CASE REPORT

The Diagnostic Odyssey: Delayed Identification of Nasopharyngeal Carcinoma Presenting as Bulbar Palsy

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ABSTRACT

Nasopharyngeal carcinoma (NPC), predominantly affecting the Chinese population in Malaysia, typically presents with diverse symptoms based on the extent of primary disease and metastasis. This case study details a 66-year-old man presenting with bulbar palsy, initially manifested as left temporal headache, slurred speech, and progressive dysphagia. There was no nosebleed, ear discharge or vertigo. Initial evaluations, including MRI brain, excluded space-occupying lesions and demyelinating disease. MRI of the whole spine incidentally revealed a mass in the Fossa of Rosenmuller with locoregional bony erosion and cervical lymph node metastasis, confirmed as undifferentiated non-keratinizing squamous cell carcinoma (T4N2M0) through biopsy. This atypical presentation underscores the diagnostic challenges and the need for heightened clinical awareness of NPC. By presenting this case, we aim to highlight the importance of considering NPC in differential diagnoses for patients with bulbar palsy to avoid delayed treatment and improve patient outcomes.
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Keywords: Nasopharyngeal carcinoma, Nasopharyngeal cancer, Squamous cell carcinoma, Bulbar palsy, Neurological symptoms

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INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a primary malignancy of squamous cell origin that arise from the lateral aspect of the nasopharynx and Fossa of Rosenmuller (FOR). It is predominantly seen in Southeast Asia and is the fourth commonest cancer in Malaysia, primarily affecting the Chinese ethnicity, followed by the aborigines of Sabah and Sarawak (1). Men are 2-3 times more commonly affected than women. Genetic susceptibility, tobacco smoking and the consumption of large amount of preserved salted fish and meat are recognizable risk factors (1). Clinical presentations are often late, with 60-85% of patients presenting with cervical lymph node metastasis at the time of diagnosis (2). The variable clinical symptoms depend on the extent of primary disease and distant metastasis. It can be broadly divided based on nasal, otology, neurology and nodal involvement. Most of the patient will present with nasal symptoms for examples nasal blockage, epistaxis, post-nasal drip and nasal speech. Abducens nerve palsy is the commonest involved nerve in the case of intracranial extension. Nodal involvement which can present as neck fullness, pain or swelling is the late presentation (3). In this case report, we present a patient whose NPC diagnosis was significantly delayed due to an initial presentation as bulbar palsy. This uncommon presentation not only obscured the underlying malignancy but also led to an intricate and prolonged diagnostic journey.

CASE REPORT

A 66-year-old non-smoker man with hypertension presented with a severe left temporal headache for 1 month, and temporarily relieved with over-the-counter painkillers. He also reported slurred speech and progressive dysphagia over 3 weeks, leading to a significant weight loss of 6kg. There were no associated symptoms such as body weakness, nosebleed, ear discharge, or vertigo. Neurological examination showed mild tongue atrophy and fasciculation, with the rest of the central nervous system examination being unremarkable. No trapezius weakness or facial nerve palsy. A diagnosis of bulbar palsy was made. Initial clinical evaluation suggested a neurological disorder, leading to multiple consultations and extensive testing. Tumour markers, infective parameters, and autoimmune panels were normal. Lumbar puncture and CSF analysis were negative for autoimmune and paraneoplastic antigens. Electromyography showed motor neuropathy

with anterior horn cell disease. An MRI brain performed at another institution, revealed multifocal old lacunar infarcts but no space-occupying lesions or demyelination features. MRI whole spine was performed to rule out Guillain-Barre syndrome and spinal cord demyelination following negative MRI brain findings.

MRI of the whole spine ruled out syringomyelia, spinal cord oedema or lesion. Within the imaged lower cranium, a lobulated mass measuring approximately 3.4cm x 3.9cm x 5.3cm (AP x W x CC) is observed in the posterior nasopharynx. This mass appears T1 isointense (Fig 1a) and heterogeneously hyperintense on T2-weighted imaging (Fig 1b), demonstrating heterogeneous enhancement in post gadolinium (Fig 1c). It invades the sphenoid sinus, clivus and eroding of the odontoid dens. Notably, the pre-pontine cistern and basilar artery remain intact. The mass obliterating both Fossa of Rosenmuller, Eustachian tubes, and torus tubarius (Fig 2a), with more extensive infiltration into both parapharyngeal spaces. This has led to the loss of normal fat demarcation with the levator palatini muscle and pharyngobasilar fascia, along with lateralization of the right tensor palatine muscle (Fig 2b). Infiltration into the adjacent pre-vertebral muscle is evident (Fig 2b), alongside bilateral mastoid effusions. Additional findings include a rounded, T2 hyperintense retropharyngeal metastasis cervical lymph node (Fig 2c) and enlarged metastatic cervical lymph nodes anterior to the right internal jugular vein and internal carotid artery (Fig 2d). These incidental MRI findings prompted a shift in patient management, leading to referral to Otorhinolaryngology specialist for naso-endoscopy. An irregular reddish right posterior nasopharynx mass obscuring the FOR noted in naso-endoscopy. No enlarged palpable cervical lymph node felt. Tru-cut biopsy confirmed undifferentiated non-keratinizing squamous cell carcinoma (T4N2M0). A contrasted CT Neck performed prior to oncology centre referral for chemoradiation therapy better delineate the bone destruction by NPC. There was a permeative pattern observed in the clivus, sphenoid bone, both occipital condyles, and the hypoglossal canal (Fig 3a, 3b, 3c).

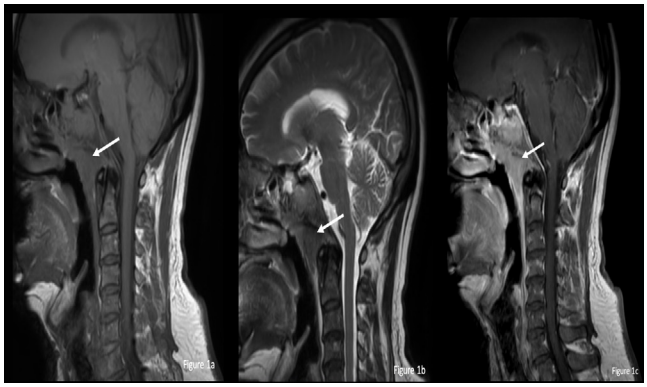

Fig. 1: MRI of lower cranium sagittal view reveals a T1 isointense (1a) and T2 heterogenous hyperintense (1b) lobulated mass in the nasopharynx with heterogenous enhancement in T1 post gadolinium sequence (1c). It measures approximately 3.4cm x 3.9cm x 5.3cm (AP x W x CC). The mass invades the sphenoid sinus, clivus and eroding of the odontoid dens. The normal T1 clivus fat marrow signal intensity is loss. Pre-pontine cistern is preserved.

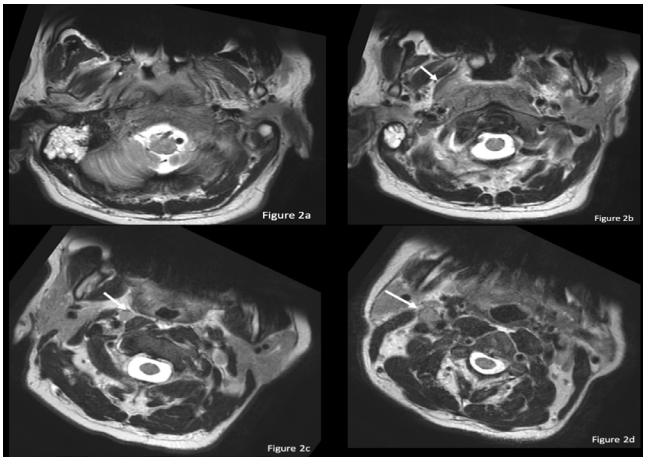

Fig. 2: MRI of lower cranium axial view in T2WI demonstrating the mass obliterating both Fossa of Rossenmuller, Eustachian tubes and torus turbaris (2a). There are extension into both parapharyngeal space (right > left). The normal levator palatini muscle, pharyngobasilar fasica and fat space are lost. The right tensor palatine muscle is bulky with lateralization by the tumour (arrow 2b). Pre-vertebral muscle is involved as well.

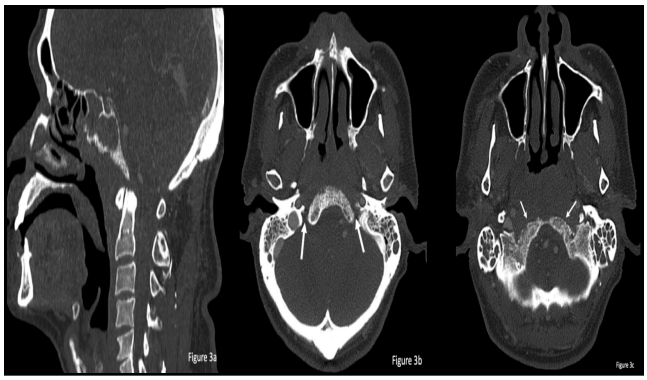

Fig. 3: MRI of lower cranium axial view in T2WI showed rounded, T2 hyperintense retropharyngeal metastasis cervical lymph node (arrow in Fig 3a) and enlarged metastatic cervical lymph nodes anterior to the right internal jugular vein and internal carotid artery (arrow in Fig 3b).

DISCUSSION

Bulbar palsy, characterized by lower motor neuron involvement affecting cranial nerves IX, X, XI, and XII, manifests through symptoms such as nasal speech, drooling, absent gag reflex, tongue atrophy, and fasciculations, leading to significant dysphagia. Common aetiologies include brainstem strokes, tumours, neurodegenerative diseases, autoimmune disorders (Guillain-Barre syndrome, myasthenia gravis), and infectious neuropathies. In this index case, the patient's initial presentation of slurred speech, and progressive dysphagia, coupled with the absence of more common NPC symptoms, significantly complicated the diagnostic process. Despite the thorough investigations, the diagnosis of bulbar palsy was made, directing the clinical focus away from an oncological aetiology. The eventual diagnosis of NPC was incidental, identified through MRI of the whole spine aimed at ruling out spinal pathologies. This serendipitous discovery underscores the diagnostic challenges posed by atypical presentations of NPC and highlights the necessity for a broad differential diagnosis when encountering bulbar palsy. There is a paucity of cases where bulbar palsy was the initial presentation of NPC, although hypoglossal nerve infiltration and paralyzed tongue in recurrent NPC has been documented (4). Table I summarize the common types of cranial nerve involvement secondary to NPC.

Table I: Common types of cranial nerve palsy secondary to nasopharyngeal carcinoma

Authors	Title	Cranial nerve involvement
Sarada Sreenath et al (2023)	Rochen-Duvigneaud syndrome with nasopharyngeal carcinoma	III, IV, V1, VI
Handy Hernandy Yuliawan (2023)	Abducens Nerve Palsy as The First Manifestation of Nasopharyngeal Malignancy	VI
Lekskul A et al (2021)	Isolated Sixth Nerve Palsy as a First Presentation of Nasopharyngeal Carcinoma: A Case Series	VI
Alexa J Denton et al (2021)	Case of Nasopharyngeal Carcinoma Presenting With Rare Combination of Multiple Cranial Nerve Palsies	III, V, VI, VII, IX, and XII
Daniela Rego-Lorca et al (2021)	Abducens palsy as first manifestation of a nasopharyngeal carcinoma	VI
Kaveh Abri Aghdam et al (2019)	Isolated unilateral sixth nerve palsy in a patient with nasopharyngeal carcinoma	VI
An-Guor Wang (2018)	Nasopharyngeal Carcinoma with Right Abducens Palsy	
X Liu et al (2014)	Prognostic value of Magnetic Resonance Imaging-detected cranial nerve invasion in nasopharyngeal carcinoma	II, III, IV, V, VI, IX, X, XI, and XII
H Becker et al (2011)	MRI findings delay the diagnosis of nasopharyngeal carcinoma	VI
A. Baharudin et al (2006)	A Rare Isolated Bilateral Abducens Nerve Palsy In Nasopharyngeal Carcinoma	VI
Jane W. Chan (2003)	Sixth nerve palsy in nasopharyngeal carcinoma	VI
J S Sham et al (1991)	Cranial nerve involvement and base of the skull erosion in nasopharyngeal carcinoma	III, IV, V, and VI
Shoji Bitoh et al (1983)	Nasopharyngeal Malignancies Causing Abducens Palsy	VI

Cranial nerve palsy in NPC indicates advanced disease and is associated with a poorer prognosis. The incidence of cranial nerve palsy in NPC ranges from 12% to 35%, typically resulting from disease extension to the skull base or infiltration through skull base foramina such as the foramen ovale and foramen lacerum. Trigeminal (CN V) and abducens (CN VI) are the commonest affected nerves (5). The prognosis is worse in those with multiple cranial nerves involvement compared to

those with single cranial nerve involvement (5). The proposed mechanisms for cranial nerve involvement include direct tumour invasion, nerve compression, and perineural spread. The latter is of particular interest as it occurs without regional lymph node or organ metastasis. Tumour growth within the nasopharynx can extend in any direction with posterolateral extension posing a risk to the last four cranial nerves. The hypoglossal nerve, in particular, is vulnerable as it traverses the hypoglossal canal, where it comes into close proximity with the glossopharyngeal, vagus, and accessory nerves. Paralysis of hypoglossal nerve result in tongue atrophy of the affected size. Fatty infiltration usually occur in chronic cases. Radiological evidence of hypoglossal canal erosion and soft tissue fullness in the carotid space supported the presentation of bulbar palsy in our patient, despite the sparing of the accessory nerve. Perineural spread through the foramen ovale is another important route for metastasis. Nerve fibres itself are relatively resistant to tumour invasion. MRI, with its superior soft tissue contrast and ability to detect nerve denervation and oedema, is preferred for evaluating cranial nerve involvement.

Submucosal NPC presents significant diagnostic and therapeutic challenges due to its concealed anatomical location, making early detection difficult. Transnasal endoscopic ultrasound-guided fine-needle aspiration biopsy (FNAB) has been shown to be a highly effective method for sampling submucosal lesions, offering enhanced visibility especially in cases where conventional imaging methods fail. In addition to endoscopic methods, MRI is pivotal in the detection and staging of submucosal NPC, as it can identify tumours that are often missed during standard endoscopic examinations as our index case. Generally, management of NPC emphasizes a combination of radiotherapy, chemotherapy, and targeted therapies. Radiotherapy remains the primary treatment for early-stage NPC, providing high curative potential. For advanced stages, concurrent chemoradiotherapy (CCRT) is standard, enhancing the effectiveness of radiotherapy. Apart from the standard management of NPC, endoscopic submucosal dissection (ESD) has emerged as a promising surgical option for early-stage disease enabling en bloc resection of submucosal tumours while minimizing complications like perforation and bleeding. In more advanced cases, where tumours may infiltrate deeper tissues or involve adjacent structures, surgical resection alone is often insufficient. For these scenarios, radiotherapy is considered the cornerstone of treatment. Intensity-modulated radiotherapy (IMRT) is widely preferred due to its ability to deliver high-dose radiation precisely to the tumour while sparing critical nearby structures like the brainstem and optic nerves. IMRT has been associated with better local control and reduced toxicity, making it the standard of care for locally advanced submucosal NPC. Furthermore, when nodal involvement or distant metastases are present, CCRT is recommended. The use of platinum-based chemotherapeutic agents, combined with IMRT, has been shown to enhance radiosensitivity and improve overall survival rates. The integration of these novel therapies into clinical practice, along with advancements in endoscopic and radiotherapeutic techniques, is expected to significantly improve patient outcomes in submucosal NPC management. Comprehensive management strategies also include regular screening, and continuous monitoring to address recurrence and improve overall survival rates.

CONCLUSION

The atypical presentation of bulbar palsy, which mimics more common neurological conditions for example stroke, underscores the need for comprehensive diagnostic evaluation and awareness of NPC as a potential underlying cause. NPC is a highly radiosensitive tumour and submucosal NPC may be missed on routine endoscopy, necessitating a combined approach of MRI and deep endoscopic biopsy to avoid misdiagnosis. Early detection and appropriate management are essential to enhance patient quality of life and survival rates.

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