CASE REPORT

Extensive choroidal infarction in a case of mixed essential cryoglobulinaemia in a postpartum female

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SUMMARY

A case of mixed essential cryoglobulinaemia resulting in massive choroidal infarction and irreversible vision loss in a postpartum female is discussed. Cryoglobulinaemia can rarely involve ocular vessels and, in this case, was adjunctive to mild hypertension in causing acute choroidopathy. Although the systemic condition of the patient improved after steroids and immunosuppressive agents, the visual loss was permanent.

BACKGROUND

Hypertensive retinopathy is important due to its relationship with target end-organ damage due to hypertension and as a guiding marker for systemic complications.¹ Cryoglobulinaemia, characterised by the presence of cryoglobulins in the serum, commonly presents with vasculitis-related damage of the skin or the renal tissue, and rarely affects the ocular vessels.² Herein, we discuss a case of cryoglobulinaemia with mild secondary hypertension complicated by irreversible visual loss due to choroidal infarction in a postpartum female.

CASE PRESENTATION

A 27-year-old female presented with bilateral and severe visual loss since 3 days. She had delivered a healthy male child more than a month back after been diagnosed as pre-eclampsia and having undergone a lower segment caesarean section. The patient was undergoing medical evaluation for proteinuria, renal dysfunction and features of volume overload. On general examination, she was found to have a pulse rate of 100/min, respiratory rate of 24/min and blood pressure of 160/90 mm Hg along with pedal oedema. Systemic examination revealed crepitations in bilateral basal lung lobes, an ejection systolic murmur and shifting dullness on abdominal examination. On ocular examination, her best corrected visual acuity (BCVA) was found to be perception of light with inaccurate projection of rays bilaterally, while anterior segment of both the eyes was normal. Fundus examination of both the eyes revealed papilledema, retinal haemorrhages, patchy choroidal oedema and macular oedema suggestive of severe hypertensive retinopathy with choroidopathy (figure 1A, B).

Three days after the ophthalmic examination, she developed fever, vomiting and petechial rash with palpable purpura associated with pruritus and burning sensation on both the lower limbs.

INVESTIGATIONS

She was extensively evaluated for small vessel vasculitis and was found to have low serum

complement (C3 and C4) levels with highly elevated rheumatoid factor. Although serum cryoglobulins were not detected, renal biopsy showed membranoproliferative glomerulonephritis with immunofluorescence pattern compatible with mixed cryoglobulinaemia. The skin biopsy revealed features of leucocytoclastic vasculitis.

DIFFERENTIAL DIAGNOSIS

Infective endocarditis was ruled after multiple echocardiograms.

Differential diagnosis of choroidopathy and papilledema like malignant hypertension, polyarteritis nodosa, giant cell arteritis, intracranial hypertension and other thrombotic diseases was also ruled out.

TREATMENT

She was, therefore, diagnosed as mixed essential cryoglobulinaemia and given high dose steroids and immunosuppressive therapy with rituximab. Thereafter, her general condition improved with stable blood pressure at 130/90 on oral medication only.

OUTCOME AND FOLLOW-UP

However, 3 months hence, her BCVA had improved only marginally and gradually to 3/60 in the right eye (OD) and 6/36 in the left eye (OS). She developed optic atrophy and triangular wedge-shaped pigmented lesions suggestive of choroidal infarcts in OU (both eyes), with extensive macular involvement in the OD (figure 2A, B). Swept source optical coherence tomography revealed loss of inner choroidal layers, dilated large choroidal vessels and loss of foveal outer retinal layers in the OD, with thin maculas and disorganised retinal layers in OU (figure 3). Prognosis was explained and she was counselled for further immunosuppressive therapy with rituximab.

DISCUSSION

Cryoglobulinaemia can occur secondary to various other systemic disorders and its idiopathic occurrence is referred to as essential cryoglobulinaemia.³ Diagnoses of essential cryoglobulinaemia principally rest on the demonstration of cryoglobulins or the cryocrit.³ However, due to the stringent requirement of the laboratory temperature conditions for the same, there are often false-negative results.⁴ The diagnoses in our case were made on the basis of pathological evidence, skin and renal biopsy results.

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Figure 1 (A and B) Fundus photo of OU depicting severe hypertensive retinopathy, papilledema, macular oedema and choroidal infarcts.

Ocular involvement in cryoglobulinaemia is rare and has been seen as retinal vascular occlusion,² anterior uveitis,⁵ corneal deposits,⁶ central serous chorioretinopathy and pigment epithelial detachment,^{7–8} rubeosis,⁹ scleritis and peripheral ulcerative keratitis¹⁰ and even orbital inflammation.¹¹ Commonly postulated hypothesis for these ocular findings includes ischaemia secondary to paraproteinemia-related hyperviscosity, cryoglobulin-induced inflammation and occlusive phenomenon due to the unusual temperature-dependent globulin solubility.^{2–11} Retinal findings, like cotton wool spots and retinal vascular proliferation, have been reported multiple times,^{12–14} but choroidal ischaemia has not been reported. Although the vision recovered partially in both the eyes, recovery was poor in the OD which had totally lost the foveal outer retinal layers consequent to choroidal ischaemia (figure 3). Loss of the capillary layers and dilated large vessel layers is also a sign of previous acute choroidal injury in the OD.

The 'triangular sign' as wedge-shaped lesions due to infarcts was described by Amalric as evidence of choroidal ischaemia.¹⁵ Such multiple infarcts, as also seen in our case, are characteristic of halted choroidal blood flow. Until, the described aetiology of choroidal infarcts include accelerated hypertension, cocaine abuse, arteritis, periocular injections, ocular tumours, in relation to raised intracranial hypertension, thrombotic diseases and even common therapeutics like refractive surgery and photodynamic therapy. While there were no signs of cryoglobulinaemia-induced vasculitis in our patient, the relatively low levels of blood pressure, surrounding the period of vision loss (systolic around 160–170 mm Hg and diastolic around 90–100 mm Hg; stage 2 hypertension as per the Eighth Joint National Committee),¹⁶ are not sufficient enough to effect a potent vasospasm singularly.

Essential cryoglobulinaemia is known to precipitate acute cerebrovascular ischaemic stroke.¹⁷ Akin to such a pathogenesis, we believe that cryoglobulinaemia complicated the course of the ocular disease in our patient due to hyperviscosity. Current literature lacks regarding temperature of the anterior human suprachoroidal space and it would be conjectural to blame it for precipitation of the cryoglobulins in the long posterior arteries. OCT proved to be useful in planning therapy in this case by

Figure 2 (A and B) Ultrawide images of OU fundus showing massive triangular wedge-shaped choroidal infarcts with altered pigmentation in all the quadrants. Note the optic atrophy.

Figure 3 (A) Swept source optical coherence tomography (SS-OCT) image of the OD showing thin macula, split middle retinal layers and disorganisation and loss of foveal outer retinal layers. Note the loss of choroidal capillaries and dilated large choroidal layers. (B) SS-OCT image of the OS showing splitting and disorganisation of outer and middle retinal layers. Note that outer retinal and choroidal architecture are preserved in comparison to OD (A).

ruling out oedema and confirming the macular atrophy during follow-up. It also highlighted the choroidal vascular changes occurring as a consequence of infarction.

This case presents an interesting additive effect of two morbidities, pre-eclampsia and cryoglobulinaemia, producing a rare occurrence—choroidal infarction. Either one alone may not have been sufficient to cause infarction. Choroidal changes due to eclampsia have been documented with OCT¹⁸ and perfusion changes are known to occur in pre-eclampsia which result in serous retinal and retinal pigment epithelium detachments.^{18–20} The prognosis is generally good with recovery which occurs over weeks to months.²⁰ In an experimental study in monkey eyes, Kishi *et al*²¹ proved histopathologically that choroidal recovery from acute hypertension takes time with a long chronic reparative phase that involves recanalisation of the vasculature. The association between cryoglobulinaemia and pregnancy has been reported before. Patients with known history of cryoglobulinaemia may rarely worsen during pregnancy, while some patients may develop cryoglobulinaemia during pregnancy.²² Activation of complement system can occur during pregnancy and pre-eclampsia.²³ In our patient, the ocular symptoms developed 1 month postpartum after near normalisation of the hypertension and were followed 3 days later by the skin rash. The choroidal infarction resulted in permanent visual loss with partial and gradual recovery. The temporal sequence of events indicates a more than coincidental role of cryoglobulinaemia in causing infarction in an already 'stressed' choroidal vasculature due to recent recovery from pre-eclampsia.

Learning points

- ▶ Choroidal infarction in the absence of malignant hypertension should alert the physician to search for other causes contributing to ischaemia.
- ▶ While such patients may improve systemically with appropriate therapy, visual prognosis largely depends on the functional status of the macula and the optic nerve.
- ▶ Tissue diagnosis may be pathognomonic in a few cases of cryoglobulinaemia, and biological modifiers may arrest the disease progression, thereby preventing further morbidity.

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