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Acute Sixth Cranial Nerve Palsy as the Presenting Manifestation of Locally Advanced Nasopharyngeal Carcinoma: A Case Report

Assiya Lemkhoudem[1]*, Laalou Amine[1], Manal Abboubi[1], Salah Eddine Bouabbadi[1], EL Houssine Ait El Haj[1], Fouad El Asri[1]

[1]Avicenne Military Hospital of Marrakech, Morocco

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***Corresponding author:** Assiya Lemkhoudem
Avicenne Military Hospital of Marrakech, Morocco

Abstract | **Case Report**

Introduction: Nasopharyngeal carcinoma can remain clinically silent until it extends to adjacent structures, including the skull base and cavernous sinus. In some cases, ophthalmological symptoms may be the first indication of an underlying malignancy. ***Case presentation:*** We report the case of a 47-year-old patient with no significant medical history who presented with sudden-onset binocular diplopia that had persisted for one month, accompanied by weight loss and asthenia. Ophthalmological examination revealed esotropia and limitation of right-eye abduction, with preserved visual acuity and no optic disc abnormalities. Lancaster testing confirmed right sixth cranial nerve palsy. Given the associated general symptoms, further investigations were performed. MRI revealed a nasopharyngeal mass measuring 42 × 26 × 29 mm, extending to the skull base and right cavernous sinus and involving the intracavernous internal carotid artery. Histopathological examination confirmed undifferentiated nasopharyngeal carcinoma. No distant metastases were identified, and the disease was classified as T4N2M0. The patient received three cycles of induction chemotherapy. As subsequent assessment showed stable disease, concurrent chemoradiotherapy was planned. A follow-up Lancaster test was performed three months after treatment. ***Conclusion:*** This case illustrates how acute binocular diplopia may reveal an advanced nasopharyngeal carcinoma, even in the absence of typical nasal or otological symptoms. Careful ophthalmological examination, followed by appropriate neuroimaging, can play a decisive role in identifying the underlying cause and facilitating timely multidisciplinary management.

Keywords: Nasopharyngeal carcinoma; sixth cranial nerve palsy; diplopia; cavernous sinus; ophthalmology.

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is an epithelial malignancy characterized by a marked geographic variation in incidence, with endemic rates in Southeast Asia and intermediate incidence in the Mediterranean basin, including North Africa [1,2]. In Morocco, NPC represents an important oncological concern, reflecting the relatively high incidence observed across the Maghreb region [2,3]. Its deep anatomical location and close relationship with the skull base, cavernous sinus, and orbital structures account for its potential to extend locally and involve the cranial nerves, particularly the oculomotor nerves and the trigeminal nerve [4,5]. Although cranial neuropathies most commonly occur in advanced disease, they may occasionally constitute the initial manifestation of NPC, preceding the diagnosis of the primary tumor. Among these neurological presentations, sixth cranial nerve palsy can result from skull base invasion or cavernous sinus involvement, leading to acute-onset binocular diplopia. We report the case of a 47-year-old patient presenting with acute diplopia secondary to right sixth cranial nerve palsy, which led to the diagnosis of locally advanced undifferentiated nasopharyngeal carcinoma with skull base and cavernous sinus extension. [1 -3]

CASE PRESENTATION

Patient history

This is a 47-year-old patient with no significant past medical history, particularly no diabetes mellitus, hypertension, history of substance use, or known systemic disease. The patient presented with a sudden onset of diplopia one month prior to presentation, in an afebrile setting, associated with a deterioration in general condition characterized by weight loss and asthenia. There was no history of trauma or recent surgery. No other associated symptoms were reported.

Ophthalmological examination

1. Right eye (OD)

- Visual acuity: 20/20; manifest refraction: −1.00 (−0.25 × 150°).
- Intraocular pressure (IOP): 15 mmHg.
- Ocular alignment: Esotropia.
- Ocular motility: Limitation of abduction; all other eye movements were preserved.
- Pupillary light reflexes: Preserved.
- Anterior segment: Nasal corneal scarring and inferior keratic precipitates (KPs).
- Fundus examination: No optic disc edema or retinal folds.

2. Left eye (OS)

- Visual acuity: 20/20; manifest refraction: −0.50 (−0.75 × 140°).
- Intraocular pressure (IOP): 11 mmHg.
- Ocular alignment: Esotropia.
- Ocular motility: Full.
- Pupillary light reflexes: Preserved.
- Anterior segment: Nasal corneal scarring and inferior keratic precipitates (KPs).
- Fundus examination: No optic disc edema or retinal folds.

3. Orthoptic assessment

a. Lancaster red-green test:

- Hypoaction of the right lateral rectus muscle and hyperaction of the left medial rectus muscle.
- Findings consistent with right sixth cranial nerve (abducens nerve) palsy.

b. Red glass test:

- Homonymous binocular diplopia.

Diagnostic work-up

1. Orbital and brain MRI

- Near-complete opacification of the tympanic cavity and mastoid air cells.
- Soft-tissue thickening involving the right posterolateral wall of the nasopharynx.
- An osteolytic and osteosclerotic mass involving the roof of the nasopharynx, extending to the floor of the sphenoid sinus and the clivus. The lesion had irregular contours, showed contrast enhancement, and protruded into the sphenoid sinuses.

2. Dedicated nasopharyngeal MRI

A nasopharyngeal mass centered on the basiocciput was identified, with obliteration of the right pharyngeal recess. The lesion exhibited heterogeneous T2 signal intensity, isointense T1 signal, diffusion hyperintensity with focal areas of restricted diffusion on ADC maps, and heterogeneous post-contrast enhancement.

The mass measured 42 × 26 × 29 mm (transverse × anteroposterior × craniocaudal dimensions).

Anatomical extent:

- Right lateral extension: Infiltration of the right parapharyngeal space, with involvement of the cavernous sinus and encasement of the right intracavernous internal carotid artery.
- Anterior extension: Bulging into the choanae.
- Superior extension: Bulging into the right sphenoid sinus.

  Bilateral upper jugulocarotid lymphadenopathy was noted, with the largest right-sided lymph node measuring 8 × 19 mm.

3. Nasopharyngeal biopsy

- Histopathological examination: Features of an infiltrative malignant neoplasm.
- Immunohistochemical profile: Findings consistent with undifferentiated nasopharyngeal carcinoma.

4. CT scan of the chest, abdomen and pelvis (CT CAP)

No distant metastatic lesions were identified.

Diagnosis and staging

The findings were consistent with locally advanced nasopharyngeal carcinoma, staged as:

- T4: Intracranial extension involving the cavernous sinus.
- N2: Bilateral cervical lymph node involvement.
- M0: No distant metastases.

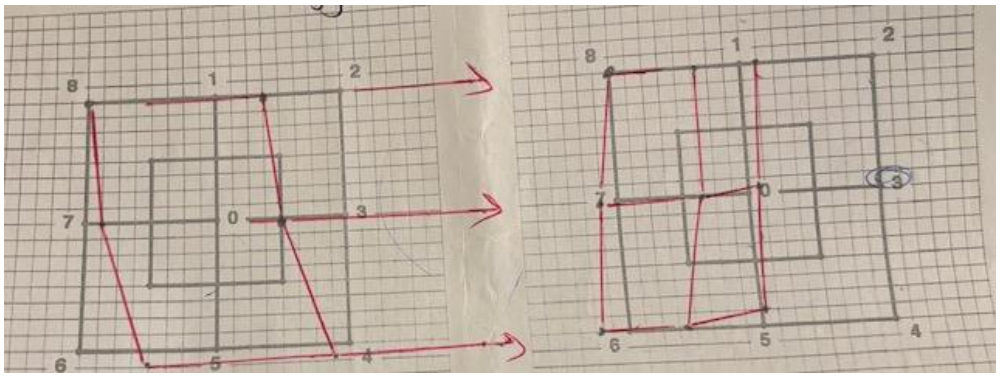
Overall clinical stage: T4N2M0.

Treatment and follow-up

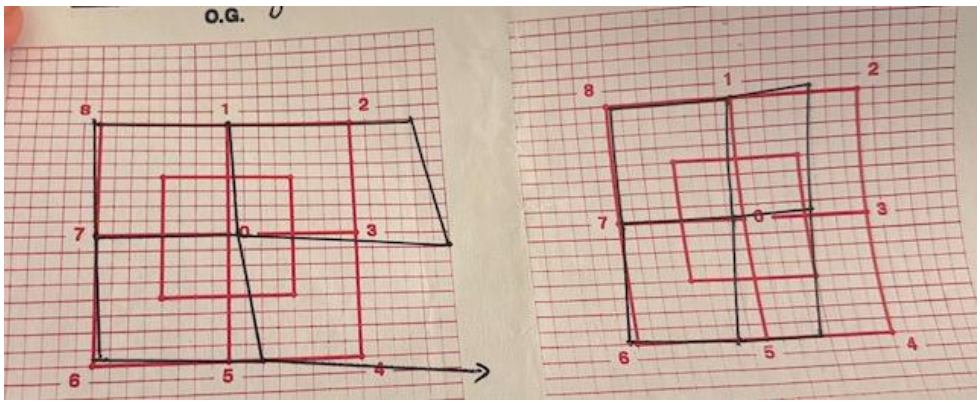
- The patient received neoadjuvant chemotherapy according to the TPX protocol.
- After three cycles, the response assessment demonstrated stable disease, with no significant change in the primary tumor.
- Following multidisciplinary tumor board review, the decision was made to proceed with concurrent chemoradiotherapy.



Clinical photograph showing right esotropia in our patient



Lancaster test demonstrating right sixth cranial nerve palsy (right lateral rectus palsy) before initiation of treatment



3 Months after treatment

DISCUSSION

Nasopharyngeal carcinoma (NPC) is characterized by a wide range of clinical manifestations, which may delay diagnosis, particularly when the initial symptoms result from invasion of adjacent structures rather than the primary tumor itself. Cervical lymphadenopathy, nasal obstruction, epistaxis, and otological symptoms are among its most common presenting features. However, neurological manifestations may occasionally precede the recognition of the primary lesion, representing a diagnostic challenge for clinicians [1,2].

In our patient, the presenting symptom was acute-onset binocular diplopia of one month's duration, associated with asthenia and significant weight loss. No nasal or otological symptoms were reported. Ophthalmological examination revealed esotropia with impaired right-eye abduction, while visual acuity, pupillary responses, and funduscopic findings remained preserved. Lancaster testing confirmed right lateral rectus hypoaction, consistent with right sixth cranial nerve palsy. This presentation illustrates how NPC may initially manifest through an isolated neuro-ophthalmological deficit in the absence of typical nasopharyngeal symptoms.

The abducens nerve is particularly susceptible to lesions involving the skull base because of its long intracranial course and its close anatomical relationship with the clivus, Dorello's canal, and the cavernous sinus. Tumor extension into these structures can impair lateral rectus function, producing esotropia and horizontal binocular diplopia. In a case series of five patients, Lekskul *et al.,* demonstrated that isolated sixth cranial

nerve palsy may be the initial manifestation of NPC, with imaging revealing tumor involvement of the clivus, Dorello's canal, or cavernous sinus [3]. The findings in our patient are consistent with this anatomical mechanism: MRI demonstrated extensive skull base involvement and extension into the right cavernous sinus, providing a plausible explanation for the right abducens nerve palsy.

The absence of optic disc edema, retinal folds, pupillary abnormalities, or decreased visual acuity in our patient suggests that the visual disturbance was primarily attributable to ocular misalignment rather than optic nerve dysfunction. Although the bilateral inferior keratic precipitates and nasal corneal scarring were additional ophthalmological findings, no causal relationship with the nasopharyngeal malignancy was established. These findings should therefore be interpreted independently of the sixth nerve palsy unless further investigations demonstrate an association.

Magnetic resonance imaging is the preferred imaging modality for evaluating the local extent of NPC, particularly skull base invasion, intracranial extension, cavernous sinus involvement, and perineural spread. Compared with computed tomography, MRI provides superior soft-tissue delineation and is particularly valuable for assessing structures that may account for cranial neuropathies [1,2]. In our case, MRI identified a 42 × 26 × 29 mm nasopharyngeal mass centered on the basiocciput, with extension into the right parapharyngeal space and cavernous sinus, involvement of the intracavernous internal carotid artery, and superior extension into the sphenoid sinus. These findings established the locally advanced nature of the lesion and directed the diagnostic work-up toward nasopharyngeal malignancy. Histopathological examination and immunohistochemistry subsequently confirmed an undifferentiated nasopharyngeal carcinoma.

According to the eighth edition of the AJCC/UICC TNM classification, intracranial extension or cranial nerve involvement qualifies as T4 disease. Bilateral cervical lymph node metastases measuring 6 cm or less and located above the caudal border of the cricoid cartilage are classified as N2 [4]. In our patient, the tumor was classified as T4N2M0, corresponding to stage IVA, provided that the bilateral cervical lymph nodes met the criteria for metastatic involvement. No distant metastases were identified on CT of the chest, abdomen, and pelvis. Nevertheless, the final nodal classification should be based on the complete radiological assessment and the documented anatomical location of the lymph nodes, as bilateral upper jugulocarotid lymphadenopathy alone does not definitively establish N2 disease.

The management of locoregionally advanced NPC relies primarily on radiotherapy combined with systemic chemotherapy. Current clinical guidelines recommend induction chemotherapy followed by concurrent chemoradiotherapy for eligible patients with stage III–IVA disease, except for selected lower-risk subgroups [5]. In a randomized phase III trial, Zhang *et al.,* demonstrated that adding gemcitabine–cisplatin induction chemotherapy to concurrent chemoradiotherapy improved 3-year recurrence-free survival compared with concurrent chemoradiotherapy alone (85.3% versus 76.5%) [6]. These results support the use of induction chemotherapy in appropriately selected patients with advanced locoregional disease.

Our patient received three cycles of neoadjuvant chemotherapy according to the institutional TPX protocol. The subsequent assessment showed stable disease, and the multidisciplinary tumor board recommended concurrent chemoradiotherapy. Stable disease after induction chemotherapy does not, by itself, preclude definitive treatment. The decision to proceed with concurrent chemoradiotherapy is consistent with the established management principles for locoregionally advanced NPC. The exact chemotherapy agents constituting the TPX regimen should be specified to permit accurate comparison with published protocols.

Cranial nerve involvement reflects locally advanced disease and may be associated with an increased risk of neurological morbidity. Nevertheless, neurological improvement following treatment has been reported in patients with NPC presenting with sixth nerve palsy. In the case series reported by Lekskul et al., symptoms improved in four treated patients, although the small sample size and limited follow-up preclude reliable conclusions regarding the probability of recovery [3]. In our patient, the neurological outcome after concurrent chemoradiotherapy remains to be documented. Serial assessment of ocular motility, ocular alignment, and diplopia, together with radiological evaluation of tumor response, will be essential to determine whether the sixth nerve palsy resolves, persists, or progresses.

This case highlights the diagnostic importance of considering a skull base lesion in patients presenting with acute sixth cranial nerve palsy, particularly when constitutional symptoms such as weight loss and asthenia are present and common microvascular risk factors are absent. Prompt neuroimaging and appropriate ENT evaluation can facilitate early diagnosis of an otherwise clinically occult malignancy. Ophthalmologists may therefore play a crucial role in the recognition of advanced NPC and in initiating the multidisciplinary management required for these patients.

CONCLUSION

Nasopharyngeal carcinoma may initially present with neuro-ophthalmological manifestations, occasionally in the absence of typical ENT symptoms. In our patient, acute binocular diplopia due to right sixth cranial nerve palsy led to the diagnosis of locally

advanced nasopharyngeal carcinoma with skull base and cavernous sinus invasion. This case highlights the crucial role of ophthalmologists in recognizing atypical neurological signs and initiating prompt neuroimaging. Early diagnosis is essential to facilitate timely multidisciplinary management and potentially improve neurological and oncological outcomes [4-6].

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