COVID-19-associated central retinal vein occlusion treated with oral aspirin

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SUMMARY

This is a case report of central retinal vein occlusion (CRVO) associated with COVID-19 treated with oral aspirin therapy. A 56-year-old woman reported decreased vision in her left eye. Her left eye vision was 6/18, N10. Anterior segment was within normal limits. Left eye fundus was suggestive of CRVO and macular oedema. Optical coherence tomography showed cystoid macular oedema and neurosensory detachment. Blood work-up revealed elevated D-dimer levels and erythrocyte sedimentation rate (ESR). She was started on treatment with low-dose aspirin 150 mg/day. After 1 month, her vision improved to 6/6, N6. Left eye fundus showed reduced retinal haemorrhages and complete resolution of macular oedema. Her repeat blood work-up showed reduced D-dimer and ESR levels. The patient was asked to be reviewed after 3 months. This case highlights that specific treatment for reducing the hypercoagulable state caused by COVID-19 with oral aspirin therapy can result in complete resolution of CRVO macular oedema.

BACKGROUND

Retinal findings following infection with SARS-CoV-2 virus occur due to complement activated thrombotic microangiopathy and hypercoagulable state.[1 2] This can lead to retinal artery and venous occlusions. There are a few papers on retinal vein occlusion associated with COVID-19 infection in literature.[3 4] We report a case of central retinal vein occlusion (CRVO) and macular oedema associated with COVID-19 infection. The highlight of this case is the improvement in visual acuity and macular oedema following reversal of hypercoagulable state with oral antiplatelet therapy.

CASE PRESENTATION

A 56-year-old woman, a healthcare worker by profession in a dedicated COVID-19 hospital in South India, presented to the retina clinic of a tertiary eye care hospital with decreased vision in her left eye for the last 1 month. She was a known diabetic for the past 5 years, well controlled on oral hypoglycaemic agents. Her best-corrected visual acuity in the right eye was 6/6, N6 (+2.00 DS) and left eye was 6/18, N10 (+1.75 DS). She had no history of hypertension and her blood pressure on the day of presentation was 124/82 mm Hg. Pupillary reaction, anterior segment examination and intraocular pressure of both eyes were within normal limits. Fundus examination of the right eye was normal. Left eye fundus examination demonstrated presence of few microaneurysms, scattered retinal haemorrhages in all four retinal quadrants, hyperaemic disc and dilated retinal vessels suggestive of non-ischaemic CRVO and macular oedema and coexistent mild stage of non-proliferative diabetic retinopathy.

INVESTIGATIONS

Spectral domain optical coherence tomography was performed using Spectralis machine (Heidelberg Engineering, Heidelberg, Germany) which showed cystoid macular oedema, shallow neurosensory detachment and intact outer retinal layers (figure 1). Due to the ongoing global pandemic and having a high risk of exposure to SARS-CoV-2 virus, she was tested for COVID-19 antibodies. She tested positive for SARS-CoV-2 IgG and negative for IgM. PCR testing was not performed because she was not ill enough for hospital admission, which at that time was required for testing. Her initial blood work-up was done which revealed elevated D-dimer levels (707 ng/mL; normal <500 ng/mL) and raised erythrocyte sedimentation rate (ESR; 52 mm at the end of first hour) (haemoglobin—111 g/L; complete blood count—normal; platelet count —3.03×10^9/L ; serum fibrinogen—194 mg/dL; prothrombin time—14.8 s; partial thromboplastin time —30.5 s; international normalised ratio—1.18; glycosylated haemoglobin—6.5%; C reactive protein—negative; serum ferritin—5.26 ng/mL, normal lipid profile, normal serum homocysteine, negative Mantoux test and normal chest radiograph).

TREATMENT

She was started on treatment with low-dose aspirin 150 mg/day and advised intravitreal anti-vascular endothelial growth factor (VEGF) therapy.

OUTCOME AND FOLLOW-UP

The patient presented 1 month later without having undergone intravitreal anti-VEGF therapy, at which point her visual acuity had improved to 6/6, N6 in the left eye. Fundus examination of the left eye showed reduced retinal haemorrhages and optical coherence tomography showed complete resolution of macular oedema. Fluorescein angiography was done to check for retinal vascular leakage which was absent. Fluorescein angiography of both eyes showed few non-leaking microaneurysms at the posterior pole (figure 2). Her repeat blood work-up at this time revealed reduced D-dimer (419 ng/mL) and ESR (16 mm at the end of 1 hour) levels compared with the previous readings. No ocular therapy was advised, and the patient was continued

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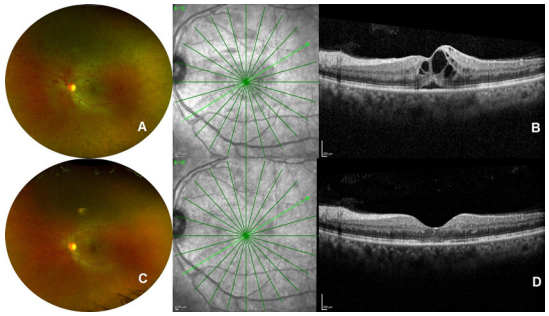

Figure 1 Fundus photographs and optical coherence tomography (OCT) images of the left eye of a patient with central retinal vein occlusion (CRVO) associated with COVID-19 infection. (A) Optomap, Daytona image of the left eye showing multiple retinal haemorrhages spread in all four quadrants of the fundus with optic disc hyperaemia and dilated retinal vessels suggestive of CRVO. (B) OCT image of the left eye at presentation showing cystoid macular oedema, shallow neurosensory detachment and intact outer retinal layers. (C) Colour fundus image of the left eye at 1-month presentation showing reduction of the retinal haemorrhages. (D) OCT image of the left eye at 1-month follow-up visit showing resolution of the macular oedema.

on daily low-dose tablet aspirin 150 mg and was asked to be reviewed after 3 months.

DISCUSSION

The common mechanisms responsible for the development of CRVO in general include arteriosclerosis, hypercoagulability, vasculitis secondary to systemic inflammation or a combination of all.[5] In the current case, the patient had developed a fresh CRVO with macular oedema and no other comorbidities aside from underlying COVID-19 existed. As a result, a diagnosis of CRVO with macular oedema secondary to COVID-19 infection was made. COVID-19 is believed to cause CRVO by (1) inducing a hypercoagulable state resulting in venous thromboembolism or (2) by causing retinal vasculitis secondary to thrombo-inflammatory cascade due to a 'cytokine-storm' immune response.[2 3 6] Both these mechanisms cause endothelial cell dysfunction, leading to breakdown in the inner blood–retinal barrier and increased capillary permeability and subsequent development of macular oedema.[7] In the current case scenario, the elevated D-dimer and ESR levels and the lack of retinal vascular leakage on fluorescein angiography favoured the hypercoagulable state theory rather than the inflammatory theory for the development of CRVO and macular oedema.

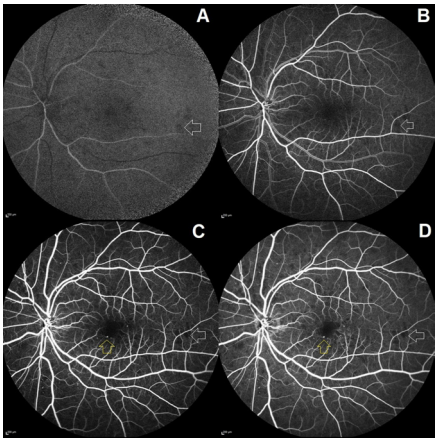

Figure 2 Sequential left eye fluorescein angiography images done at 1-month follow-up visit. (A–D) The arm–retina time was 16 s. Progressive early and late fluorescein angiography frames of the left eye showing blocked choroidal fluorescence patches spread over the posterior pole suggestive of resolving intraretinal haemorrhages (white arrow). Few non-leaking hyperfluorescent dots are seen at the macula suggestive of non-leaking microaneurysms (yellow arrow). There is no retinal vessel leakage or disc leakage in the late phase of the fluorescein angiogram.

Multiple treatment modalities have been used for treating macular oedema secondary to CRVO. Currently, the most common therapy used is by blocking intraocular VEGF by injecting intravitreal anti-VEGF agents such as aflibercept, bevacizumab or ranibizumab. In addition, intraocular and systemic steroids can be used to treat macular oedema as well.[8] Previous case reports of CRVO following COVID-19 infection were treated with intravitreal ranibizumab injections and oral corticosteroid therapy for reducing the macular oedema.[3 4] In this particular case, the patient had elevated D-dimer levels which indicated high propensity to develop blood clots. The patient was treated with non-ocular oral antiplatelet agent alone. Aspirin, due to its antiplatelet action, reduces the blood hypercoagulability and blood viscosity and acts as a blood thinner and prevents clot formation.[9] In this case, following therapy with oral aspirin tablets, there was reduction in blood hypercoagulability and restoration of blood flow in the retinal veins leading to reduction of retinal haemorrhages and macular oedema. This is further strengthened by the fact that the D-dimer and ESR levels showed lower values at the follow-up visit compared with the initial visit. Also, the natural history of CRVO does not support spontaneous resolution of CRVO or macular oedema unlike branch retinal vein occlusion.[10]

To conclude, the treatment of macular oedema in CRVO following COVID-19 infection can be guided by identifying prothrombotic or proinflammatory causative factors and can be directed specifically against it.

Learning points

- The treatment of macular oedema in central retinal vein occlusion (CRVO) following COVID-19 infection can be guided by identifying prothrombotic or proinflammatory causative factors and can be directed specifically against it.
- This case highlights that specific treatment for reducing the hypercoagulable state caused by COVID-19 with oral aspirin therapy can result in complete resolution of CRVO macular oedema.

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