Case Report:

Orbital apex syndrome secondary to nasopharyngeal carcinoma

C. S. Sandhya,[1] D. Murali Krishna,[1] C. Jagannath,[1] G. Srinivas,[2] K. Radhika[3]

Departments of [1]Ophthalmology, [2]Otorhinolaryngology, Sri Venkateswara Medical College, Tirupati and Department of [3]Pathology, Sri venkateswara Institute of Medical Sciences, Tirupati

ABSTRACT

We report the rare occurrence of unilateral orbital apex syndrome with neurotrophic keratitis secondary to nasopharyngeal carcinoma in the left eye in a 40-year-old lady. The patient presented with complaints of left-sided headache, loss of smell sensation, defective vision, and restriction of movements and drooping of left upper lid of one year duration. Computed tomography revealed hyperdense lesion involving left nasal cavity, nasopharynx and oropharynx, extending to left maxillary, sphenoid and ethmoid sinuses. Magnetic resonance imaging also confirmed the same.

Key words: *Orbital apex syndrome, Nasopharyngeal carcinoma, Neurotrophic keratitis*

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is considered to be uncommon in Western countries; however, it is common in southern China, Hong Kong, Taiwan and Singapore, with an incidence 30 times higher among the Chinese compared with whites.[1] Although NPC is rare in India, a higher incidence has been observed in north-eastern states of India. Nagaland had incidence of 6.2/100,000 and 2.1/ 100,000 among males and females respectively.[2]

NPC usually arises from the lateral wall of the nasopharynx, especially around the fossa of rosenmuller and Eustachian invasion. It may spread superiorly to involve the skull base and intracranium, resulting in cranial nerve involvement. It may also invade anteriorly to the nasal cavity, paranasal sinuses, pterygo-palatine fossa and apex of orbit. The incidence of skull base and brain invasion has been reported in some studies to be 12%-31%.[3.4]

Orbital involvement in NPC is classified as T4 disease[3] and anterior orbital involvement is rare. In a review of non-disseminated NPC patients in Singapore the incidence of orbital involvement was reported to be 2.6%.[4] Orbital involvement from NPC occurs due to recurrence of the primary tumour, with 44% having had multiple recurrences before orbital involvement. Eyelid swelling or an eyelid mass, and limitation of extraocular motility are the most common presenting features.[5]

The most common pathway for orbital invasion occurs via the pterygopalatine fossa and inferior orbital fissure. Orbital involvement may also occur through the ethmoid and sphenoid sinuses.[5] Occasionally, the route of orbital invasion may be difficult to determine, particularly in cases with extensive tumour extension but direct invasion of orbit is rare in NPC. We describe a patient diagnosed with recurrent NPC and document the rare occurrence of orbital involvement.

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Corresponding author: Dr C.S.Sandhya, Professor and Head Department of Ophthalmology, Sri Venkateswara Medical College Tirupati, India.
e-mail: ophthalmologysvmc@gmail.com

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CASE REPORT

A 40-year-old lady presented to the Ophthalmology out-patient service of Sri Venkateswara Ram Narain Ruia Government General Hospital (SVRRGGH), Tirupati the teaching hospital attached to Sri Venkateswara Medical College, Tirupati with a history of left-sided headache, defective vision, drooping of left upper eyelid and loss of smell of 9 months duration. The illness started with left-sided headache and loss of smell. Defective vision and drooping of lid followed after one month. There was no history of diplopia. She was not known to have diabetes mellitus or hypertension. The patient gave history of being evaluated earlier at a local hospital in March 2013, was diagnosed to have NPC and had taken incomplete treatment.

General physical examination was normal except for the presence of mild degree of anaemia. Local examination of the right eye was normal. The left eye showed total ptosis with poor *levator palpebrae superioris* (LPS) action (Figure 1A). Circum corneal congestion was present. Cornea showed a 7 mm oval central ulcer involving the epithelium and superficial stroma with rolled out edges. Corneal sensations were absent (Figure 1B).

The surrounding epithelium was loose. A diagnosis of neurotrophic keratitis grade 2 was made (Table1).[6] The lens was clear. Pupil showed relative afferent pupillary defect (RAPD). All the extra ocular movements were absent suggesting involvement of III, IV and VI cranial nerves (Figure 1C). Sensations on the forehead were absent suggesting

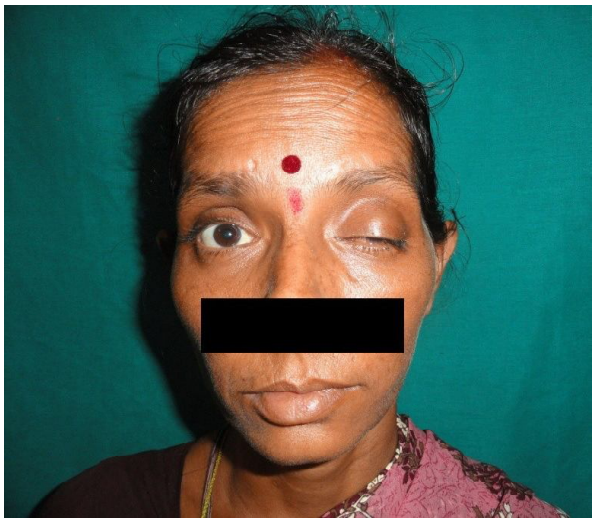

Figure 1A: Clinical photograph in primary position showing ptosis in the left eye

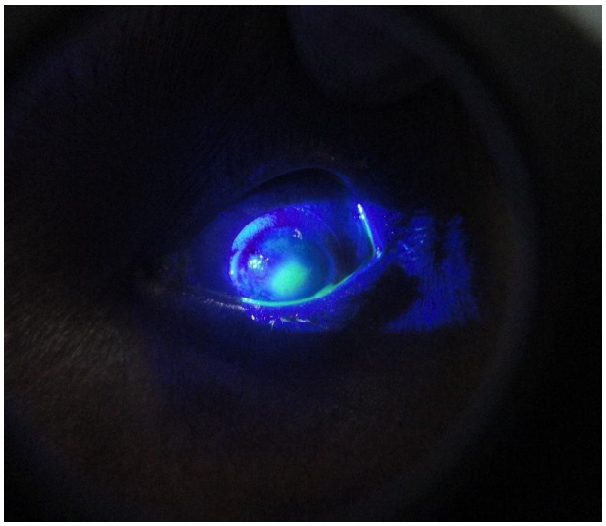

Figure 1B: Clinical photograph showing corneal ulcer left eye evident on fluorescein stain

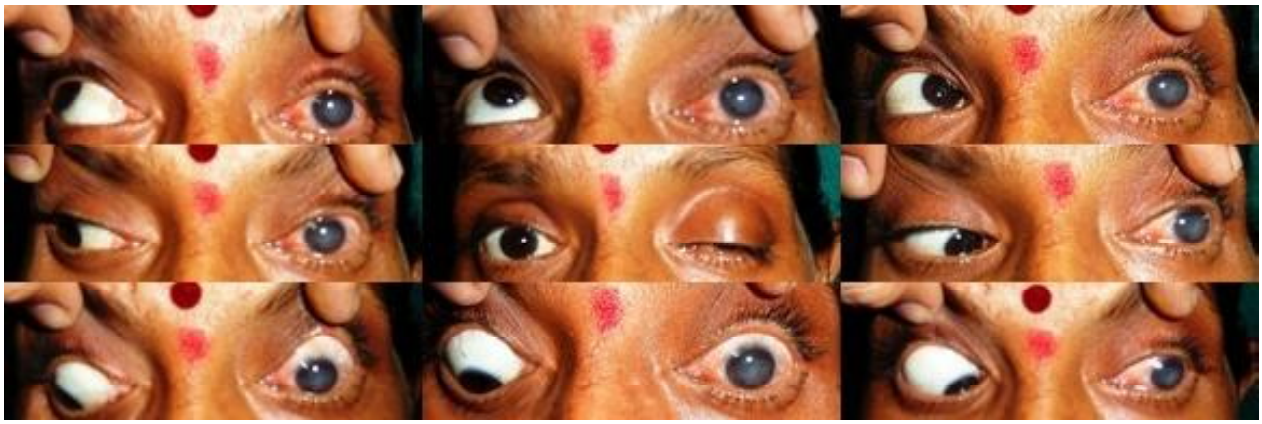

Figure 1C: Clinical photographs showing ocular movements in all 9 positions of gaze

Table 1: Mackie classification

Stage	Feature
Stage 1	Rose Bengal staining of the inferior palpebral conjunctiva Decreased tear break up time Increased mucous viscosity Punctate epithelial fluorescein staining
Stage 2	Epithelial defect- Oval and in the superior cornea Defect surrounded by a rim of loose epithelium Edges may become smooth and rolled Stromal swelling with folds in the Descemet s membrane. With inflammatory cells in anterior chamber
Stage 3	Stromal lysis/melting Perforation

Source: reference 6

involvement of ophthalmic division of trigeminal nerve.

Fundus examination showed mild pallor of the optic disc in right eye. Best corrected visual acuity (BCVA) was 6/6 in right eye and counting figures (CF) at 1 m in the left eye. Schirmer's test showed 3 mm / 5 minutes in left eye. Colour vision and visual fields are normal in right eye. Red green colour vision defect was present in left eye and visual field testing could not be done due to poor vision. Exophthalmometry readings were 21 mm in right eye and 22 mm in left eye. Regional lymph nodes were not enlarged. Rhinological examination revealed a mass in nasopharynx.

Laboratory investigations revealed erythrocyte sedimentation rate (ESR) 42 mm at the end of one hour. Chest radiograph (postero-anterior view) was normal. Abdominal ultrasonography was normal. Computed tomography (CT) of the orbits and paranasal sinuses showed a hyperdense lesion in the left nasal cavity, naso-pharynx and oropharynx extending to left sphenoid, ethmoid and maxillary sinuses and obliteration of cavernous sinus on left side (Figure 2A). The mass extended to seller and parasellar region (Figure 2B). Gadolinium contrast enhanced magnetic resonance imaging (MRI) confirmed the CT findings (Figure 3).

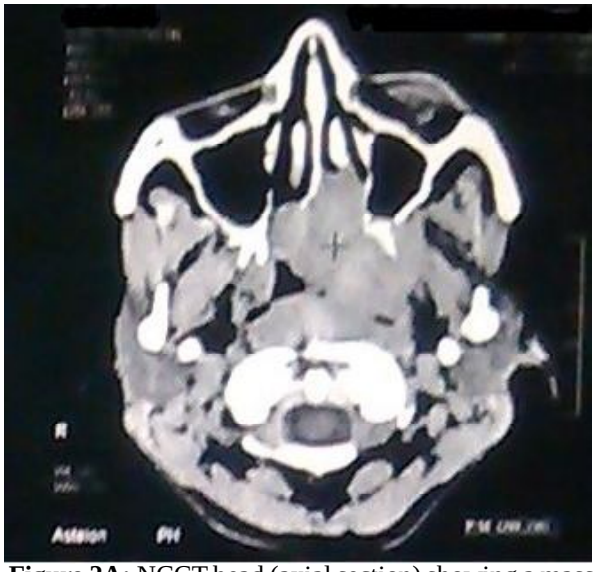

Figure 2A: NCCT head (axial section) showing a mass in the left ethmoidal sinus and obliterating left cavernous sinus

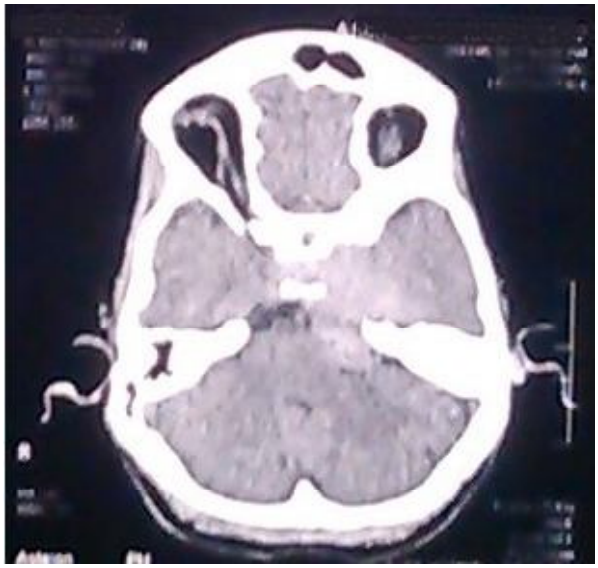

Figure 2B: NCCT of the head (axial section) showing mass in sellar and para sellar area

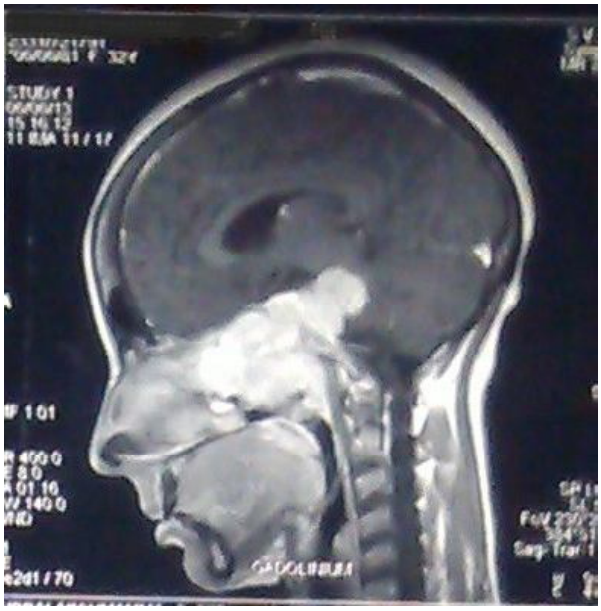

Figure 3: T1-weighted gadolinium contrast-enhanced MRI of the head showing mixed density lesion seen in nasopharynx extending to left eth- moid sinus and cavernous sinus

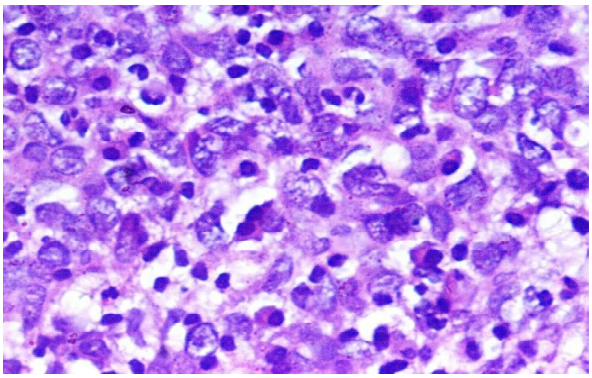

Figure 4: Photomicrograph showing polygonal cells with pleomorphic vesicular nuclei, prominent nucleoli and scant cytoplasm suggestive of undifferentiated squamous cell carcinoma (Hematoxylin and eosin, × 40)

Diagnostic nasal endoscopy was carried out and a biopsy specimen was obtained from the lesion. Histopathological examination of the biopsy specimen was suggestive of undifferentiated squamous cell carcinoma (Figure 4).

The patient was diagnosed to have NPC (Stage 4) with total ophthalmoplegia due to involvement of cavernous sinus and orbital apex and neurotrophic keratitis. The patient was started on topical treatment with 0.5% moxifloxacin, 1% carboxymethyl cellulose, 2% homatropine and 0.25% fluorometholone eye drops. In addition lubricating eye ointment was administered at bed time.

She was referred to neurosurgery and medical oncology services for further management. The patient was started on oral phenytoin and once-a-week cisplatin for 3 weeks followed by radiotherapy (60 Gy in 30 cycles). The neurotrophic ulcer responded to treatment, ptosis improved and visual acuity improved to 5/60 (Figures 5A and 5B) at 6 months follow-up.

DISCUSSION

NPC is a unique disease with clinical behaviour, epidemiology and histopathology that is different from that of squamous cell carcinomas of the head and neck. NPC is considered as an Asian disease, particularly in southern Chinese population. It is rare in the rest of the world. Intermediate rates are recorded in areas such as South-East Asia, Taiwan, Hong Kong and locations with large number of immigrant Chinese.[7] The elevated nitrosamine content in salted or preserved food and fermented dietary items are thought to be a causative factor.[8]

Epstein-Barr virus (EBV) genome is clonal in dysplastic NPC cells indicating the EBV infection is an early event in the multi-stage progression of NPC.[9] The NPC is most commonly seen in the 40-60 years age groups with peaks also being described in the second and sixth decades of life; men are more frequently affected than women (male: female ratio = 2.5:1).[10]

Pathologically the World Health Organization (WHO) classification of NPC recognizes three histological types. These include Type 1, keratinizing squamous cell carcinoma found in non-endemic areas. It is associated with smoking and alcohol use and has the worst prognosis. Type 2, nonkeratinized carcinoma behaves in a fashion similar to Type 3. Undifferentiated carcinoma that was previously

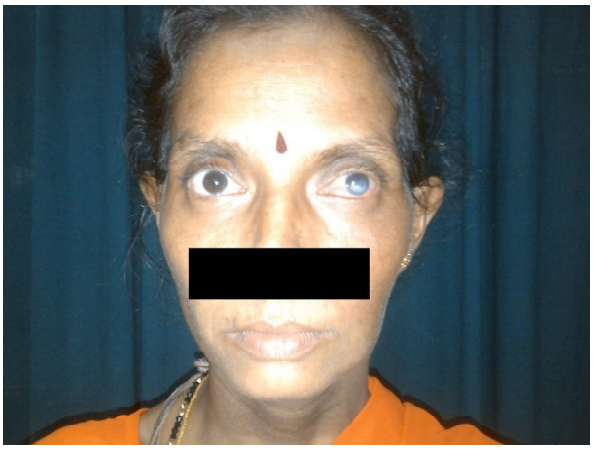

Figure 5A: Clinical photograph showing improvement of ptosis in primary position at 6 months of follow-up

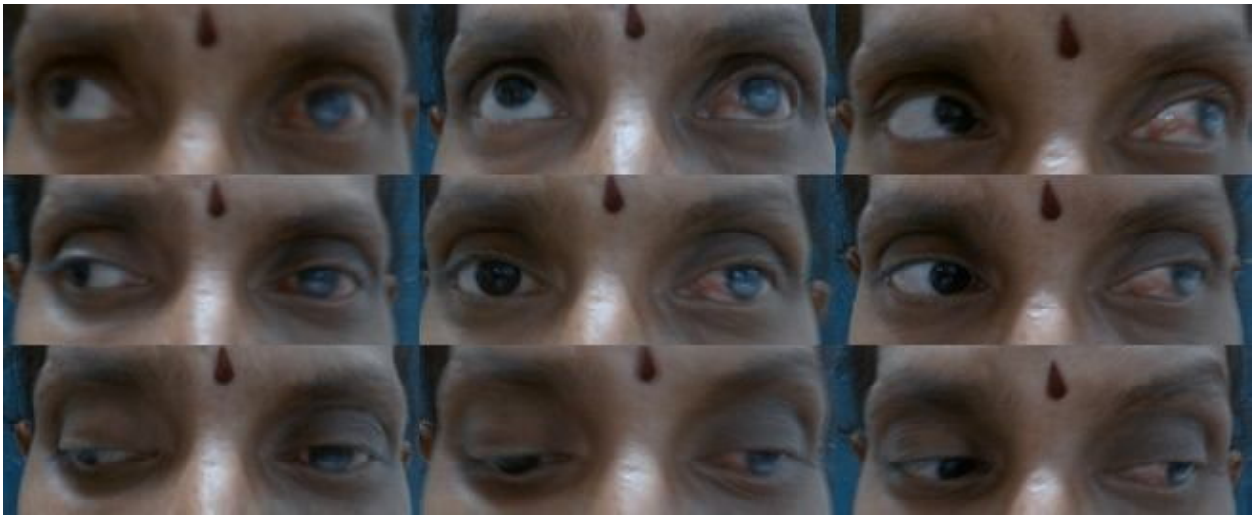

Figure 5B: Photograph showing ocular movements in 9 positions of gaze after radiotherapy and chemotherapy at 6 months of follow-up

called B lymphoepithelioma constitutes Type 3. Types 2 and 3 are radiosensitive and have a much better prognosis. In North America the prevalence of Types 1, 2 and 3 NPC has been reported to be 25%, 12% and 65% respectively.[11] Our patient had Type 3 disease.

Staging of NPC relies on evaluation of the primary tumour (T category), the draining nodal groups (N category) and evidence of metastatic disease (M category).[12] Orbital invasion is staged as T3 disease. Orbital invasion is a marker of extensive disease.

Direct extension from the pterygopalatine fossa and inferior orbital fissure represents the most common route of orbital involvement.[13] The tumour can infiltrate further superiorly into inferior orbital fissure and extend to the orbital apex. From the orbital apex it can extend intracranially via superior orbital fissure. Infiltration occurs as a result of direct extension from the nasal cavity, with 15% of patients having evidence of infiltration at diagnosis. Extension from the ethmoid and or sphenoid sinuses is the second most common route.[14]

Orbital extension from the superior orbital fissure via the cavernous sinus is the, least common route. Other orbital manifestations include nasolacrimal duct involvement, although the mechanism is uncertain, direct reflux has also been postulated.[15] Orbital invasion indicates a poor prognosis.[16] Optic neuritis has been described, possibly secondary to a paraneoplastic syndrome. Radio-

therapy is the main stay of treatment for NPC followed with chemotherapy in ad- vanced cases . In an earlier study[16] a 5-year survival rate of 35% was reported. During the follow-up period ptosis of right eye had improved with a good LPS action of 8 mm. Neurotrophic ulcer responded and fluorescein stain was negative. Extraocular movements improved significantly. Visual acuity improved from counting finger close to face to 5/60. Fundus showed normal study in right eye. This case highlights the importance of considering NPC as one of the causes total ophthalmoplegia and neurotrophic keratitis.

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