

Case Series

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Covid associated orbital apex syndrome: Madras ENT Research Foundation experience

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ABSTRACT

The second wave of corona virus pandemic is currently raging through India since last few weeks. Since last year, COVID-19 has brought in a multitude of challenging manifestations in the ENT regions. One such rare and complex entity is OAS (orbital apex syndrome). This case series highlighted our experience in 2020 with managing two such cases of OAS associated with COVID-19 infection. Their clinical and radiological presentation was discussed and their management protocol was explained with references from relevant literature. Although elderly patients with comorbidities were considered to have highest risk for COVID-19 associated neurologic and ophthalmic complications earlier, now it was found to affect younger healthy individuals as noted in our cases. Knowledge about such virulent complications of COVID-19 is essential for otolaryngologists, to manage this life-threatening entity in a timely manner.

Keywords: COVID-19, Diplopia, Ophthalmoplegia, Stroke, Orbital apex syndrome, Mucormycosis

INTRODUCTION

On the 30 January 2020 the WHO declared the outbreak of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), causing coronavirus disease (COVID-19), a new infectious disease which spread to several other countries worldwide. It became a worldwide pandemic. COVID-19 is primarily a disease with respiratory manifestations including cough, sore throat and anosmia, it mainly presented as a viral pneumonia. There are also increasing reports of cardiovascular and thromboembolic complications. More recently reports have emerged regarding complications like OAS leading onto life-threatening cavernous sinus thrombosis and further sequelae like sepsis and stroke.

OAS is a rare life-threatening complication mainly due to inflammatory etiology like sarcoidosis, Tolosa Hunt

syndrome, systemic lupus erythematosus, microscopic polyangiitis, granulomatosis with polyangiitis, Churg Strauss syndrome, IgG4-related variant form as well as caused by infections like bacterial, fungal, viral or parasitic. It can also occur due to septic foci from facial infection, sinusitis, orbital cellulitis, pharyngitis or otitis or following traumatic injury or surgery, especially in the setting of a thromboembolic disorder commonly in old age, diabetics and immunocompromise. It is difficult to differentiate between cavernous sinus syndrome and orbital apex because of similar involvement of ocular motor nerves and trigeminal nerves, however, the main differentiator is the optic nerve involvement in OAS. OAS rarely occurred due to viral infections in the past. The current COVID-19 pandemic has brought in this entity, the pathophysiology of which needs to be explored further. We presented two cases of COVID-19 afflicted patients with OAS and their management.

CASE SERIES

These two cases presented to us in the time period between August and September 2020. The case details of these patients are presented below.

Case 1

A 39 year old male suspected with left orbital cellulitis was referred to our institute, a tertiary care centre, for further evaluation and management. He presented to us with complaints of left sided visual loss, proptosis, ptosis and retro-orbital pain with the congestion of eye and left sided headache with numbness as well as left facial palsy (House-Brackmann Gr-4). It was inferred that the facial palsy happened in association with the ophthalmoplegia as a sequence of covid related viral multi-neuropathy. He gave a history of COVID-19 infection confirmed by RT-PCR 16 days back, which was managed in a covid care centre. He also gave a history of typhoid infection prior to COVID-19 infection which was treated and he recovered.



Figure 1: (a-d) Case 1 clinical images of LT facial palsy and ptosis.



Figure 2: MRI brain and orbit of case 1.

On examination, he had left orbital congestion, edema, proptosis, ophthalmoplegia and ptosis (Figure 1 a-d). Radiological and hematological evaluation were done. Magnetic resonance imaging (MRI) of the brain and orbit were done which confirmed left sided OAS with suggestion of impending cavernous sinus thrombosis (Figure 2). His blood glucose levels were found to be increased HbA1c was 10.8%, fasting blood sugar was

293 mg/dl, post prandial blood sugar was 457 mg/dl and urine glucose positive, hence opinion of diabetologist was sought and insulin was titrated accordingly. Since he appeared toxic with fever spikes, lumbar puncture was done, normal flow was noted and cerebrospinal fluid (CSF) was transparent. CSF analysis was within normal limits, potassium hydroxide (KOH) preparation showed no fungal elements, CSF culture was negative and Quantiferon TB gold test was also negative. He was treated with intravenous antibiotics (piperacillin/tazobactam 4.5 g BD, meropenem 500 mg BD), anticoagulants (enoxaparin a low molecular weight heparin or LMWH), IV steroid and tablet acyclovir 800 mg thrice daily. He showed gradual improvement in his general condition with the above.

Case 2

A 53 year old female presented with complaints of acute swelling in the right side of face of sudden onset associated with drooping of eyelid, numbness over the right half of the face, visual loss in the right eye, ophthalmoplegia and proptosis. She had a history of hypertension, diabetes and hypothyroidism. On neurological examination her right side 3, 4, 5, 6 cranial nerves paresis were noted. All other cranial nerves were found to be clinically normal. Diagnostic nasal endoscopy revealed bilateral edematous mucosa obstructing both osteomeatal complex, fungal mucin and blood clot was present (Figure 3). CT scans confirmed right orbital cellulitis, along with fungal pan-sinusitis (Figure 4) obstructing her right osteomeatal complex and diagnosis of fungal rhinosinusitis probably mucormycosis was made associated with OAS. Patient was found to be covid positive on RT-PCR testing. Hence, with adequate barrier nursing precautions, she was managed in the covid ward with IV antibiotics and antifungal drugs injection liposomal amphotericin B and syrup posaconazole. Her sugars were monitored and brought under control. She did not have lung signs on CT-chest and did not require oxygen support or steroids. She eventually recovered from her COVID-19 infection in 2 weeks. Her orbital symptoms settled with medications. Subsequently she underwent endoscopic sinus surgery for debridement of the fungal colonies. Her post-op recovery was uneventful.



Figure 3: DNE-right nasal cavity edematous middle meatus (*), fungal mucin and unhealthy mucosa.



Figure 4: Arrow showing heterogenous intensity suggestive of fungal elements in the right ethmoid.

DISCUSSION

Orbital cellulitis is an inflammatory process involving the tissues that are located posterior to the orbital septum. The common presentation included red and swollen eyelids, chemosis, periocular pain, limited and painful eye movements, proptosis and impaired vision with afferent pupillary defect. *Staphylococcus aureus*, *Streptococcus anginosus*, non-typeable *Haemophilus influenzae*, *Mucorales* and *Aspergillus spp.* have been identified in association with orbital cellulitis.² OAS in immunocompromised persons mainly occurs as a result of invasive fungal sinusitis mainly caused by mucormycosis and *Aspergillus* species and rarely by species like *Alternaria*.⁸

OAS was characterized by involvement of optic nerve, oculomotor nerve, trochlear nerve, abducens nerve and the first division of the trigeminal nerve.³ This resulted in sudden vision loss, ophthalmoplegia and ocular pain. The etiologies for OAS included trauma, infections, inflammations, malignancies and vascular or endocrine diseases. OAS was characterized by vision loss from optic neuropathy and ophthalmoplegia due to the involvement of ocular motor nerves in the orbital apex. Due to anatomical proximity, two other syndromes with overlapping features included superior orbital fissure syndrome and the cavernous sinus syndrome.³

Co-existing (bacterial) pan or ethmoid rhinosinusitis was described in 86-98% of patients with OAS or Jacob syndrome. Fungal rhinosinusitis was more common in immunocompromised patients. Hypercoagulability induced by COVID-19 caused complications like pulmonary embolism, VTEs, disseminated intravascular coagulation (DIC) and stroke. OAS also occurred in COVID-19 infection. Postulated mechanisms of hypercoagulability included disruptions in the renin-angiotensin (RAS) system with reduction in ACE-2 and angiotensin 1 and 7 and alterations in the coagulation cascade leading to a consumption coagulopathy and cytokine storm including IL-1, IL-6 and TNF- α . In the

case of invasive *Aspergillus* infection, first infection from the paranasal sinuses will cause erosion of nearby bone or soft tissue which can later lead to cavernous thrombosis, embolism.⁶

Bagheri et al reported on a 37 year old male with OAS who had no underlying systemic disease. They hypothesized that upper respiratory congestion in the setting of COVID-19 had contributed to compromised mucociliary clearance, secondary sinus obstruction, immunodeficiency due to disease and resultant bacterial orbital super-infection led to OAS, in the background of a hypercoagulable state induced by the covid virus.¹

Orbital apex disorder was diagnosed by a detailed history and physical examination, a complete ophthalmic evaluation, followed by serial examinations was mandatory. MRI or HRCT imaging was helpful in characterizing neoplastic, infectious or inflammatory disorders and trauma.⁴ Magnetic resonance angiography or CT angiography helped diagnose vascular causes. Laboratory tests needed to be ordered depending on the history, physical examination and imaging findings.

Peripheral facial nerve palsy associated with COVID-19 has been described by Lima in eight patients. Seven out of his eight patients were treated with steroids and all patients have complete or partial recovery. Possible mechanisms related to nerve damage in idiopathic facial nerve paralysis included ischemia of vasa nervorum and demyelination induced by an inflammatory process. Microthrombi and other vascular changes may be implicated in the development of facial nerve ischemia in COVID-19 patients.⁵ Direct viral damage or an autoimmune reaction toward the nerve producing inflammation and causing facial palsy had been reported. In one of our patients, peripheral facial palsy was noted in association with OAS. All cases need a thorough understanding of the cause and requires judicious use of steroids whenever needed.⁷

CONCLUSION

Prompt identification and management is mandatory for proper treatment and preservation of vision in OAS. Establishing the etiology of OAS is particularly important for its management. These two cases highlighted here have indicated that COVID-19 should be considered as a likely aetiology while evaluating patients for cranial nerve palsy with orbital swellings. In the current setting of the COVID-19 pandemic, this is becoming a more serious picture due to the rapid resurgence of invasive mucormycosis infections. In retrospect we believe that these manifestations could have been also due to associated mucormycosis infection which is now declared as an epidemic in these 2nd COVID-19 wave across India. The ENT fraternity in the present day need to be well aware and appropriately armed with medical and surgical treatment protocols to face such fatal complications arising due to this COVID-19 pandemic.

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