

Orbital Apex Syndrome with Central Retinal Artery Occlusion in a COVID patient: Is there more than what meets the eye?

Dr. Dipika Sainath¹, Dr. Anujeet Paul²

¹(Department of Ophthalmology, ACS Medical College/ Dr.MGR University, Chennai)

²(Fellow, BB Eye Foundation/ Kolkata)

Abstract: Ocular presentations of coronavirus disease (SARS-CoV2) are varied, though infrequent. A 46-year old SARS-CoV2 positive female, an uncontrolled diabetic presented with sudden onset loss of vision in the right eye with complete ptosis and low-grade fever for two days. She has no perception of light in the right eye, with proptosis, chemosis and total external ophthalmoplegia. The pupil was fixed, mid-dilated and unresponsive to both direct and consensual light reflexes. This painted a picture of Orbital Apex Syndrome (OAS). Fundus examination revealed a central retinal artery occlusion (CRAO). Computerised tomography disclosed extra sinus involvement in relatively innocent sinuses pointing towards a fungal etiology. The setting of OAS with CRAO within two days in a SARS-CoV2 who was an uncontrolled diabetic with no history of corticosteroid use and a radiological profile indicating a fungal origin is presented for its rarity.

Key Words: Orbital Apex Syndrome. Central Retinal Artery Occlusion. Coronavirus. COVID

Date of Submission: 06-01-2023

Date of Acceptance: 20-01-2023

I. Introduction:

The coronavirus disease (SARS-CoV2) has presented with an assorted variety of ophthalmic manifestations ranging from conjunctivitis, corneal epithelial defects to retinal arterial occlusions and cavernous sinus thrombosis.^{1,2} The setting of SARS-CoV2 and a compromised immunity, has led to a rise of secondary fungal infections at an alarming rate.^{2,3} We report an unusual presentation of Orbital Apex Syndrome (OAS) with Central Retinal Artery Occlusion (CRAO) in a mildly symptomatic SARS-CoV2 patient, with presumed fungal etiology.

II. Case Report:

A 46-year-old SARS-CoV2 positive diabetic female with poor glycemic control, maintaining adequate oxygen saturation in room air, presented with sudden loss of vision in right eye associated with headache, low-grade fever and drooping of the right upper eyelid for two days. She was not on any corticosteroid or immunosuppressive therapy. There was no history of nasal discharge or bleed. She had no perception of light in the right eye and 20/20 vision in the left eye.

Right eye examination revealed complete ptosis with absence of movements in all gazes. Corneal sensation was reduced on the right side with hypoesthesia noted along the division of the infraorbital nerve. There was axial proptosis of 4mm (22mm) and chemosis. Pupil was fixed, mid-dilated and non-reactive to both direct and consensual light reflexes.



Figure 1: (a) Clinical photo showing complete ptosis of the right eye. (b) Clinical photo showing proptosis and chemosis of the right eye.

Fundus revealed a pale disc, arteriolar attenuation, segmentation of blood columns in the veins, a cherry red spot at macula and retinal edema suggesting central retinal artery occlusion (CRAO). Left eye examination was within normal limits. There was no evidence of necrotic eschar or facial palsy. Examination of nasal and oral cavities were unremarkable. Tenderness was elicited in frontal, ethmoidal and maxillary sinuses.

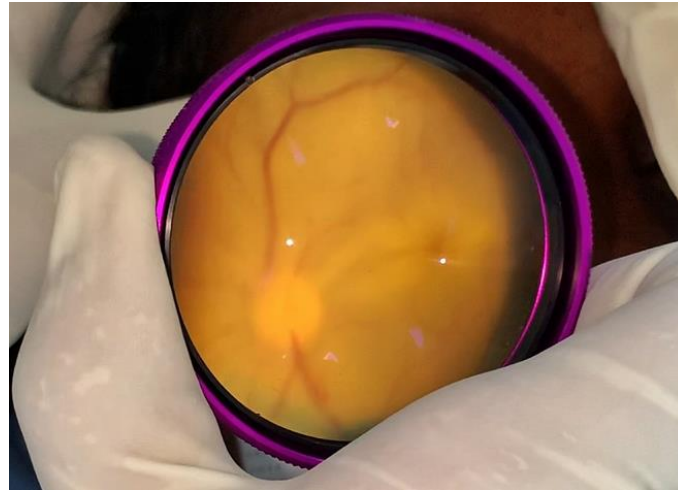


Figure 2: Smartphone fundus photo showing central retinal artery occlusion with a pale disc, arteriolar attenuation, segmentation of blood columns of vein, a cherry red spot at macula and retinal edema.

There were no signs of meningeal irritation. Reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV2 was positive. Blood investigations revealed D-dimer 733 ng/ml, Ferritin 1200ng/ml, fasting and post prandial blood sugar of 205 and 375 mg% respectively. Computerized tomography (CT) scan of the paranasal sinuses showed soft tissue opacification of all sinuses with mucosal thickening. Peri-antral fat stranding was seen around the right maxillary sinus.

This clinico-radiological profile was suggestive of an acutely invasive fungal etiology giving rise to OAS and CRAO. The patient was unwilling for magnetic resonance imaging, diagnostic endoscopy, tissue biopsy and further treatment, so was discharged against medical advice.

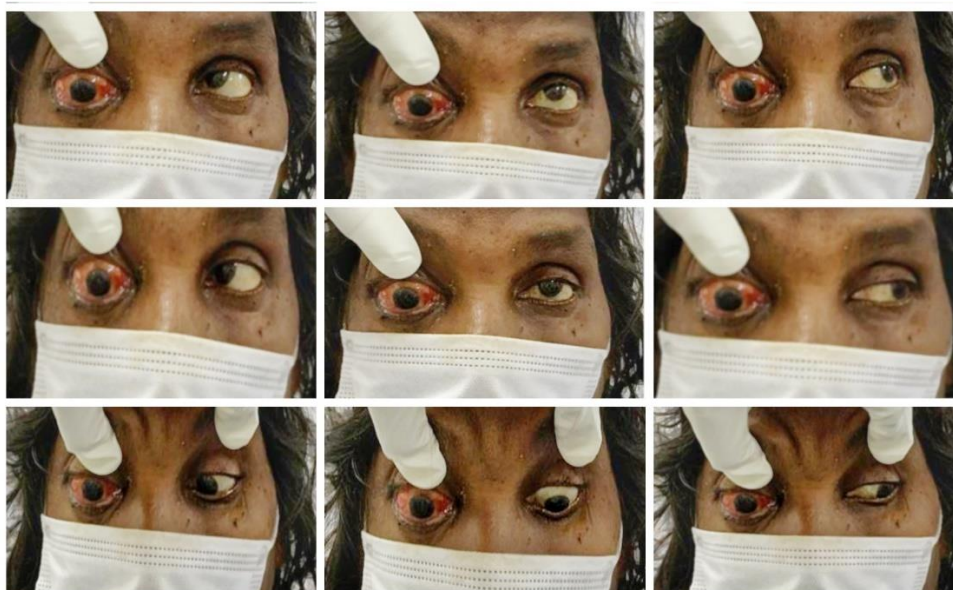


Figure 3: Nine cardinal gaze photo showing proptosis, chemosis and total external ophthalmoplegia of the right eye.

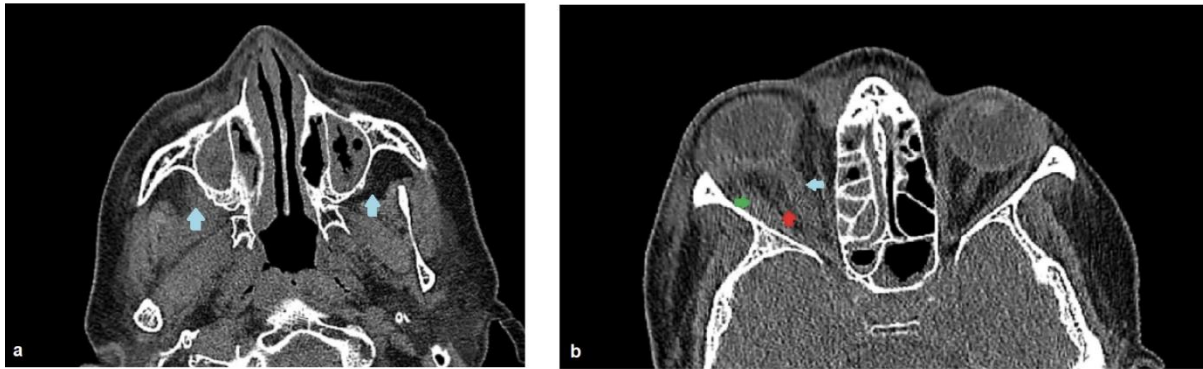


Figure 4: (a) Computerised tomography of the brain and orbit in coronal section showing peri-astral inflammation (blue arrow). (b) Computerised tomography of the brain and orbit in coronal section showing thickened optic sheath (blue arrow) with intra-conal fat stranding (red arrow) and bulky lateral rectus (green arrow).

III. Discussion:

Ophthalmic manifestations have been reported sporadically as a presenting feature as well as a complication to SARS-CoV2 infection.^{2,4} Ocular presentations elucidated range from conjunctivitis, episcleritis, keratitis to arterial and venous occlusions, acute macular neuroretinopathy (AMN).^{1,5} The authors speculate the pathogenesis to be a direct viral infection, its cytopathological effect, prolonged intensive care stay and alteration in the immune host response.^{2,5} Additionally, retinal features occur either by direct tissue damage by SARS-CoV2 and its immunogenicity or by thrombotic complications in patients requiring critical care.^{2,6}

The inherent immunocompromised state in the background of SARS-CoV2 has played host to rhino-orbital infections^{1-3,7} Common fungal species reported in SARS-CoV2 are *Aspergillus*, *Rhizopus*, *Mucor* and *Rhizomucor*. The mortality rate here is high, ranging from 50% to 80%.⁷ Poor prognosis has been linked to intracranial or orbital involvement alongside an irreversible immune suppression.^{2,7} Subramaniam et. al. stated SARS-CoV2 positivity and concurrent steroid use dramatically reduce immunity in 61.2% of his studied patients.⁸

White et. al. remarked that SARS-CoV2 patients had an increased incidence of invasive fungal infections upto 27%, most common being *Aspergillus* and *Candida*.³ El Kholyet. al. reported 77.8% *Mucor* species and 30.6% *Aspergillus fumigatus* after histopathological confirmation.⁹ Angioinvasion, thrombosis and ischemic necrosis of the host tissue are speculated to be responsible for spread of such infections.^{2,5,7} On CT, extra sinus involvement in relatively innocent sinuses rules in a fungal etiology.¹⁰ In our patient, the radiological profile of peri-antral fat stranding around right maxillary sinus, intra-conal fat stranding with a bulky lateral rectus, a thickened optic sheath with proptosis along with a combination of clinical features and their nature of onset, alarmed us to a fungal etiology.

The orbit communicates via valveless vessels with sinuses, nasopharynx, eyelid and cavernous sinus. This may be attributed to the shorter latent period for spread of infection, especially in an immunocompromised host.¹¹ Involvement of the orbit in the setting of a fungal invasion presents as OAS, characterized by proptosis, ophthalmoplegia and sudden loss of vision.^{8,11} Untreated OAS may progress to epidural and subdural empyema, meningitis, cavernous sinus thrombosis, brain abscess and may transmit via the optic canal, optic nerve or the ophthalmic vein.¹² An isolated report stated that a SARS-CoV2 patient developed OAS after nine days of positivity.¹³ Our patient developed OAS with CRAO within the period of two days.

CRAO, cavernous sinus thrombosis and endophthalmitis have been variably reported in OAS.⁸ Incidence of CRAO in OAS accounts to 16%–20%.⁶ In a backdrop of SARS-CoV2, the presentation of OAS and CRAO within two days in a mildly symptomatic patient with a distinct radiological profile heralds in an acute fungal origin. This amalgamation wherein the only high risk features include uncontrolled diabetes and raised free iron has not been reported to the best of our knowledge and is presented for its rarity.

IV. Conclusion:

In the setting of uncontrolled diabetes mellitus in SARS-Cov2, a patient who is not seriously ill may harbor a latent fungal infection. Therefore, a high level of suspicion is warranted in the management, with early diagnosis and prompt, well-coordinated treatment involving a multi-disciplinary approach. This is essential to save the sight and the life of the patient.

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Dr. Dipika Sainath, et. al. “Orbital Apex Syndrome with Central Retinal Artery Occlusion in a COVID patient: Is there more than what meets the eye?.” *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 22(1), 2023, pp. 06-09.