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Case Report

LOSS OF CONSCIOUSNESS IN NASOPHARYNGEAL CARCINOMA WITH BRAINSTEM INFILTRATION

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ABSTRACT

Introduction: Nasopharyngeal carcinoma (NPC) is prone to intracranial infiltration in advanced stages due to its proximity to the skull base, despite the protective bony structures. Loss of consciousness in NPC patients with brainstem involvement should be distinguished from other causes.
Case Report: A 70-year-old man developed progressive symptoms, including left otalgia and trismus, within eight months before admission. CT revealed a nasopharyngeal mass infiltrating the medullary and pontine cisterns, confirmed as nonkeratinized NPC from biopsy. One month prior, he underwent tracheostomy for airway obstruction. Ten days before admission, he experienced nausea, vomiting, and altered consciousness. During hospitalization, severe hyponatremia was detected and confirmed as the main etiology, further proven by the fact that the patient only regained consciousness after hypertonic saline infusion while being unresponsive after prior dexamethasone administration. After four days, he was discharged with plans for chemotherapy and radiotherapy.
Discussion: Brainstem infiltration in NPC is rare, even in advanced stages, due to the protective skull base. However, intracranial spread can occur via foramina or direct bony destruction. Loss of consciousness in NPC patients with suspected brainstem infiltration requires careful evaluation, as non-tumoral causes like hyponatremia should be considered. Tumor-induced malnutrition, impairing mastication and intake, may contribute to electrolyte imbalances.
Conclusion: In NPC patients with brainstem infiltration, loss of consciousness should not be immediately attributed to direct tumor invasion. Other treatable causes, such as hyponatremia, must be promptly detected to ensure appropriate management.

Keywords: nasopharyngeal carcinoma, loss of consciousness, brainstem infiltration, hyponatremia

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a malignant tumour that originates in the nasopharynx and has a strong tendency for local invasion and distant metastasis. Due to its anatomical proximity to the skull base, NPC can extend intracranially, including into the brainstem, in advanced stages. While the skull

base provides some structural protection, tumour infiltration may occur through foramina or direct bony erosion. Neurological complications from brainstem involvement, such as altered consciousness, are rare but can significantly impact prognosis and treatment decisions.

Loss of consciousness in NPC patients with suspected brainstem involvement presents a diagnostic challenge. While direct tumour infiltration is a possible cause, other factors such as metabolic disturbances, infections, or paraneoplastic syndromes may also contribute. Hyponatremia, a common complication in cancer patients, can lead to severe neurological impairment. Differentiating between direct brainstem invasion and alternative causes is essential for appropriate clinical management and therapeutic intervention.

Despite extensive research on NPC progression and metastasis, reports focusing on brainstem infiltration and its neurological consequences remain limited. The misattribution of symptoms to direct tumour infiltration may delay appropriate corrective measures, such as electrolyte correction, leading to unnecessary interventions and poorer patient outcomes.

This case highlights an instance where severe hyponatremia, rather than direct tumour invasion, was the primary cause of loss of consciousness in an NPC patient with radiological evidence of brainstem infiltration. The patient's recovery following hypertonic saline administration highlights the importance of ruling out metabolic abnormalities before attributing neurological decline to tumour progression. This report aims to emphasize the need for thorough clinical evaluation in similar cases, preventing misdiagnosis and optimizing patient care.

CASE REPORT

A 70-year old male presented with inadequate contact, inability to vocalize or to follow instructions, however the patient was able to localize pain. The patient had a history of difficulty opening his mouth and left auditory disturbances eight months prior.

CT-scan from two months prior at Cipto Mangunkusumo Hospital (RSCM) revealed nasopharyngeal malignant mass with parapharyngeal and masticator space involvement**.**

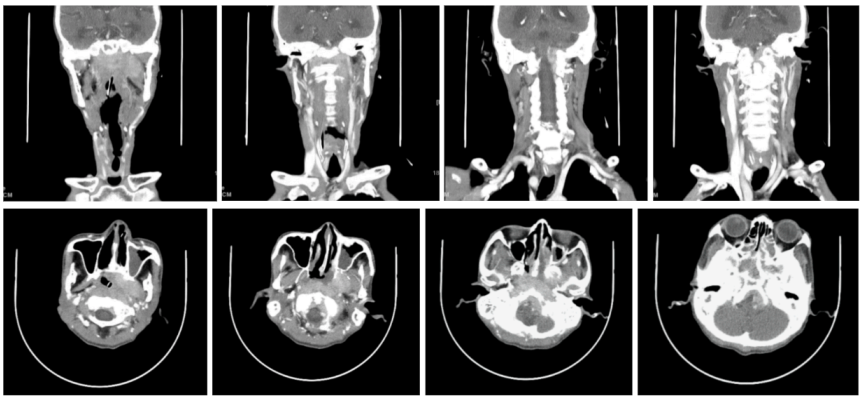

Figure 1. A collage of coronal (top) and axial (bottom) view of nasopharyngeal CT-scan of the patient. Observed on December 2025

The patient underwent biopsy, confirming undifferentiated squa-mous cell carcinoma of the nasopharynx with T4N2Mx staging, corresponding to at least stage IVA NPC. A month prior to current admission, the patient was admitted to RSCM for tracheostomy due to impending airway obstruction. Chemotherapy was planned on an outpatient basis, and the patient was discharged in a bedridden state, communicating via writing.

Ten days before the current admission, the patient experienced two days of nausea and vomiting followed by lethargy. After nine days in another hospital, the patient was discharged but readmitted to RSCM due to persistent symptoms. On admission, vital signs were normal except for hypertension (179/94 mmHg). General examination and showed no abnormalities, while speculum inspection of the cavum nasi by ENT-Oncology division was also normal, but this is attributed to the fact that the tumor mass is located further back in the nasopharynx and not readily visualized through speculum. Neurological assessment revealed a GCS of E3M5Vtrach, mild right-sided hemiparesis (motor strength 4+), and the use of a nasogastric tube, suggesting obstruction and cranial nerve palsy, which was corroborated by indirect

signs in nasopharyngeal CT-scan namely the sail sign which indicates lesion to the tenth cranial nerve, fatty atrophy of left tongue which indicates lesion to the twelfth cranial nerve, and atrophy of left shoulder which corresponds to eleventh cranial nerve lesion. Lab results showed thrombocytosis (467,000/uL) and significant hyponatremia (121 mmol/L). Initial 10 mg intravenous dexamethasone challenge did not improve conscious-ness, thus further administration was halted. The patient was then treated with 3% NaCl via central access twice daily while further planning by the ENT and Medical Hematology-Oncology department also continues in determining the best definitive treatment tailored for the patient.

Over four days, consciousness gradually improved, reaching full recovery after two days. The patient was discharged with plans for nasopharyngeal MRI, induction chemotherapy (Cisplatin and 5-FU), and consideration for radiotherapy.

DISCUSSION

Nasopharyngeal Carcinoma

Nasopharynx

NPC is a type of malignant tumour which arises from the nasopharynx which serves the function of passage for air and food, resonance space in phonation, and pharyngeal articulation. The nasopharynx is bordered laterally by Rosenmüller's fossa, orificium of eustachian tube, and torus tubarius and lined by ciliated pseudostratified epithelium with goblet cells at its mucosal lamina.[1]

Pathogenesis

NPC in many patients usually arises from fossa of Rossenmüller which is a deep recess located at the superior part of nasopharynx, close to the ostium of the Eustachian tube. The

WHO Classification	Epidemiology	Prognosis
Keratinizing	~25% NPC cases Rare <40 y of age Men greater than women Weak EBV association Environmental risk factors	20%-40% 5-y survival
Nonkeratinizing	Overall ~ 75% NPC cases Most common fifth to seventh decades 70% men, 30% women Strong EBV association Genetic & environmental risk factors	

Differentiated	~ 15% NPC cases	~75% 5-y survival
Undifferentiated	~60% NPC cases May occur in children	~75% 5-y survival
BSCC	Rare Sixth to seventh decades, mean age = 55 y Men greater than women Associated with excessive alcohol and tobacco use	Seems to be less aggressive than BSCC in other sites but overall poor prognosis

Table 1 WHO classification of NPC

growth of tumour might obstruct the tube which causes effusion, and otalgia which was present in the patient presented in this case.[1]

One model of pathogenesis given by Wong, et.al. states that normal nasopharyngeal epithelial cells are influenced by exposure to environmental carcinogens which causes genetic lesions, such as deletions in chromosomes 3p and 9p, leading to the inactivation of tumor suppressor genes, predisposing nasopharyngeal epithelial cells to Epstein–Barr virus (EBV) infection. Infected cells harbor episomal viral genomes and express viral proteins and non-coding RNAs which activate cancer hallmarks and clonal expansion, furthering NPC progression. Somatic genomic alterations, such as mutations in the NF-κB pathway and antigen presentation, shape the tumor microenvironment and enhance immune evasion. Additionally, acquired mutations in TP53, chromatin remodeling genes, and the PI3K–MAPK pathway contribute to tumor growth, local recurrence, and metastasis.[2]

Types of NPC

The WHO classifies NPC into three types: keratinizing squamous cell carcinoma (SCC), non-keratinizing SCC, and basaloid SCC. NPC primarily affects men at fifth to seventh decade of life. Non-keratinizing NPC, strongly associated with EBV, results from genetic and environmental factors. It has two subtypes: differentiated (15% of cases) and undifferentiated (60%), both with a 75% five-year survival rate. The patient in this report was diagnosed with non-keratinizing NPC via nasopharyngeal biopsy, though differentiation was not confirmed.

This diagnosis aligns epidemiologically with the patient presented, informing a better prognosis overall.[3]

Furthermore, the authors of this article investigated through literature searches and discussions whether NPC subtypes have distinct infiltration patterns but found nothing conclusive. Most literature suggests NPC spreads randomly, though its extent can be classified following the American Joint Committee on Cancer (AJCC) staging system which states that T-staging for NPC can be divided into the following: (1) Tis: Tumor in situ; (2) T1: Involves oropharynx/ nasal cavity without parapharyngeal extension; (3) T2: Extends to parapharyngeal fat; (4) T3: Invades skull base/paranasal sinuses; (5) T4: Extends intracranially, affecting cranial nerves, orbit, hypopharynx, or infratemporal/masticator spaces.[3]

The patient in this report had T4 staging due to confirmed intracranial and masticator space invasion on clinical and radiological assessment.

Intracranial Infiltration of NPC

In relation to its location, NPC can extend towards any direction, including into the cranial fossa. This was enabled by the fact that the skull base, which lies superior to the nasopharynx, has several foramina which can be utilized by cancer cells for perineural invasion into the cranium. Cranial nerve involvement in NPC thus can be related and hypothesized even before imaging by relating each cranial nerve palsy with which skull base foramen it passes through. For example, foramen lacerum and foramen ovale, which act as the passage for the third branch of fifth cranial nerve and petrosal nerve respectively, are responsible for medial fossa extension of NPC, while internal acoustic meatus and hypoglossal canal, where the seventh and eighth cranial nerve, and the twelfth cranial nerve passes respectively, play a role in posterior fossa extension.[4,5]

In the patient presented in this article, extension was observed through imaging into the posterior fossa, specifically into the medullary and pontine cisterns. Coupled with apparent twelfth cranial nerve palsy

in this patient, it can be inferred that intracranial NPC extension in this patient passes perineurally through the hypoglossal canal. Despite this, brainstem infiltration in this patient was not thought to cause loss of consciousness due to its relatively superficial infiltration and minimal mass effect, thus lowering the chance of disruption into the ascending reticular activating system which lies dorsally in the brainstem. However, the slight right sided hemiparesis in this patient can be attributed to the tumor pressing towards left pyramid of medulla, right above the decussation of pyramids.[4,5,6]

Other Possible Causes of Loss of Consciousness

Hyponatremia

Hyponatremia, which is indicated by sodium level below 135 mEq/L, is a common complication in many types of cancers, including head and neck cancers. Hyponatremia in cancer patients is often in the form of Syndrome of Inappropriate Anti-Diuretic Hormone (SIADH), which, in absence of other causes such as hypothyroidism and hypoadrenalism or specific organ failures, is characterized by lower serum osmolarity (hypoosmolar) and normal volemic status (euvolemia).[7]

Head and neck cancer is the second most common cancer to cause SIAD after small-cell lung cancer. The proposed mechanism of this condition is the increase of Y neuropeptide which leads to endogenous vasopressin production, and carotid compression which stimulates the baroreceptor of carotid bulbus. Still there were reports where head and neck cancer patients had elevated plasma vasopressin without any indicators of ectopic production.[8]

Severe hyponatremia (sodium level below 125 mEq/L) will cause low plasma osmolarity. Within the brain, this causes extravasation of plasma into the interstitial space of brain parenchyma, causing interstitial edema of the brain. This further causes the increase of intracranial pressure, causing nausea, vomiting, and delirium. Left untreated, hyponatremia will cause osmotic demyelination of neurons causing further deterioration which leads to death.[8,9]

In the patient presented in this article, the apparent hypoosmolar

and hypovolemic state at presentation pointed towards SIADH as a cause of hyponatremia, which might be induced by NPC. However, other possible causes of hyponatremia also existed in this/ patient as discussed below.

Low Intake

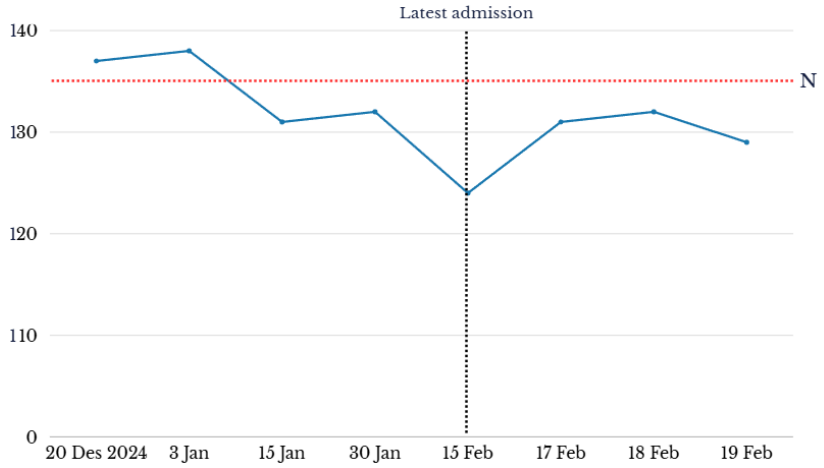

Figure 2 The patient's sodium level from first diagnosis of possible nasopharyngeal mass to latest admission

Masticator space and parapharyngeal space infiltration of NPC can have debilitating effects on the ability to eat normally. Masticator space is located laterally from nasopharynx and contains the lateral and medial pterygoid muscles which helps to pull the condyle head of mandible for jaw protrusion, and elevation and lateral deviation of the mandibula, respectively, which are essential in eating and chewing. Parapharyngeal space, which lies posterolaterally to the nasopharynx also contains the carotid sheath, which houses the internal carotid artery, internal jugular vein, and the ninth, tenth and twelfth cranial nerves, which innervate various muscles of the Naso oropharynx and tongue. Compression or destruction in this area will result in further difficulty of oral intake.[10]

In this patient, low intake should have manifested as overall lowering of nutritional laboratory indicators such as low blood glucose, and low blood electrolytes. Since hypo-natremia is the only abnormality observed, low intake is not thought of as the main factor in causing loss of consciousness in this patient.

Management

Hyponatremia

Hyponatremia in this patient is classified as SIADH due to hypoosmolar and euvolemic status. The duration of hyponatremia is chronic and persistent with fluctuating levels; thus, the current recommendation dictates administration of hyperosmolar saline (NaCl 3%) with the targeted increase of no more than 10 mmol in 24 hours, followed by fluid restriction if the patient's consciousness improves. The patient in this article showed marked improvement after both procedures, further cementing hyponatremia as the main cause of loss of consciousness.[11]

Nasopharyngeal Carcinoma

In accordance to the 2024 NCCN guidelines on Head and Neck Cancer, the definitive therapy for NPC patients should be tailored and personalized for each individual. The guideline stated that for patients with NPC staging of T3-4, N1-3, M0 should undergo induction chemotherapy followed by systemic therapy/radiotherapy. The choice of induction in this patient is preferred (category 1) to reduce the tumor mass including its intracranial infiltration. Upon further evaluation, if the patient is deemed fit, radiotherapy can be administered after induction while minimizing the risk of unnecessary radiation to adjacent areas. Docetaxel/cisplatin/5-FU is indica-ted for EBV associated disease (category 2A), which is histopathologically and epidemiologically consistent with the patient in this case report.[12]

Neurosurgery Consideration

Literature searching was performed regarding the consideration of neurosurgery in patients with brainstem infiltration of NPC. The search yielded only one relevant case report article which reports two cases of NPC with skull base involvement, one in cerebellopontine-tine angle and the other in mastoid antrum. The article stated that the main choice of therapy is chemotherapy and re-irradiation, while neurosurgery was indicated only to alleviate the mass effect of the tumor. Neurosurgery should only be performed only if the risk of

damage to eloquent areas can be minimized and then followed further by chemotherapy and radiotherapy.[13]

CONCLUSION

Nasopharyngeal carcinoma is often located near the brainstem, and although rare, it can infiltrate the brainstem through various skull base foramina. This infiltration may cause neurological deficits and impaired consciousness due to brainstem compression. However, decreased consciousness in NPC patients can also result from other factors such as SIADH-related hyponatremia, hypoxemia from airway obstruction, or malnutrition due to swallowing and mastication difficulties.

In cases of NPC with brainstem infiltration, it is crucial not to immediately attribute decline of consciousness solely to tumour infiltration. Other reversible causes, such as SIADH, should be promptly identified and managed to ensure appropriate treatment.

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