DOI: 10.7860/JCDR/2023/61308.18300

Case Report

Radiology Section

Orbital Apex Syndrome and Pituitary Metastasis in Lung Carcinoma: A Case Report

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ABSTRACT

Orbital Apex Syndrome (OAS) is a spectrum of Orbital Apex Disorder (OAD) in which progressive vision loss occurs due to the involvement of oculomotor nerve at the orbital apex, resulting in optic neuropathy and ophthalmoplegia. Generally patients represents with the associated symptoms related to the structures involved, specifically the orbital fissure, orbital appex or cavernous sinus, collectively known as OAD. The present study reports a case of in 38-year-old female patient, detected to have carcinoma bronchus on further evaluation. The patient presented with bilateral progressive blurring of vision, diplopia, and headache. The Magnetic Resonance Imaging (MRI) brain and orbits revealed thickening of the intracanalicular portion of the right optic nerve, thickening of the intracranial portion of bilateral bilateral optic nerves, a soft tissue intensity lesion at the planum sphenoidale, pituitary gland with out a bright spot, nodular thickening of infundibulum, and thickening of the bilateral cavernous sinus showing near homogeneous postcontrast enhancement. A Chest X-ray (CXR) followed by High Resolution Computed Tomography (HRCT) thorax confirmed a soft tissue density mass lesion with spiculated margins in the posterior segment of the right upper lobe, along with an abrupt termination of the posterior segmental bronchus. Fibreoptic bronchoscopy revealed narrowing of the right upper lobe segmental bronchus. Bronchial lavage fluid revealed features of adenocarcinoma. A whole-body Positron Emission Tomography (PET) scan performed elsewhere showed a well-defined hypermetabolic, heterogeneously enhancing soft tissue in the posterior segment of the right upper lobe and at the right orbital apex. Tissue diagnosis could not be confirmed as the patient's health deteriorated. The MRI brain and orbits with contrast is the most important modality in evaluating OAD. The OAS is rarely reported as the first symptom of an occult lung carcinoma.

Keywords: Adenocarcinoma, Carcinoma bronchus, Cavernous sinus, Oculomotor nerves, Ophthalmoplegia

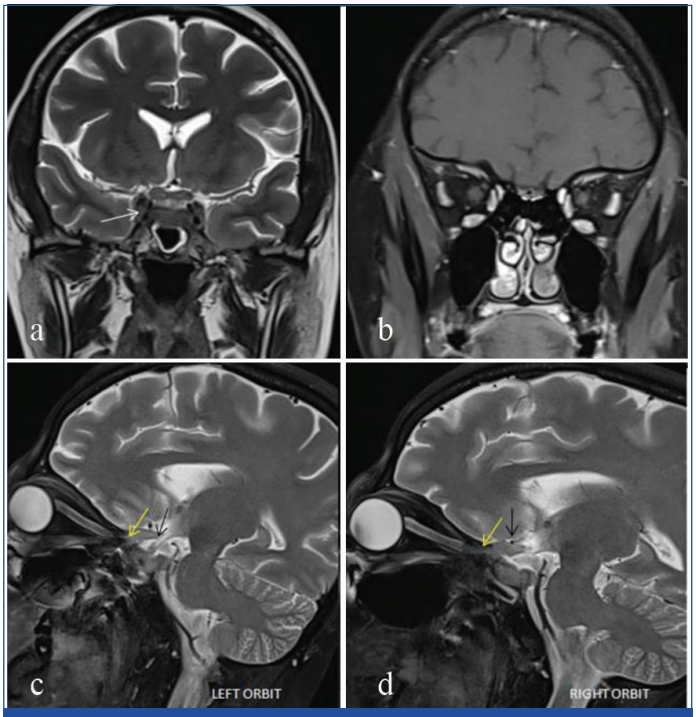
CASE REPORT

A 38-year-old female presented with bilateral acute and progressive blurring of vision along with diplopia for past 10 days. She had similar complaints one month ago, which were partially relieved with three doses of intravenous methylprednisolone (1 gm). Other associated symtoms reported were, intermittent holocranial headaches, mild breathlessness for three months, and weight loss. However, she had no known co-morbidities, phonophobia, photophobia, associated episodes of emesis, or trauma. No abnormalities were detected in the routine blood investigations and Reverse Transcription Polymerase Chain Reaction (RT-PCR).

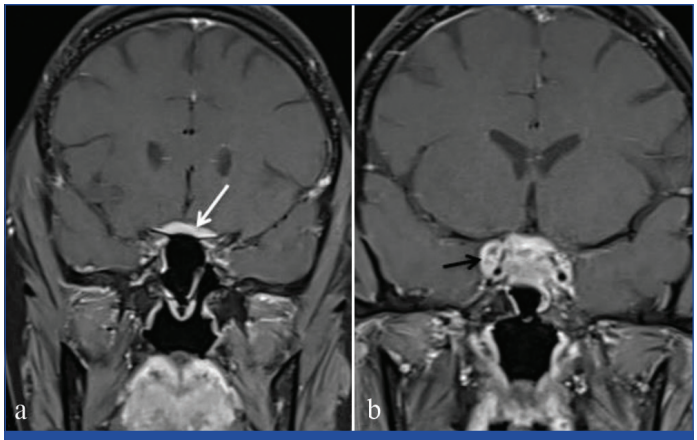
On general examination, the right eye showed only light perception, while the left eye showed only finger counting with restricted eye movements. Fundic examination revealed atrophy in the right fundus, while the left fundus appeared to be normal.

The MRI brain and orbits [Table/Fig-1 (a-d)-4(a-c)] with contrast showed thickening of the intracanalicular portion of right optic nerve with effacement of the surrounding subarachnoid space, thickening of the intracranial portion of the bilateral optic nerves (right>left), a soft tissue intensity lesion at the planum sphenoidale and pituitary gland with the absence of a bright spot, nodular thickening of the infundibulum, and thickening of the bilateral cavernous sinus (right>left, with convex outer margin) showing near homogeneous postcontrast enhancement. There were no overt signs of pituitary insufficiency, which were probably masked by OAS.

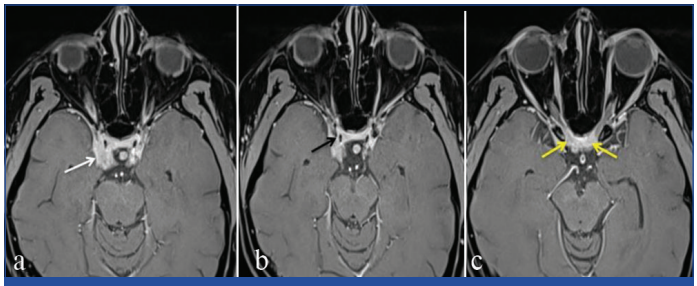
Considered differential diagnos were as follows: (1) granulomatous sarcoidosis (2) lymphoma (3) Immunoglobulin G4 (IgG4)-related disease (4) Tolosa Hunt syndrome, however the underlying cause of orbital apex involvement remained unclear. Intravenous injection of methylprednisolone, injection of monocef and injection of optineuron were not effective in subsiding the symptoms for five days. No abnormalities were detected in ultrasound of abdomen and pelvis. The CXR revealed an inhomogeneous opacity in the right upper zone in the perihilar region with slightly spiculated margins [Table/Fig-5]. HRCT thorax [Table/Fig-6] was performed, revealing a solid mass lesion of soft tissue density (CT value+25-40 HU) measuring 1.7×3.1×3.5 cm (craniocaudal×transverse× anteroposterior, respectively) with spiculated margins in the posterior segment of the right upper lobe, adjacent to the posterior segmental



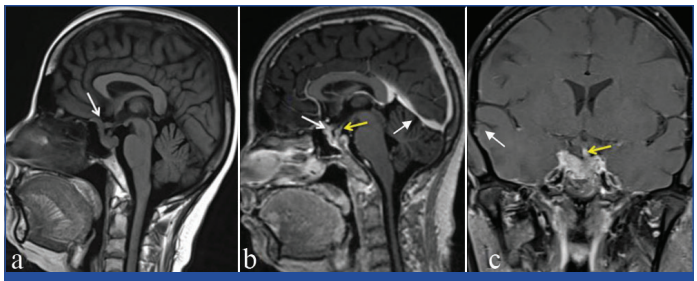
[Table/Fig-1]: (a) Coronal T2WI-showing bulky right cavernous sinus with outer convex margins (marked by white arrow). (b) Coronal T1 FS-showing normal intra-orbital optic nerve on either side. Sagittal T2FS for right (c) and left optic nerve. (d) Showing effacement of subarachnoid space around intracanalicular portion of bilateral optic nerves (marked by yellow arrow) and thickening of intracranial portions of optic nerves (marked by black arrow).



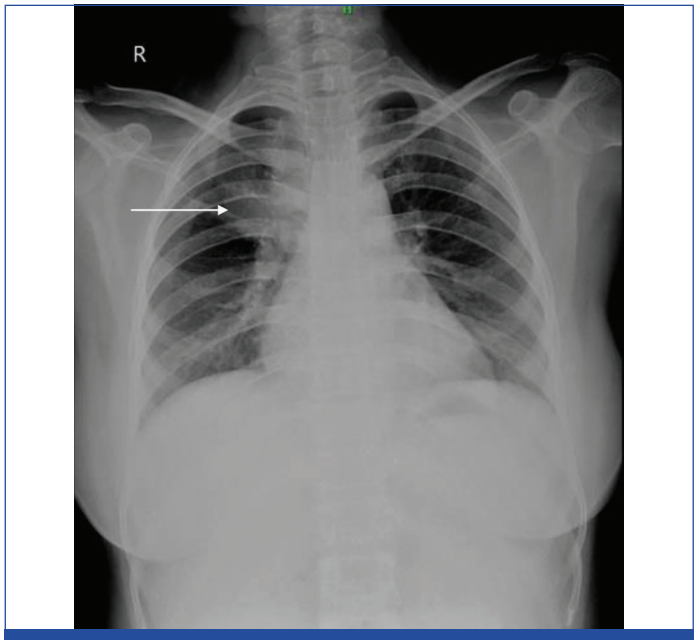
[Table/Fig-2]: Postcontrast T1VIBE coronal images-showing homogenously enhancing soft tissue intensity lesion along planum sphenoidale (marked by white arrow in (a) extending to involve pituitary gland and bilateral cavernous sinus (marked by black arrow in (b).



[Table/Fig-3]: (a-c) Postcontrast T1VIBE axial images-showing homogenously enhancing lesion in right cavernous sinus (marked by white arrow), right orbital apex (marked by black arrow) and around intracanalicular portions of bilateral optic nerves (right>left) (marked by yellow arrow).

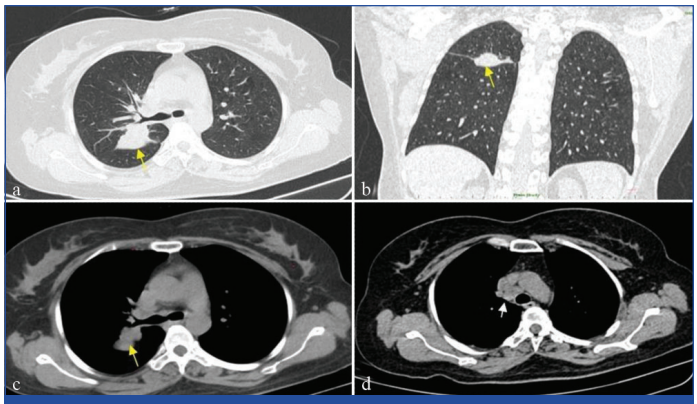


[Table/Fig-4]: (a) Sagittal T1W images (b) postcontrast T1 sagittal (c) postcontrast coronal T1FS showing soft tissue intensity lesion along planum sphenoidale (marked by white arrow) extending to involve pituitary gland with absent bright spot of posterior pituitary, nodular thickening of infundibulum (marked by yellow arrow) showing moderate, near homogenous contrast enhancement.

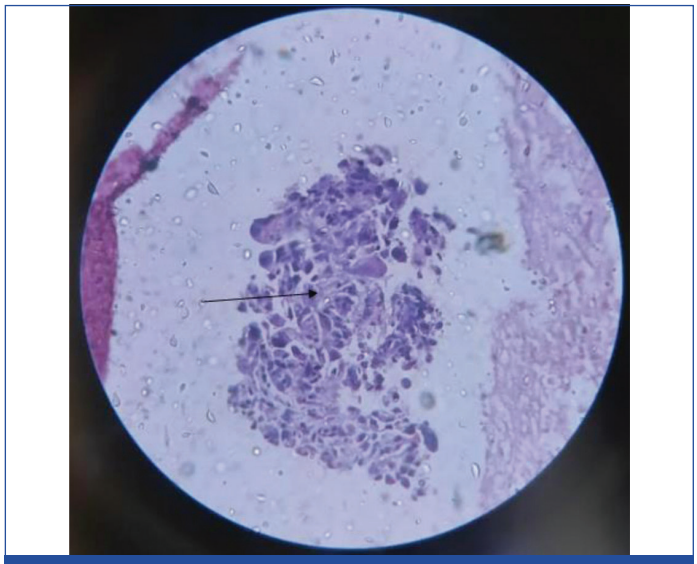


[Table/Fig-5]: Chest Posteroanterior (PA) view showing inhomogeneous opacity in right upper zone in perihilar region (marked by white arrow).

bronchus, which showed abrupt termination [Table/Fig-6a,b]. No obvious air bronchogram, cavitation, or calcifications were noted within the lesion. It abutted the superior portion of the oblique fissure. Enlarged non necrotic right paratracheal [Table/Fig-6c,d], right hilar, and sub carinal lymph nodes were noticed. Fibre-optic bronchoscopy revealed narrowing of the right upper lobe segmental bronchus with extensive congestion. Cartridge-based Nucleic Acid Amplification Test, solid/liquid cultures, and malignant cytology were performed on the bronchial lavage fluid, which revealed features of adenocarcinoma [Table/Fig-7].



[Table/Fig-6]: HRCT Lung (a) axial, (b) coronal), CT Thorax at mediastinal window (c, d) showing Soft tissue density mass with spiculated margins in relation to posterior segmental bronchus of right upper lobe (marked by yellow arrow), right paratracheal lymph node (marked by white arrow).



[Table/Fig-7]: Photo micron showing tumour cells arranged in solid sheets-features suggestive of lung adenocarcinoma (H&E, 40x).

A whole-body PET scan was performed externally, which revealed a well-defined hypermetabolic, heterogeneously enhancing soft tissue in the posterior segment of the right upper lobe (SUV 12.1) with mediastinal involvement, right hilar nodes, and right supraclavicular nodes. An ill-defined lesion was also observed in the right orbital apex (SUV 11.2). Furthermore, routine blood investigations were within normal limits. A CT-guided biopsy was planned but could not be performed due to the deterioration of the patient's health leading to death on the 10th day of admission.

These findings were suggestive of a high-grade primary neoplastic lesion of the lung (adenocarcinoma) that presented as OAS.

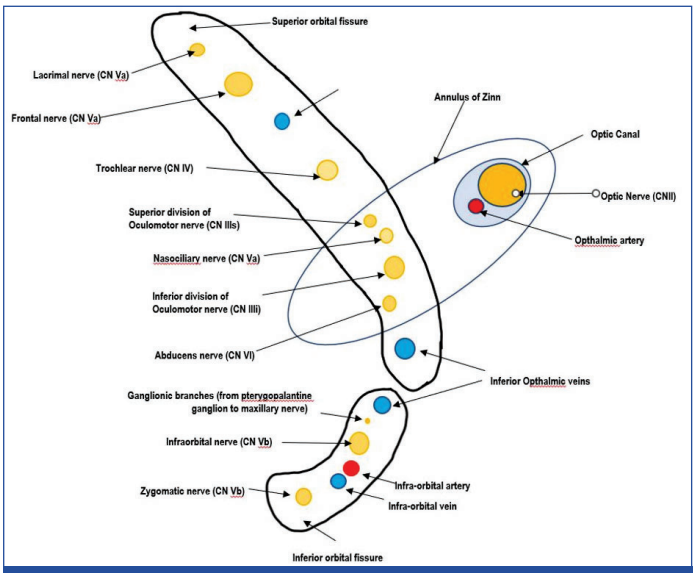
DISCUSSION

OAS results by virtue of dysfunction and damage to the optic nerve, oculomotor nerve (3), trochlear nerve (4), abducens nerve (6), and the ophthalmic branch of the trigeminal (V1) cranial nerve [Table/Fig-8]. It is characterised by ophthalmoplegia and vision loss. Involvement of the optic nerve causes an afferent pupillary defect. Involvement of the first division of fifth cranial nerve causes

hypoaesthesia of the forehead. Cavernous Sinus Syndrome (CSS) includes all the features of OAS and involvement of the maxillary branch of the trigeminal nerve (V2) and oculo-sympathetic fibres. As cavernous sinus is a venous plexus with communication with contralateral cavernous sinus, bilateral cranial neuropathy can occur. Superior Orbital Fissure Syndrome (SOFS) is characterised by the involvement of cranial nerves 3, 4, 6, and V1 with the absence of involvement of the optic nerve [Table/Fig-9] [1]. The orbital apex region is a complex region which has immense degree of anatomical variations that contains the optic nerve, cranial nerves, vessels, soft tissue, and bony structures (optic canal and superior orbital fissure) [2]. Pathology of the orbital apex can affect the optic nerve sheath complex, conal and intraconal space, extraconal space, and bony orbit. Optic nerve and three layers of the meninges form optic nerve sheath complex. The conal space is composed of 4 recti and intermuscular membranes joining them, which extend posteriorly to the insertion of the muscle tendons at the orbital apex on the annulus of Zinn. The intraconal space contains cranial nerves 3, 6, nasal ciliary branch of V1, ophthalmic artery, and orbital fat [3]. The extraconal space and bony orbit are defined by the superior orbital fissure, extraconal orbital fat, and the osseous orbital apex.

Syndrome	Cranial nerve involvement	Cranial nerve not involved
Orbital Apex Syndrome (OAS)	II, III, IV, V1+/-V2	-
Cavernous sinus syndrome	III, IV, V1+/-V2	II
Superior orbital fissure syndrome	III, IV, V1	II, V2

[Table/Fig-8]: Depicts algorithm for localisation of lesions in and around orbital apex [3].



[Table/Fig-9]: Adapted from Hacking C. Orbital apex (diagram). © 2017 Craig Hacking; CC-BY-SA-NC. Radiopedia.org. Available from: https://radiopaedia.org/cases/orbital-apex-diagram-1?lang=us).

The orbital apex, has four walls of bony orbit and a bony canal. The bone canal is made up of the optic canal, as well as the superior and inferior orbital fissures [Table/Fig-9] [4]. Various pathologies affect the orbital apex, including traumatic (cranio-maxillofacial injuries), infective, inflammatory, vascular (cavernous sinus thrombosis, carotico-cavernous fistula, carotid artery aneurysm), neoplastic, endocrinal (thyroid orbitopathy), and others (such as fibrous dysplasia, neurofibromatosis, and mucocele). Infections can be bacterial, fungal, viral, or parasitic. Inflammatory conditions include sarcoidosis, Tolosa Hunt syndrome, systemic lupus erythematosus, IgG4-related disease, granulomatosis with polyangiitis, Churg-Strauss syndrome, and non specific orbital inflammation [1,5,6]. Neoplastic causes of OAS include head and neck cancer (including nasopharyngeal carcinoma, adenoid cystic carcinoma) with locoregional and perineural spread, haematologic cancers (leukaemia, non-Hodgkin's lymphoma, Burkitt's lymphoma), and metastatic lesions (breast carcinoma [7], lung carcinoma [8], renal carcinoma [9], local tumours like meningioma, schwannoma, neurofibroma causing extrinsic compression of the contents at the orbital apex [4,5]). Metastatic spread to orbit occurs in 7% of all cancers. Orbital metastasis occurs and remarkably noted in 20% of these patients as a primary lesion. Breast, lung, and prostate carcinoma are the usual primaries [10].

Metastasis can involve intraconal space at the orbital apex. Haematogenous bony metastasis can occur at the bony orbital apex. Metastasis can also involve the cavernous sinus. These result in the involvement of cranial nerves and hence OAS. Cavernous sinus thrombosis can occur due to aseptic and septic causes [11]. In malignancies, there is a hypercoagulable state that can result in aseptic cavernous sinus thrombosis, which is unusual and typically associated with other disorders. [12].

Pituitary gland metastasis is extremely rare, accounting for about 1% of pituitary gland diseases [13]. Pituitary gland metastasis is frequently asymptomatic due to the lower predilection of malignancies to metastasize to the anterior lobe of the pituitary gland [14]. Rarely, it can present as pituitary insufficiency. There is a predilection to metastasize to the infundibulum and posterior pituitary due to the anatomy and blood supply of the gland. The posterior pituitary receives direct blood supply from the systemic circulation [14]. While the anterior pituitary receives blood supply via portal circulation via hypothalamus. The posterior pituitary has a greater area of contact with the sella turcica and adjacent dura. Hence, posterior pituitary gland may involve directly, if the malignancy with bony metastasis occurs, while the anterior lobe involvement occurs due to the continuous spread from metastasis in the posterior lobe [15,16].

Neuroimaging with CT and MRI are required in every suspected instance of OAS. Brain and orbital MRI with thin sections and contrast study can diagnose soft tissue involvement, bone marrow involvement, perineural spread of tumours seen as focal or diffuse thickening of the cranial nerves involved, and involvement of the cavernous sinus. The cavernous sinus appears bulky with an outer convex margin when involved [5]. However, a CT scan can provide useful information in both soft tissue and bony windows. Bony windows can demonstrate a destructive lesion or osteoblastic lesion involving the orbital apex. Plain and contrast studies at the soft tissue window can demonstrate an enhancing soft tissue component obliterating the intraconal fat [1,17]. Trauma, infection, inflammation, autoimmune, and vascular causes were excluded in this case. ANA blot tests were negative, p-ANCA and c-ANCA tests were negative. Angiotensin Converting Enzyme (ACE) test was normal. Chest X-ray, CT thorax, and Positron Emission Tomography-Computed Tomography (PET-CT) were diagnostic of lung cancer. However, a lesion at the orbital apex could not be biopsied.

Ookuma T et al., reported a case of a 53-year-old male having stage 4B lung adenocarcinoma hospitalised for chemotherapy. He complained of diminished vision of right eye with diplopia. On examination, there was drooping of the right eyelid with protrusion of the right eyeball. Neurological examination revealed limited adduction, abduction and vertical movements of the right eyeball. MRI brain with the orbit showed a heterogeneously enhancing mass in the right orbit in the retrobulbar compartment extending to the orbital apex. The patient was diagnosed with OAS associated with intraorbital metastasis of lung cancer. He was treated with carboplatin, pemetrexed, and pembrolizumab. There was partial improvement in his ocular symptoms after chemotherapy [18].

Xu L et al., reported a case of a 66-year-old male presenting with diplopia and blepharoptosis of the right eye which worsened after admission and developed near-complete ophthalmoplegia of the right eye. His neurological examination revealed impairment of the right II to IV, V1, and VI cranial nerves. MRI of the patient showed that he had OAS secondary to metastasis from small cell carcinoma of the lung [19].

Present study represents a case in which is primary lung carcinoma presenting simultaneously as OAS and metastasis in the infundibulum and pituitary gland on MRI. In present case, OAS and pituitary metastasis are likely due to haematogenous spread. Involvement of the anterior pituitary is likely due to contiguous spread from the posterior pituitary. Despite the involvement of the pituitary gland, there were no overt signs of pituitary insufficiency, probably masked by the orbital apex and cavernous sinus involvement.

CONCLUSION(S)

The OAS can be a presenting feature of primary malignancies. Hence, a high index of suspicion and workup is mandatory to rule out primary malignancies, apart from other aetiologies of OAS. Simultaneous metastases to the pituitary gland should also be looked for, as they can provide which can give clues to the mechanism of spread.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 23, 2023
- Manual Googling: Jan 28, 2023
- iThenticate Software: Feb 28, 2023 (16%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Nov 15, 2022**
Date of Peer Review: **Jan 02 2023**
Date of Acceptance: **Mar 02, 2023**
Date of Publishing: **Aug 01, 2023**