Mixed Retinopathy: A Unique Presentation

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Summary

We describe the case of a 24-year-old male with transplant-associated retinal thrombotic microangiopathy (TMA) secondary to hemodynamic instability following renal transplant. Presenting symptoms were ocular and examination findings were consistent with a Purtscher-like retinopathy. This case demonstrates mixed retinopathy picture of ocular TMA following hypertensive crises post renal transplant along with viral retinitis.

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Keywords: *Thrombotic microangiopathy (TMA), Purtscher-like retinopathy, Viral retinitis*

Case Description

A 24-year-old male with history of hypertension for last 3 years presented to the clinic with gradual diminution of vision OU (oculus uterque) since 1 week. Best-corrected visual acuity (BCVA) was 3/60 in oculus dexter (OD) & 2/60 in oculus sinister (OS). The patient gave history of right side renal transplant 2 months ago and was on oral immunosuppressive therapy (Tacrolimus, Mycophenolate Mofetil and Deflozocort). Physical parameters (pulse, respiration rate) were stable with documented blood pressure (BP) of 170/90 mm Hg. On slit lamp evaluation, anterior chamber cells (grade 1+) were noted with IOP of 19/19 mm Hg (OU). On fundus examination occasional vitreous cells were detected with cotton wool spots, retinal oedema with peri-arteriolar sparing and macular oedema OU. Peri-papillary mylenated nerve fibres were observed in OS. Optical coherence tomography (OCT) showed presence of sub retinal fluid (SRF) with intra-retinal cystoid oedema in both the eyes (OU). On fundus fluorescein angiography (FFA) background choroidal hypo-fluorescence with multiple pin point hyper-fluorescence leaks were observed in the late phase of angiogram in both the eyes with increased foveal avascular zone suggestive of macular ischema OU (Figure 1A, Figure 1B). Blood reports were positive for cytomegalovirus (CMV) and negative for human immunodeficiency virus (HIV). Intravitreal gancyclovir OU along with Tab Valgancyclovir 450 mg twice a day was started on line of CMV retinitis and transplant related medication were advised to continue. Follow up after 2 weeks revealed improvement in BCVA with OD 6/60 and OS 6/36. Anterior segment was unremarkable OU. Fundus examination showed dot haemorrhages and cotton wool spots along with decreased retinal oedema OU. Systemic BP was 140/90 mm Hg. SRF with decreased intra-retinal oedema was picked up on OCT (Figure 2A & 2B). The treatment plan was modified to oral steroids with alternate dosing, gancyclovir was changed to acyclovir and tacrolimus was changed to everlimus considering the toxic effects of the drug. On final visit after 2 months, the patient had BCVA of 6/36 with normal anterior segment OU. OCT confirmed resolved oedema with foveal thinning. FFA was suggestive of macular ischemia (Figure 3A & 3B). The diagnosis of Purtscher-like retinopathy secondary to hypertensive crises with serous retinal detachment caused by transplant-associated thrombotic microangiopathy with CMV retinitis was made.

Discussion

Patients undergoing organ transplantation may present with ocular changes in the preoperative, peri-operative, or postoperative periods.[1] The changes may be either related to the deterioration of retinal diseases occurring prior to

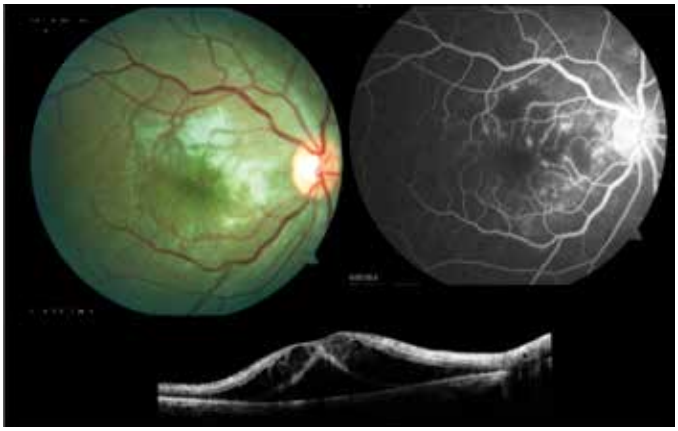


Figure 1a: *Fundus picture of the right eye showing retinal oedema with peri-arteriolar sparing. On OCT, intra-retinal cystoid oedema is apparent. FFA showing multiple pin point hyperfluorescent leaks in the late phases with macular ischemia*

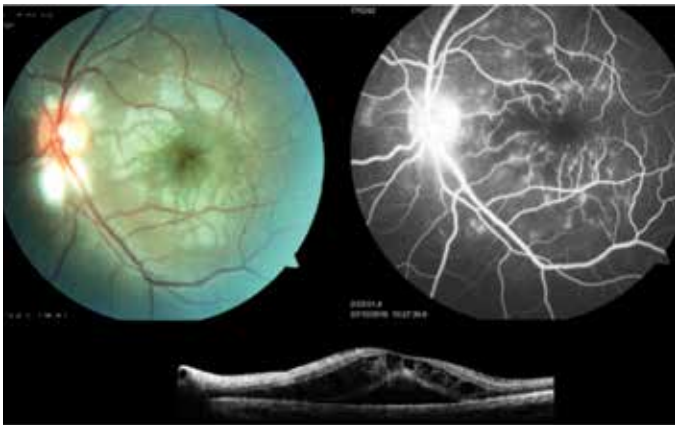


Figure 1b: *Fundus picture of the left eye showing retinal oedema with peri-arteriolar sparing. On OCT, intra-retinal cystoid oedema is apparent. FFA showing multiple pin point hyperfluorescent leaks in the late phases with macular ischemia*

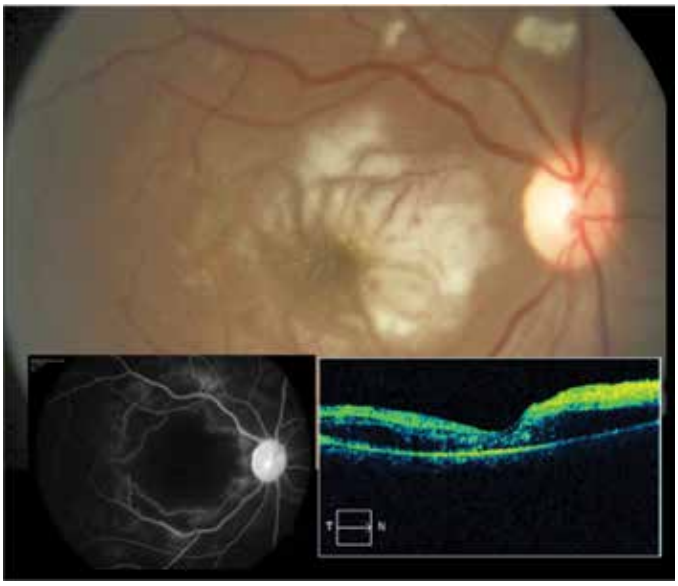


Figure 2a *Two weeks post treatment, the right eye fundus picture showing decreased macular odema with pin point haemorrhages with FFA suggestive of macular ischemia*

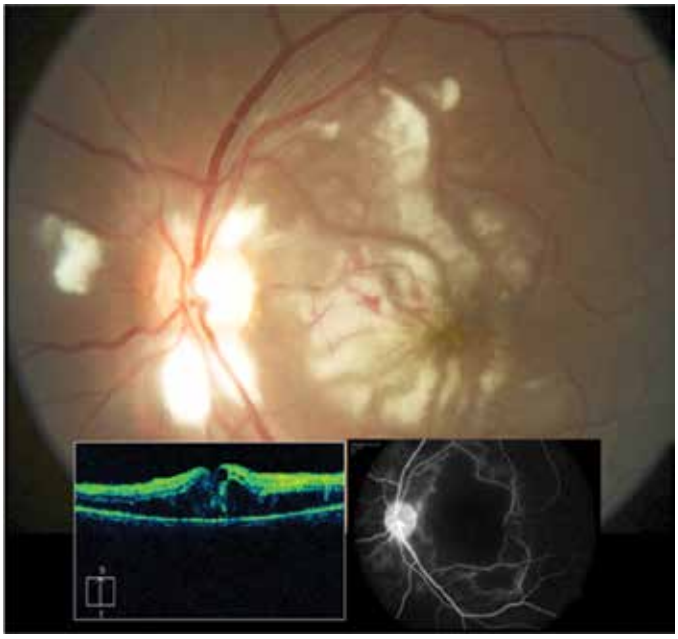
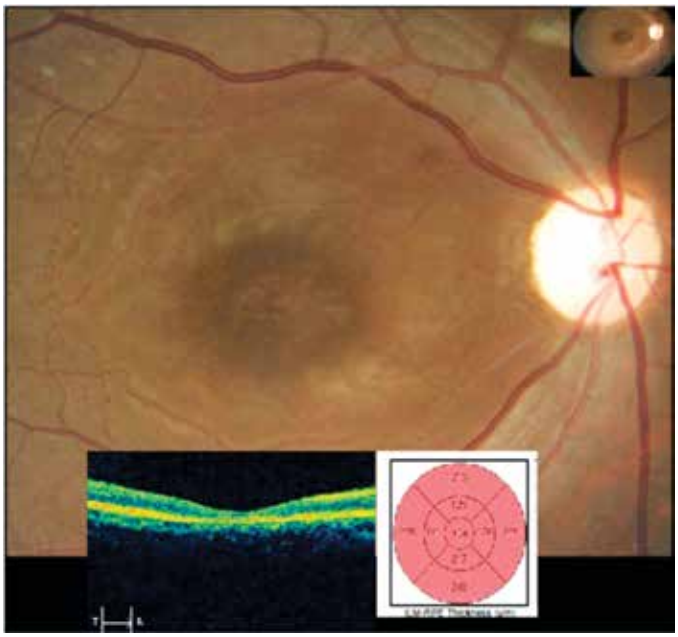


Figure 2b *Two weeks post treatment, the left eye fundus picture showing decreased macular odema with pin point haemorrhages with FFA suggestive of macular ischemia*



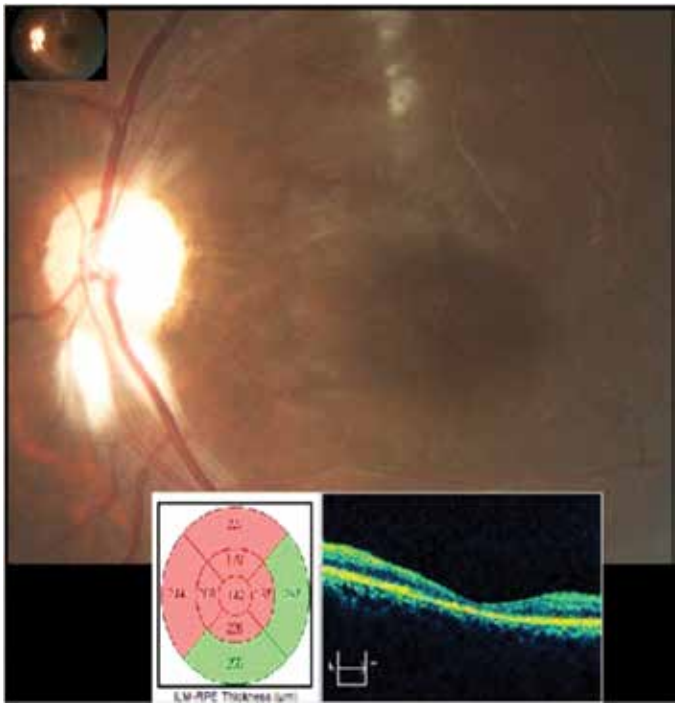


Figure 3: *Post 1 month fundus picture showing dried up macula with ghost vessels signifying macular ischemia bilaterally*

transplantation, or represent complications of the procedure or the treatment started in the postoperative period giving rise to mixed retinopathy picture. Retinal complications of solid organ transplantation may be divided into three main types: microvascular retinopathy, infection, and haematological complications.[2]

Transplant-associated thrombotic microangiopathy (TTMA) is a type of microangiopathy, which includes thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS) and TTMA.[3,4] Patients suffering from ocular TTMA may present as Purtscher-like retinopathy with decreased visual acuity or visual field defect or both. Though very few reports of ophthalmic features in transplant associated microangiopathy have been reported, retinal findings are typically bilateral and symmetric and include multiple cotton wool spots, telangiectasia, microaneurysms, macular oedema, hard exudates, Purtscher flecken and retinal haemorrhages.[5]

Purtscher's retinopathy usually occurs secondary to trauma and presents with cotton wool spots, retinal whitening and retinal haemorrhages. This can be eliminated from our differential given the absence of trauma. Another

terminology "Purtscher-like retinopathy" is used to describe retinopathy seen in condition other than trauma. Proposed mechanism responsible for this is leukoembolization of pre-capillary retinal vasculature.[6] Several systemic conditions (pancreatitis, systemic lupus erythematosus, collagen vascular diseases, fat or amniotic fluid embolus, chronic renal failure, systemic hypertension, HIV retinopathy, cytomegalovirus (CMV) retinitis, leukemias) have been known to result in a similar fundus appearance, together referred to as Purtscher-like retinopathy. Flecken are multiple discrete areas of retinal whitening in the superficial inner retina, between the arterioles and venules. The typical retinal whitening has a clear zone, which usually exists between the affected retina and an adjacent arteriole.[7] They resolve spontaneously within 1 to 3 months, and may be replaced by mottling of the retinal pigment epithelium, temporal disc pallor, and attenuation or sheathing of the retinal vessel.

Cytomegalovirus is the most common viral infection after kidney transplantation. Clinical presentations of cytomegalovirus infection range from asymptomatic infection to organ-specific involvement. CMV-induced vasculopathy and thrombosis have been reported in both immune-compromised and immune-competent individuals. Thrombosis of the jugular, cerebral, retinal, and upper-extremities veins have been reported as a complication of CMV infection in HIV-infected patients.[8] HIV retinopathy and early CMV retinitis may present with cotton wool spots. Later findings of CMV retinitis include retinal haemorrhages, necrosis and vasculitis. In our case titers for CMV were positive (>50,000 copies/ml) but vasculitis and necrosis was completely absent on retinal examination.

Additionally, the drugs used in the postoperative transplant management may cause retinal damage due to toxicity or lead to the development of retinal diseases secondary to metabolic changes.[9] But in the current scenario, it is very unlikely, given the time period of drug intake is very small. Central serous chorio-retinopathy (CSR) could have been one of the diagnoses in our case considering it presents with stress, anxiety, corticosteroid use, toxicity of immunosuppressive drugs, such as cyclosporine and tacrolimus.[10] In the absence of typical leak pattern and resolving sub retinal fluid (SRF) even on steroid continuation, it makes it an unlikely diagnosis in our case.

Conclusion

Post-transplantation retinal changes found may be related to pre-existing conditions or to complications of the surgical procedure, opportunistic infections, or drug toxicity. Patients in the transplantation program should undergo careful pre and postoperative retinal assessment whenever possible by an ophthalmologist.

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