabilizes damaged neuronal membrane and micro-vascular channels, enabling partial recovery of nerve fibres that have not been damaged irreversibly. In addition, steroid inhibits granulocyte aggregation secondary to complement activation. Beneficial effect is dose-dependent. Currently there is little evidence to support use of systemic steroid routinely.

Acknowledgements

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References