CASE REPORT

Cavernous sinus syndrome: a rare presentation of nasopharyngeal carcinoma

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SUMMARY

Cavernous sinus syndrome (CSS) encompasses a range of potential pathologies that can pose significant diagnostic challenges and often necessitate extensive evaluation. Given its potential to threaten both sight and life, timely and accurate diagnosis is critical. Here in, we present a rare case of CSS secondary to nasopharyngeal carcinoma. A 72-year-old man presented with a right eye ptosis, and diplopia lasting for two weeks, preceded by recurrent episodes of epistaxis and nasal obstruction. Clinical examination revealed right-sided cranial nerve palsy affecting the oculomotor, trochlear, and abducent nerves. Neuroimaging revealed a mass in the right cavernous sinus and another mass in the left torus tubarius. Endoscopic examination revealed a mass in the posterior left nasopharynx, which was histopathologically confirmed as a non-keratinizing nasopharyngeal carcinoma. The patient was scheduled for radiotherapy and chemotherapy but ultimately declined further treatment and succumbed to his illness eight months later. Cranial nerve involvement is a common manifestation of nasopharyngeal carcinoma, often signifying advanced disease.

INTRODUCTION

Cavernous sinus syndrome is a clinical condition arising from any pathology affecting the cavernous sinus. This condition can manifest with ophthalmoplegia, double vision, proptosis, ptosis, Horner syndrome, and decreased corneal sensation due to the involvement of cranial nerves in this region. The aetiologies of CSS include tumours, infections, inflammation, vascular disorders, and trauma. While primary tumours of the cavernous sinus are rare, more commonly, tumours involve the cavernous sinus either through direct extension from adjacent head and neck tumours or via hematogenous spread from distant sites. Nasopharyngeal carcinoma (NPC) is a type of squamous cell carcinoma that arises in the head and neck region. It is particularly prevalent in certain populations, such as those in Southeast Asia, southern China, the Middle East, and North Africa. Males are at a higher risk of developing NPC than females. Risk factors for NPC include Epstein-Barr Virus (EBV) infection, tobacco smoking, consumption of salt-preserved fish and other preserved foods, as well as a family history of NPC. Radiation therapy and chemotherapy are the standard non-invasive treatments for locally advanced NPC.[1] In this report, we present a rare case of CSS secondary to nasopharyngeal carcinoma.

CASE PRESENTATION

A 72-year-old Chinese gentleman presented to the Emergency Department with a two-week history of drooping of the right upper eyelid. He also experienced binocular horizontal diplopia, particularly noticeable in primary and left gaze positions. He reported no history of trauma, headaches, vomiting, body weakness, unsteady gait, or fever. Additionally, there were no complaints of loss of appetite or significant weight loss. His medical history included chronic smoking, hypertension, diabetes mellitus, and chronic obstructive pulmonary disease, for which he was using a Salbutamol inhaler. He was poorly compliant with his oral hyperglycaemic and antihypertensive medications.

His visual acuity was 20/40 in both eyes, with unremarkable findings in both the anterior and posterior segments. Examination revealed moderate ptosis and restricted extraocular muscle movement (EOM) indicative of right oculomotor nerve involvement. The right pupil was normal in size and reactive. Other cranial nerve examinations were unremarkable. His blood pressure was 196/90 mmHg, and blood glucose was 5.2 mmol/L. He was initially diagnosed with right oculomotor nerve palsy secondary to mononeuritis multiplex and was observed for further progression. At a follow-up visit one week later, the ptosis in his right eye had worsened, and he now experienced significant diplopia in all gazes. He also developed sharp stabbing pain in the right eye, along with episodes of mild epistaxis and nasal blockage. However, there was no history of reduced smell or hearing loss. His visual acuity remained 20/40 in both eyes, and there was no relative afferent pupillary defect. The ptosis in the right eye had become severe. EOM examination revealed

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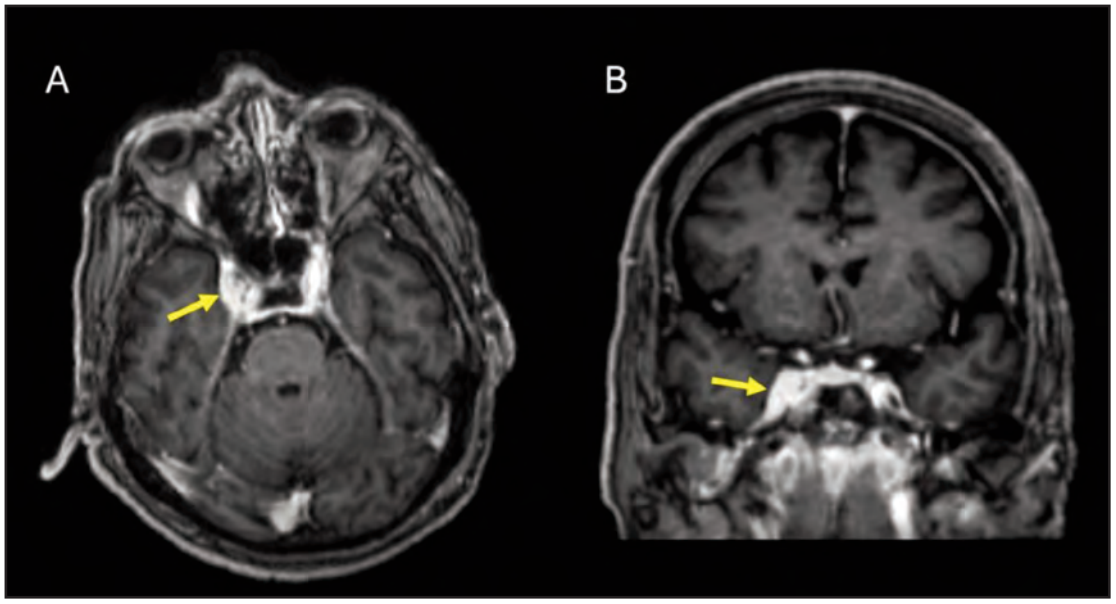

Fig. 1: MRI of the brain in T1-weighted post gadolinium in axial (a) and coronal (b) views showed a right cavernous sinus mass with enhancement post-contrast (yellow arrow)

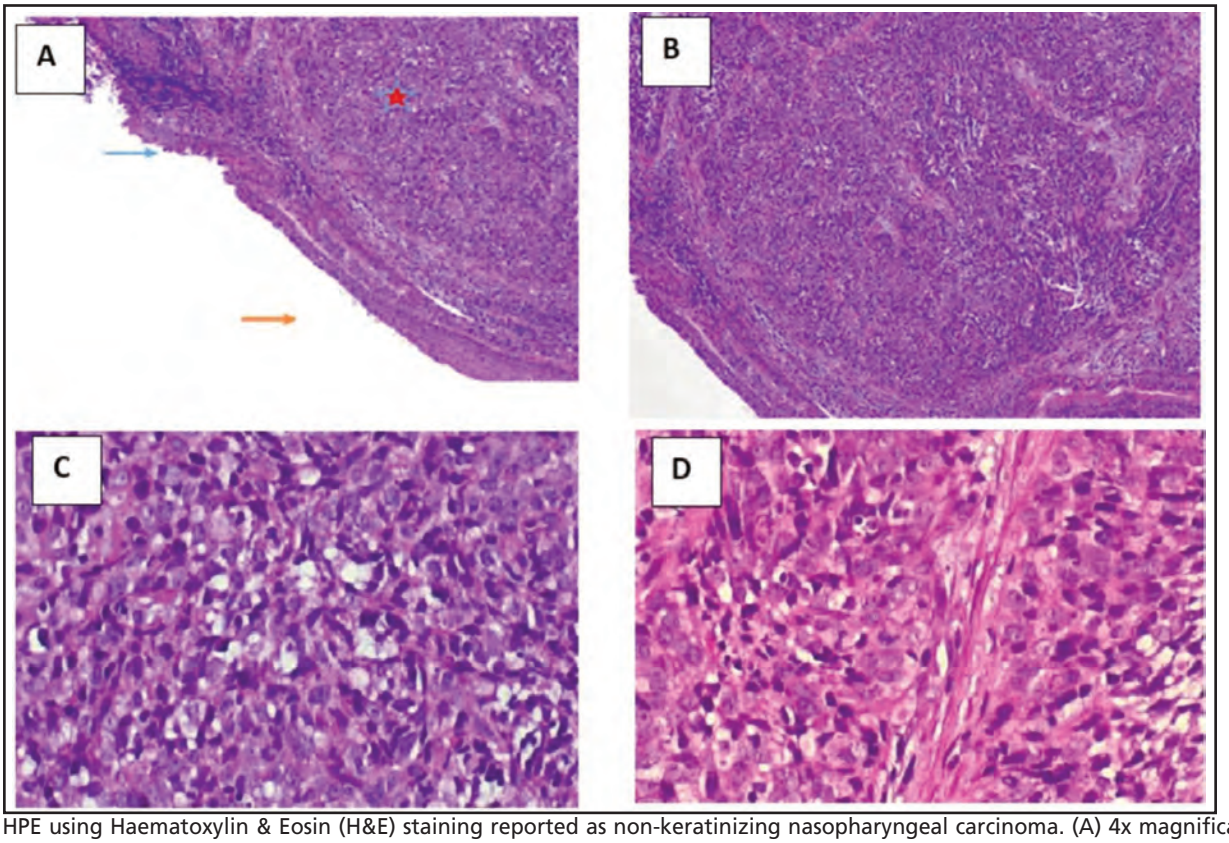

Fig. 2: HPE using Haematoxylin & Eosin (H&E) staining reported as non-keratinizing nasopharyngeal carcinoma. (A) 4x magnification, section from the fossa of Rosenmüller (FOR) partly covered by non-keratinized stratified squamous epithelium (orange arrow) and respiratory type epithelium (blue arrow), (B) exhibiting sheets of malignant tumour infiltrating the subepithelial stroma. (C) 60x magnification, the tumour cells exhibit moderate to marked nuclear pleomorphism, with irregular nuclear membranes, round to oval hyperchromatic vesiculated nuclei, prominent nucleoli, and vacuolated cytoplasm. However, keratin pearls or individual keratinization are absent. (D) 60x magnification, mitosis is seen

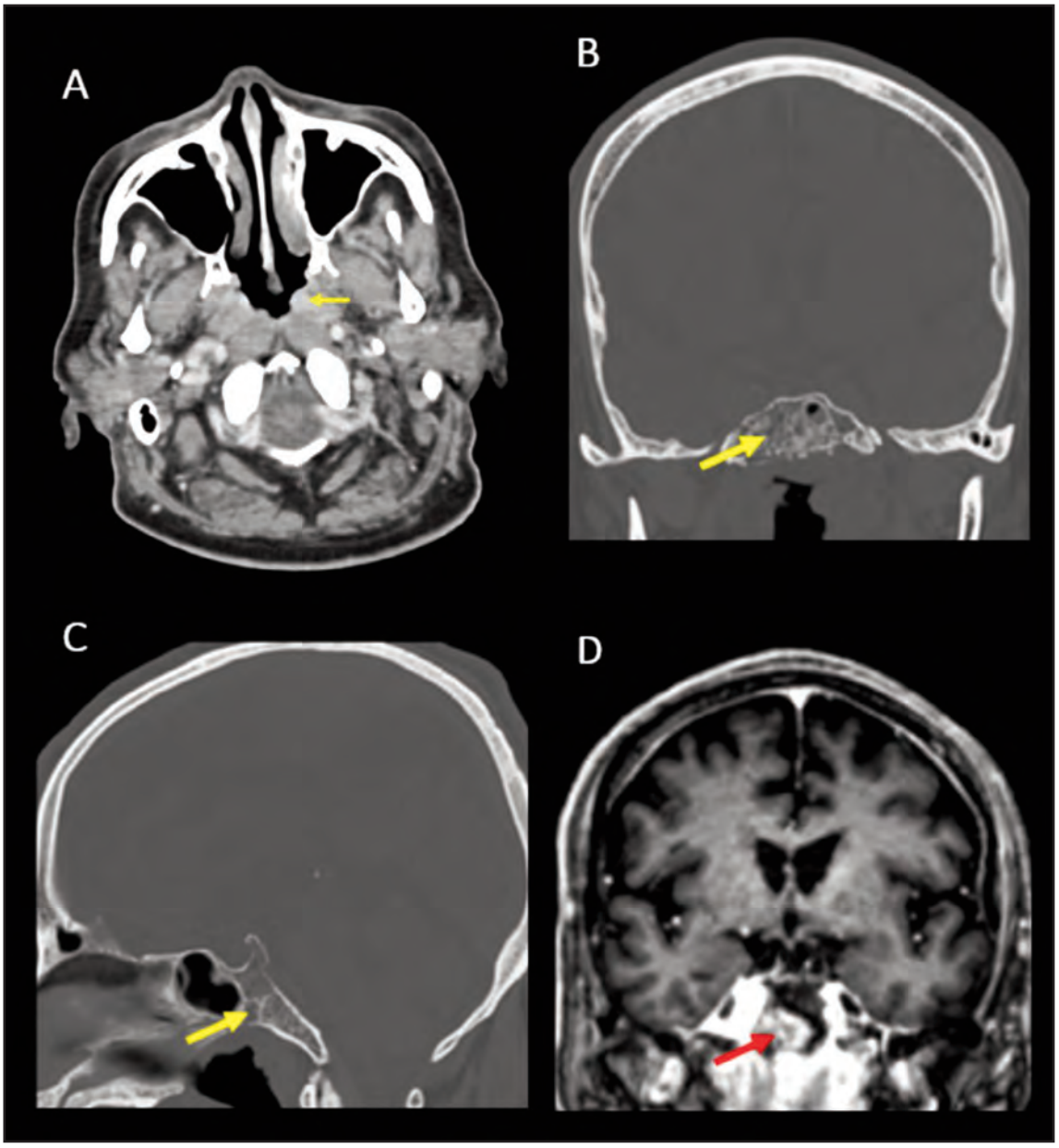

Fig. 3: Contrast-enhanced CT neck and MRI Brain. (A) A sub-centimeter enhancing mass at the left torus tubarius (yellow arrow), consistent with the primary tumour of NPC. CT Brain in bone window in coronal view (B), sagittal view (C), reveal bony erosion of the sphenoid bone (yellow arrow), sparing the clivus. (D) Contrast enhanced MRI of the brain in coronal view showed an enhancing mass (red arrow) within the bony erosion, extending towards the right cavernous sinus while sparing the left cavernous sinus

involvement of the third, fourth, and sixth cranial nerves. The right conjunctiva was white, with no dilated episcleral vessels. Intraocular pressure in the right eye was slightly elevated at 22 mmHg, while the left eye remained within normal limits at 18 mmHg. The corneal reflex in the right eye was reduced, with hypoesthesia involving the right ophthalmic and maxillary branches of the trigeminal nerve. The central nervous and cerebellar systems were normal. Submental and auricular lymph nodes were palpable, with tenderness in the right auricular lymph node. At this point, the patient was diagnosed with right CSS.

Blood investigations, including full blood count, renal profile, liver profile, erythrocyte sedimentation rate, fasting blood glucose, and C-reactive protein, were within normal limits. Contrast-enhanced computed tomography (CECT) of the brain and orbit revealed bulging of the right cavernous sinus, suggestive of a mass, which was later confirmed by magnetic resonance imaging (MRI) of the brain and orbit (Figure 1). Subsequently, the otorhinolaryngology (ORL) team performed a nasal endoscopy and biopsy. Endoscopy revealed a mass in the posterior left nasopharynx, and histopathological examination (HPE) confirmed non-keratinising nasopharyngeal carcinoma (Figure 2).

Computer tomography (CT) of the neck, thorax, and abdomen identified a primary tumour at the left torus tubarius, obliterating the fossa of Rosenmüller (Figure 3a), with bilateral cervical lymphadenopathy and no distant metastasis. During the retrospective review of the previous imaging, bony erosion with cortical break of the sphenoid bone on the right, just anterior to the clivus was revealed. There was an enhancing soft tissue component within, extending towards the right cavernous sinus, indicating the local extension of the tumour from the left nasopharynx to the right cavernous sinus, while sparing the left cavernous sinus (Figure 3b, 3c, 3d). The patient was scheduled for a series of radiotherapy and chemotherapy but ultimately refused treatment and defaulted on follow-up. He succumbed to his illness eight months after the diagnosis.

DISCUSSION

The cavernous sinus is an interconnected series of venous channels located in the middle cranial fossa on each side of the sphenoid bone. It is formed by the splitting of the dura mater at the body of the sphenoid bone. The oculomotor, trochlear, and trigeminal nerves (ophthalmic and maxillary branches) lie along the lateral walls of the cavernous sinus, while the internal carotid artery and abducent nerve run centrally within it. As a result, any pathology in this area can lead to cranial nerve palsy.

CSS is most commonly caused by tumours. In a study by Keane et al., which summarized 151 cases of CSS, 30% were due to tumours, 24% to trauma, 23% to inflammation, with the remaining cases attributed to infections, aneurysms, and other factors.[2] This finding aligns with Fernandez et al., who reported that tumours were the primary cause in 80 out of 126 cases of CSS.[3] NPC, a malignancy common in Southeast Asia, Southern China, the Middle East, and North Africa, is more prevalent in men, with a male-to-female ratio of 2 to 3:1.[1] In Malaysia, NPC is the most common head and neck cancer among men, following lung cancer.[4] Risk factors for NPC include EBV infection, consumption of salt-preserved fish and other preserved foods, tobacco smoking, and alcohol consumption, many of which were present in our patient.

NPC arises from the epithelium of the nasopharynx and spreads via local or perineural spread, hematogenous and lymphatic routes. For local spread, the tumour can invade surrounding structures and tissues. Since the nasopharynx is near the cavernous sinus, the tumour may invade posteriorly or laterally through the pharyngeal wall, leading to encroachment on the cavernous sinus. Additionally, NPC can cause perineural spread by infiltrating the maxillary (V2) and mandibular (V3) nerve branches, which have an anatomical relationship with the nasopharynx. The cancer cells may then track along the course of the maxillary nerve towards the cavernous sinus, potentially affecting other cranial nerves within the cavernous sinus. According to Chong et al., NPC can infiltrate the pterygopalatine fossa and trigeminal nerve, leading to subsequent spread to the cavernous sinus. In their study, this route was observed in 4 out of 17 patients with pterygopalatine fossa infiltration, where contrast enhancement of the maxillary nerve resulted in infraorbital neuropathy.[5] Haematogenous spread occurs through invasion of the skull base marrow and the venous plexus of the parapharyngeal region, while lymphatic spread is facilitated by the rich lymphatic tissue in the posterior nasopharynx. NPC can infiltrate the intracranial space through the skull base, particularly via the foramen ovale and lacerum, entering the cavernous sinus and presenting as CSS.

Distant metastasis commonly involves the liver, bone, and lungs. Patients with intracranial involvement, such as orbit and cranial nerve infiltration, typically have a poorer prognosis, as observed in our patient, who had a survival rate of only eight months post-diagnosis. Aziz et al. found that the common presentations of NPC include a neck mass (70.9%), unilateral nasal obstruction (33.3%), and epistaxis (29.2%). Less common symptoms (20.9%) include headaches, diplopia, and facial paraesthesia.[6] Ophthalmic manifestations as the initial presentation of NPC are rare, occurring in about 5.4% of cases, with a 1.8% risk of blindness.[7] The presence of cranial nerve involvement in NPC indicates advanced disease. The trigeminal (12.5%) and abducent (10.5%) nerves are most commonly affected.[8,9] Our patient's initial presentation with 3rd cranial nerve palsy, initially diagnosed as right oculomotor nerve palsy secondary to mononeuritis multiplex, was unusual and evolved into multiple cranial nerve palsies within a week.

Radiological imaging is crucial in identifying potential causes of CSS, including mass lesions, infections, or inflammation. However, imaging findings alone are often inconclusive, necessitating clinical correlation to establish an accurate diagnosis. In cases of cavernous sinus metastasis, CECT may reveal an enhancing mass within the cavernous sinus and sometimes associated with bony erosion. Conversely, cavernous sinus thrombosis, a life-threatening condition that must be excluded, is characterized by a filling defect in the cavernous sinus, manifesting as heterogeneous enhancement and dilation of the superior ophthalmic vein on CECT. However, MRI is superior for diagnosing NPC compared with CECT because it provides excellent contrast resolution for soft tissues allowing better differentiation between normal anatomical structure and pathological lesion.

NPC is typically diagnosed via biopsy obtained through nasopharyngeal endoscopy. MRI is the preferred imaging modality for diagnosing and staging NPC, particularly in detecting subclinical masses that may be missed by endoscopic biopsy. However, CT and PET scans remain valuable for radiotherapy planning, staging, and detecting distant metastasis. In our case, the diagnosis of NPC was confirmed by nasopharyngeal biopsy, with contrast-enhanced CT (CECT) of the neck, thorax, abdomen, and pelvis performed for staging.

Management of CSS depends on the underlying aetiology. NPC is highly sensitive to radiotherapy, making it the cornerstone of treatment. Chemotherapy is indicated for locally advanced regional disease and distant metastases. Surgery is typically reserved as a salvage option, particularly in cases of local recurrence, radiation-resistant cancer, or for lymph node removal following chemoradiation. Our patient was offered radiotherapy and chemotherapy but ultimately refused treatment.

The overall 5-year survival rate for NPC patients who seek treatment ranges from 32% to 62%.[9] Among these, the survival rate for those treated with radiotherapy alone is 22.5%, while those treated with chemoradiotherapy combined with adjuvant chemotherapy have a survival rate of 61.4%. A study by Siti-Azrin et al. identified poor prognostic factors such as advance age, stage 4 disease, and the presence of metastases. NPC with cranial nerve involvement is associated with a poorer prognosis, with a 1.74-fold higher risk of death.[10]

CONCLUSION

Clinical symptoms of CSS can be misleading, masking an underlying lethal malignancy such as advanced NPC. Given NPC's aggressive nature and rapid progression, prompt diagnosis is vital for initiating timely treatment and improving outcomes. Intracranial involvement often carries a poor prognosis, underscoring the need for vigilant assessment and swift intervention.

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