CRCP Case Reports in Clinical Practice

Case Report

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A Rare Coincidence of Non-Keratinizing Nasopharyngeal Squamous Cell Carcinoma (SCC) and Pituitary Adenoma: A Case Report

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Citation Soltaninejad S, Yazdani S, Sanjari M, Bahador M. A Rare Coincidence of Non-Keratinizing Nasopharyngeal Squamous Cell Carcinoma (SCC) and Pituitary Adenoma: A Case Report. Case Reports in Clinical Practice. 2025; 10(2): 54-58. DOI:10.18502/crcp.v10i2.19897

Running Title Coexistence of Nasopharyngeal SCC and Pituitary Adenoma

ABSTRACT

This is the first reported case of the coexistence of nasopharyngeal carcinoma and pituitary adenoma in a 36-year-old female. The case is significant due to the rarity of these two tumors occurring simultaneously and the diagnostic challenges posed by overlapping symptoms. The patient presented with a history of chronic nocturnal headaches localized to the temporal region. Initial symptoms included six months of amenorrhea, massive bilateral galactorrhea, and classic clinical signs of acromegaly.

The nasopharyngeal mass was initially missed during early evaluations, as the patient was primarily assessed for a secreting pituitary adenoma. The nasopharyngeal mass was detected for the first time during rhinoplasty using an endoscope. Histopathological examination confirmed differentiated non-keratinizing nasopharyngeal carcinoma alongside a pituitary adenoma. During radiotherapy for the nasopharyngeal carcinoma, the patient developed visual symptoms, including ptosis and outward deviation of the eye. The patient declined surgical excision of the pituitary adenoma; therefore, the radiotherapy field was expanded to include the adenoma. The radiotherapy dose was 70 Gy, delivered in 35 sessions.

After three months of expanded radiotherapy, all symptoms, including headaches and visual disturbances, were completely resolved. Follow-up after 14 months showed no evidence of recurrence or disease progression.

Article info:
Received: February 22, 2024
Revised: March 25, 2025
Accepted: April 21, 2025

Keywords:
Nasopharyngeal neoplasms;
Pituitary adenoma;
Radiotherapy

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Introduction

The World Health Organization classifies nasopharyngeal carcinomas into three types: keratinizing squamous cell carcinoma, non-keratinizing carcinoma, and basaloid squamous cell carcinoma [1]. Non-keratinizing nasopharyngeal carcinoma (NKAC) is the most common subtype and is further divided into differentiated and undifferentiated forms, though this distinction does not affect treatment or prognosis [2]. NKAC is characterized by the absence of keratin production, distinguishing it from other types. Several risk factors are associated with NKAC, including Epstein-Barr virus (EBV) infection, Asian ethnicity, positive family history, tobacco and alcohol exposure, environmental factors such as wood dust, formaldehyde, nickel, and certain genetic variations [3].

Treatment for non-keratinizing nasopharyngeal carcinoma typically involves a combination of surgery, radiation therapy, and chemotherapy, tailored to the cancer stage and patient's overall health [4]. Radiation therapy, often combined with chemotherapy, is the mainstay, especially for advanced stages, with options including intensity-modulated radiation therapy (IMRT) and concurrent chemoradiation showing improved survival and reduced toxicity. Surgery is less common but may be considered in selected cases.

Pituitary adenomas are usually benign, slow-growing tumors that can cause health issues such as acromegaly. The risk increases with age, mostly affecting adults between 30 and 50 years, and is slightly higher in women. Hormonal imbalances like excess growth hormone or prolactin increase risk. Some evidence suggests smoking and heavy alcohol use may also contribute, although further research is needed. Treatment aims to reduce excess hormone production and relieve symptoms, primarily through surgery. When tumors are large or inaccessible, medications and radiation therapy are alternative options.

This case report presents the first known instance of concomitant NKAC and pituitary adenoma, with NKAC detected incidentally during rhinoplasty performed as rehabilitation after acromegaly treatment.

Case Presentation

Here is a concise and clear summary of the case presentation with relevant radiological and clinical details integrated from the search results:

We present the case of a 36-year-old female with a history of chronic nocturnal headaches localized to the temporal region since 2020. Apart from long-term tobacco use, she reported no significant environmental exposures or family history. In 2022, she was referred to an endocrinologist due to six months of amenorrhea, profuse bilateral galactorrhea, and classic clinical signs of acromegaly, including enlarged hands and feet, broad nose, thickened lips, enlarged tongue, and headaches.

Magnetic resonance imaging (MRI) of the pituitary gland, performed with and without gadolinium contrast, revealed a sellar mass measuring approximately 30 × 28 × 15 mm with moderate homogeneous enhancement, extending superiorly into the suprasellar cistern and causing depression of the sellar floor, consistent with a pituitary macroadenoma. The lesion compressed the optic chiasm and involved the right cavernous sinus, while the left cavernous sinus appeared normal. These imaging features align with typical findings of pituitary macroadenomas, which often extend beyond the sella and show solid enhancement on T1-weighted post-contrast images.

Laboratory tests showed elevated serum prolactin (105 ng/mL), insulin-like growth factor 1 (IGF-1) at 830.7 ng/mL, and basal growth hormone (GH) level of 22.4 ng/mL, confirming a functional pituitary adenoma secreting prolactin and GH. Other pituitary hormone levels were within normal limits.

The patient was treated medically with octreotide LAR, cabergoline, and dopamine agonists. Despite partial symptomatic improvement, including reduced galactorrhea, IGF-1 levels remained elevated (267 ng/mL) after one year (Table 1). The patient declined surgical intervention for tumor excision..

In 2023, during rhinoplasty performed as part of rehabilitation following acromegaly treatment, a large nasopharyngeal mass was incidentally detected via endoscopy. The mass and an additional lesion at the skull base were biopsied. Histopathology confirmed differentiated non-keratinizing nasopharyngeal carcinoma and pituitary adenoma. Microscopy showed tumor cells arranged in interconnecting cords and trabeculae without keratinization, with well-defined borders, increased nuclear-to-cytoplasmic ratio, vesicular nuclei, prominent nucleoli, and dense lymphoplasmacytic stroma [Figure 1].

Reassessment of MRI with fat-saturated post-contrast T1 axial images revealed a large enhancing nasopharyngeal mass extending superiorly from the

Table 1. Medical Test Results

Test	Result	Unit
HGH	22.40	ng/ml
FSH	3.3	mIU/ml
Prolactin	10.5	ng/ml
Cortisol Am	5.95	µg/dL
TSH (ELISA)	1.3	µIU/ml
Total Thyroxin (T4)	6.9	µg/dL
Cortisol (8AM)	19.5	µg/dL
Glucose Tolerance Dose	75	gr
Glucose Fasting	80	mg/dL
Glucose (1 hr)	129	mg/dL
Glucose (2 hr)	106	mg/dL
GH (Growth hormone)	5.24	ng/ml
GH (Growth hormone) 60 min	2.54 H	ng/ml
GH (Growth hormone) 120 min	1.86*	ng/ml
IGF-1	267 H	ng/ml

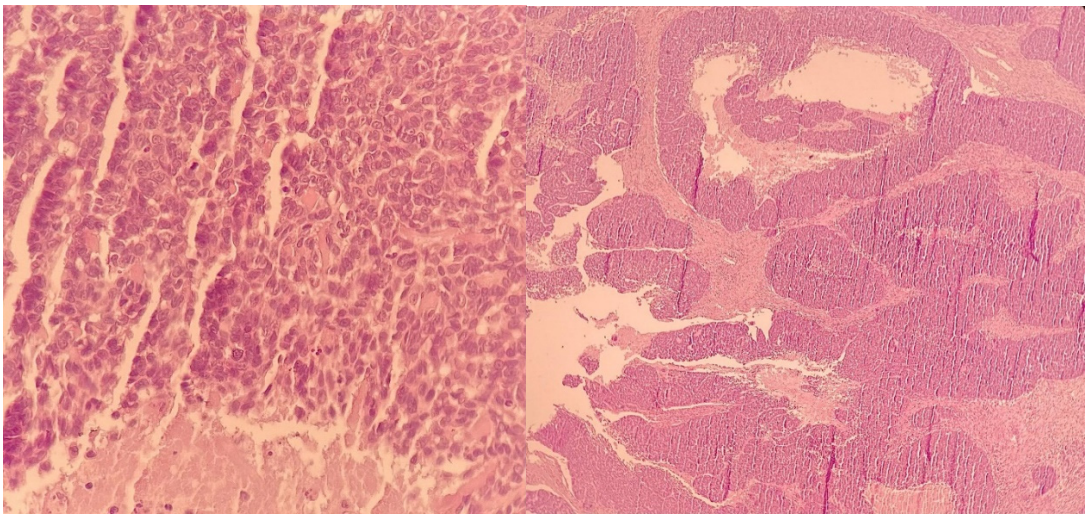

Fig. 1. Nasopharyngeal carcinoma, Nonkeratinizing, differentiated subtype.

nasopharynx roof into bilateral cavernous sinuses (more prominent on the left), crossing the skull base, and involving the dura of the left middle cranial fossa floor and left temporal lobe, consistent with nasopharyngeal carcinoma with intracranial invasion [Figure 2].

This summary reflects the clinical course, imaging findings consistent with pituitary macroadenoma (including suprasellar extension and cavernous sinus involvement per SIPAP classification), and the incidental discovery of nasopharyngeal carcinoma during rhinoplasty, integrating radiological and pathological data from the provided references.

With the new diagnosis of NKAC, the patient

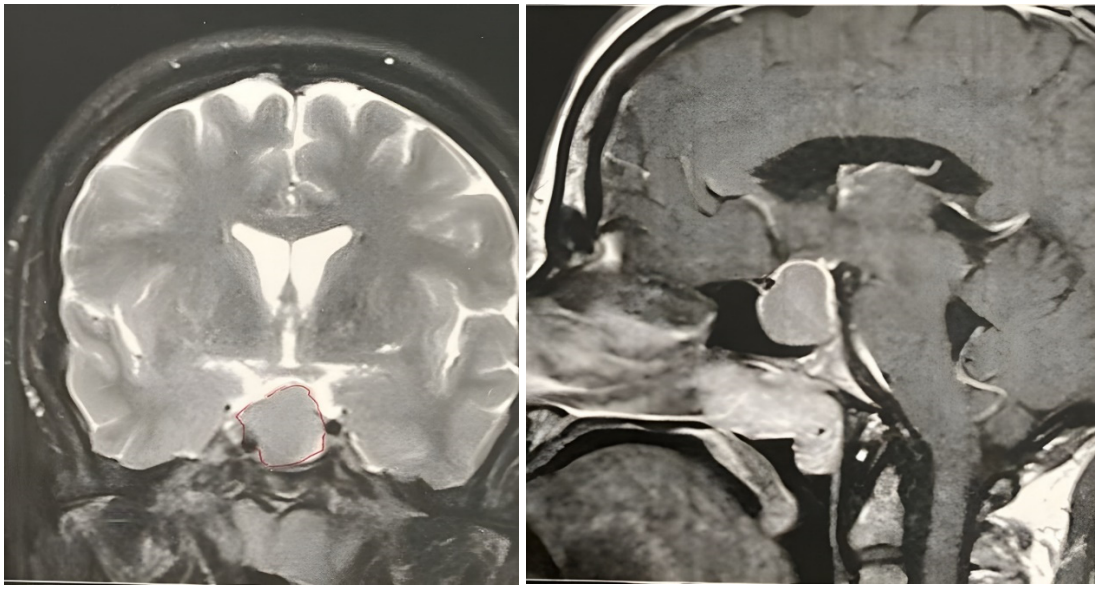

Fig. 2. A large enhancing sellar mass with suprasellar extension and optic chiasm compression is noted, consistent with pituitary macroadenoma, along with a nasopharyngeal carcinoma exhibiting intracranial invasion.

underwent a full tumor work-up, including cervical, chest, and mediastinal CT scans, as well as a PET scan. Positive findings included a 5 mm subpleural nodule in the medial segment of the right lower lobe and a hypodense nodule in the right thyroid lobe, which was reported as benign follicular (Bethesda II) following fine-needle aspiration. At the time of diagnosis, the patient showed positive plasma serology for Epstein-Barr virus (EBV).

In conclusion, we encountered a case of non-keratinizing nasopharyngeal carcinoma (NKAC), staged as T2N0M0, which was initially missed during early assessments and subsequently excised incidentally during rhinoplasty, alongside a coincidental functional pituitary adenoma managed non-surgically. To complete the treatment of NKAC, the patient underwent a standard regimen of concurrent chemoradiotherapy, consisting of weekly cisplatin (50 mg/m²) and a total radiation dose of 70 Gy delivered in 35 fractions.

During chemoradiation, the pituitary adenoma increased in size, resulting in signs of cranial nerve III and VI compression, manifested as ptosis and outward deviation of the left eye. Due to the patient's refusal of surgical excision, the radiotherapy field was expanded to encompass the pituitary adenoma. Consequently, after three months, all symptoms, including headaches and visual disturbances, resolved completely. Follow-up evaluations over 14 months, including post-treatment MRI and PET-CT scans, showed no evidence of recurrence or disease progression.

Discussion

Diagnosis of nasopharyngeal carcinoma is usually difficult in the initial stages, as patients often do not present with any nasal symptoms [5]. In this report, despite the obvious nasopharyngeal mass visible on the patient's first MRI—performed when she was referred for acromegaly and galactorrhea—the lesion was missed by both the radiologist and endocrinologist. To our knowledge, this is the first reported case of the coexistence of nasopharyngeal carcinoma (NAKC) and pituitary adenoma.

Nasopharyngeal masses typically do not produce clinical symptoms until advanced stages, when the tumor becomes large enough to obstruct the Eustachian tube (leading to serous otitis media) [6] or affect cranial nerves (causing headache or visual loss) [7]. However, in the present case, the patient did not experience any ear pain. All symptoms observed in this patient were attributable to the pituitary adenoma, as they persisted after resection of the nasopharyngeal tumor but resolved when the radiotherapy field was expanded to include the pituitary tumor.

Nevertheless, headache [5] and visual disturbances [7] have been reported as the sole symptoms of nasopharyngeal carcinoma in some cases. This underscores the importance of carefully evaluating the nasopharyngeal cavity in patients undergoing MRI for any medical suspicion. Studies have demonstrated that MRI has high sensitivity and specificity in diagnosing nasopharyngeal carcinoma [8].

A large body of evidence supports the role of Epstein-Barr virus (EBV) as the most common risk factor for nasopharyngeal carcinoma (NPC) [9]. In the present case, the patient was not only EBV-positive but was also born in an endemic region for NPC [10, 11]. Although this is the first reported case of the coexistence of these two tumor types, it is possible that some underlying causes for their occurrence are shared. Among the risk factors identified for each tumor type, tobacco exposure is the only common factor, which was also present in this patient.

Using the human gene database (GeneCards®), an RNA gene called MEG3 (Maternally Expressed 3) was identified as a common gene associated with both tumors, with a high relevance score of 92.08 [Figure 1].

Conclusion

This finding may guide future research toward elucidating the shared genomic origins of these tumors. Recent studies have highlighted the genomic landscape of nasopharyngeal carcinoma, suggesting new therapeutic targets and biomarkers for this malignancy [12]. MEG3 could be considered one such potential therapeutic target.

Until it is clarified whether the coexistence of these two tumor types in the same patient is coincidental or due to a common cause, clinicians should be vigilant for accompanying nasopharyngeal carcinomas when evaluating patients with pituitary adenoma.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

Funding

No funding was received to assist with the preparation of this manuscript.

Conflict of Interests

The authors have no conflict of interest to declare.

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