

Case Report

# Nasopharyngeal Metastasis from Lung Adenocarcinoma: A Case Report and Literature Review

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## Keywords

Lung cancer · Nasopharyngeal metastasis · Oligometastatic disease · Local treatment · Case report

## Abstract

**Introduction:** Managing uncommon metastatic sites from different solid tumors is challenging since no available guidelines define the best therapeutic approaches for these rare clinical events. Thus, malignancies giving rise to distant metastases involving infrequent anatomical regions are often associated with a poor prognosis. **Case Presentation:** We present the case of a 75-year-old man who developed uncontrolled epistaxis following the detection of a metachronous nasopharyngeal metastasis from a previous lung adenocarcinoma. The lesion was identified with a computed tomography scan and its origin from the earlier non-small cell lung cancer was confirmed by a biopsy. The patient was successfully treated with radiation therapy and is currently continuing his oncological follow-up. To the best of our knowledge, this is the fifth reported case of a lung malignancy spreading to the nasopharyngeal region. **Conclusion:** Meticulous patient monitoring and accurate radiological diagnosis followed by histological confirmation are of paramount importance for the management of uncommon metastatic sites. Likewise, a multidisciplinary approach is essential to devise the appropriate treatment strategy for each patient with locoregional interventions, such as radiation therapy, often playing a pivotal role for the management of symptomatic lesions in unusual anatomical sites.

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## Introduction

The incidence and prevalence of lung cancer is constantly rising, making it the leading cause of cancer mortality globally, with 1.8 million deaths in 2020 [1]. Non-small cell lung cancer (NSCLC) commonly metastasizes to brain (47%), bone (36%), liver (22%), adrenal glands (15%), the thoracic cavity (11%), and distant lymph nodes (10%) [2–4]. Uncommon metastatic sites represent 5% of distant dissemination, with a higher occurrence in adenocarcinoma compared to squamous cell carcinoma [5]. Soft tissue metastases, particularly in the nasopharyngeal region, are seldom documented in the literature. Moreover, these cases are prone to misdiagnosis as distinguishing metastases from primary tumors in the head and neck region can be difficult.

The lack of defined guidelines makes the management of patients with atypical localizations of lung cancer extremely challenging. Patients with uncommon metastases usually present other disease localizations, warranting systematic therapy as the standard therapeutic approach. However, in oligometastatic disease, there is a growing recognition that prioritizing local treatments such as radiation therapy may be more beneficial [6]. Here we report the case of a man with a history of lung adenocarcinoma, whose disease relapsed in the nasopharynx and was successfully treated with radiation therapy.

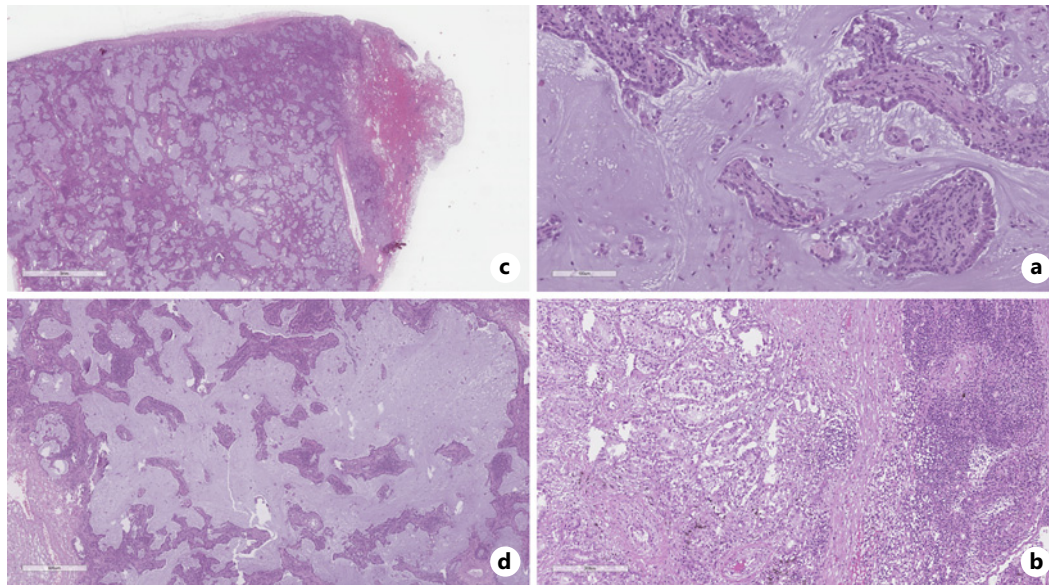
## Case Presentation

In March 2021, a 73-year-old Caucasian man was admitted to the hospital because of persistent cough and dyspnea. A total body contrast-enhanced CT showed a 44 mm heterologous mass in the left lung. The patient was a former smoker of 35 pack/years, with a history of bronchial asthma and hiatal hernia. No family history of cancer was reported. Disease staging was completed with a fluorodeoxyglucose-positron emission tomography (FDG-PET) that confirmed a hypermetabolic lesion in the left lung (maximum SUV 13.2) without nodal involvement and distant metastases.

In April 2021, the patient underwent a left lobectomy and lymphadenectomy with a histopathological exam consistent with invasive mixed mucinous and non-mucinous adenocarcinoma, with prevalent aspects of colloid mucinous carcinoma and pulmonary immunophenotype (shown in Fig. 1a–d). Tumor cells were strongly positive for CK7 and TTF-1 and negative for CD20/CDX2 (shown in Fig. 2a–d). Based on these findings, the patient was diagnosed with invasive lung adenocarcinoma, classified as pT4 (7.5 cm lesion, infiltrating the pleura, and an additional 5 mm nodule in a distinct ipsilateral lobe) pN2 (7/16 positive lymph nodes). Immunohistochemistry examination of the resected tumor tissue was negative for ALK and ROS-1 expression. Molecular analysis did not detect mutations in the *EGFR* and *BRAF* genes. Programmed cell death ligand-1 (PD-L1) testing showed a tumor proportional score <1%. From July to August 2021, he received four cycles of adjuvant chemotherapy with cisplatin and vinorelbine. Subsequently, he underwent regular follow-up evaluations.

In April 2022, an FDG-PET scan showed a single secondary metastasis in the right pubic bone treated with 3 fractions of stereotactic radiation therapy (STRT) (total dose 30 Gy, 1,000 cGy/daily). Following treatment completion, after a thorough discussion with the patient it was decided to resume follow-up.

However, in October 2022 he was admitted to the emergency department for uncontrolled epistaxis. A nasal endoscopy showed the presence of a protruding and bleeding lesion in the left choana. An ensuing CT scan showed hypodense solid tissue, entirely occupying the



**Fig. 1.** **a** Tumors appear as single, soft, jelly-like nodule with a mucoid appearance and protruding borders. **b** High magnification of the nodule reveals abundant extracellular mucin pools with distended and destroyed alveolar spaces. **c** Tumor cells show bland looking, with mild atypia, papillary architecture, mucin laden, and cuboidal to columnar appearance. **d** Metastasis to locoregional lymph node.

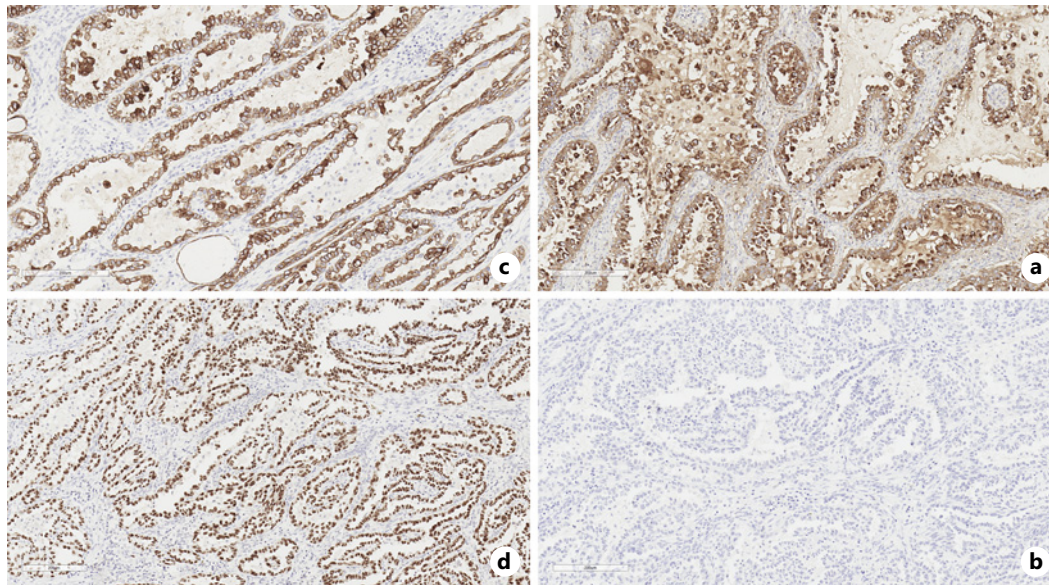
left nasal cavity, the nasopharynx, the maxillary sinus, the sphenoid sinus, the frontal sinus, and the ethmoid cells, interrupting the walls of the left maxillary sinus, partially displacing the nasal septum, and deviating the left ethmoidal lamellae. The hard palate and the left pterygoid processes were also partially eroded (shown in Fig. 3a). An FDG-PET confirmed a metabolically active nasopharyngeal lesion (with a SUV max of 12.8) (shown in Fig. 3b) and a subsequent biopsy showed that the lesion was consistent with a metastasis from lung adenocarcinoma (immunohistochemical profile: TTF-1, Pan-CK, and CK-7 positive; CK-20 and p63 negative).

From January to February 2023, the patient underwent STRT on the left nasal cavity (36 Gy), with considerable improvement of his epistaxis and no major side effects. Indeed, a CT scan performed in July 2023 showed a reduction of the nasopharynx lesion but the appearance of a lesion in the left cerebellar tonsil (shown in Fig. 4a, b). These findings were confirmed by subsequent magnetic resonance imaging of the brain (shown in Fig. 5a–c).

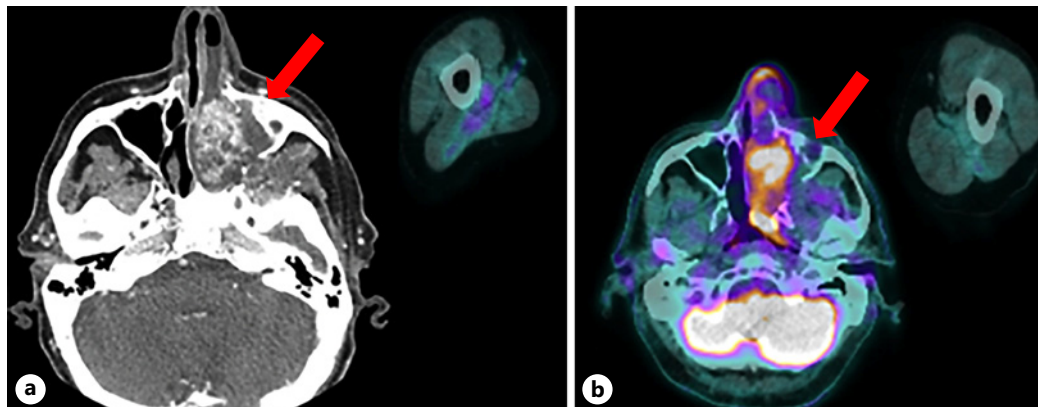
Again, in August 2023, the patient underwent STRT on the left cerebellar tonsil (27 Gy–900 cGy/daily). His last MRI in October 2023 showed further regression of the nasopharynx disease and a partial response of the cerebellar lesion. The CARE Checklist has been completed by the authors for this case report (online suppl. material; for all online suppl. material, see <https://doi.org/10.1159/000539018>).

## Discussion

Although metastases to the nasopharynx are extremely rare in clinical practice, some cases have been documented in the literature as secondary lesions originating from different primary tumors [7–9]. Clinical presentation of nasopharyngeal metastases depends on the

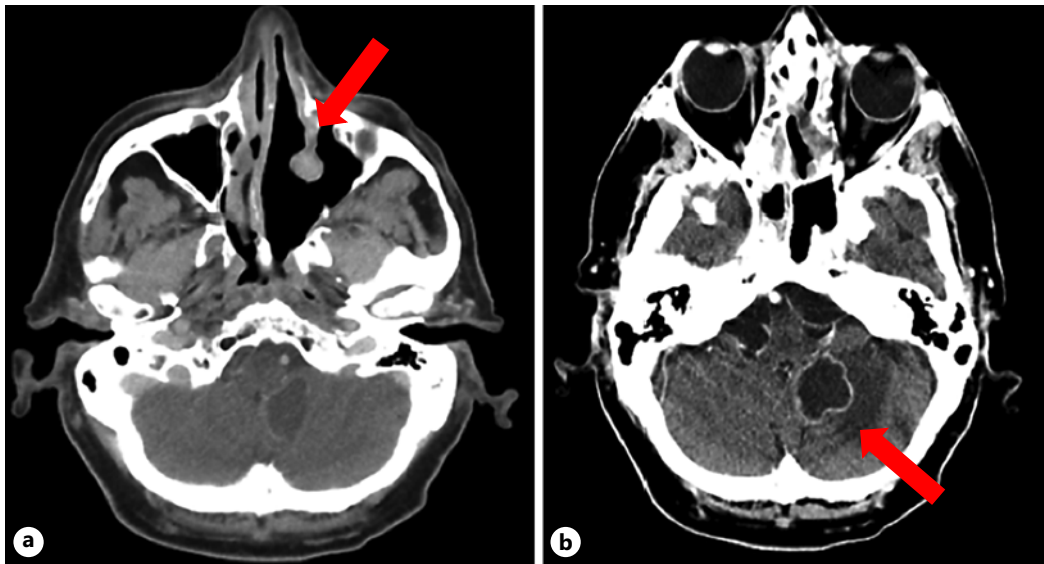


**Fig. 2.** a–d Immunohistochemistry analysis shows strong and diffuse positivity for CK7 (a), TTF-1 (b), Napsin-A (c) and no reactivity for CK20 (d).



**Fig. 3.** a CT scan (axial view) shows a nasopharyngeal mass. b FDG-PET imaging reveals a hyper-metabolic lesion in the nasopharynx.

extent and location of the disease, potentially including symptoms such as nasal obstruction, nasal discharge, epistaxis, hearing impairment, headache, and cranial nerve palsy [10–12]. These manifestations overlap with those of primary nasopharyngeal carcinoma. However, to distinguish between primary and metastatic tumors, appropriate imaging tools and thorough pathological analysis are required [13]. A comprehensive literature review from 1955 to 2023 retrieved 4 cases of lung carcinomas metastasizing to the nasopharynx (shown in Table 1). Notably, all 4 cases involved male patients, with a particularly intriguing observation being that three out of four were from an Asian population. The first case reported in the literature involved a 36-year-old Japanese man diagnosed with adenocarcinoma of the lung. This patient presented with metastases to the palatine tonsils, nasopharynx, and right nasal cavity. Following unsuccessful systemic chemotherapy and worsening of his epistaxis, the patient underwent inhalation therapy with 5-fluorouracil and received local radiation therapy,

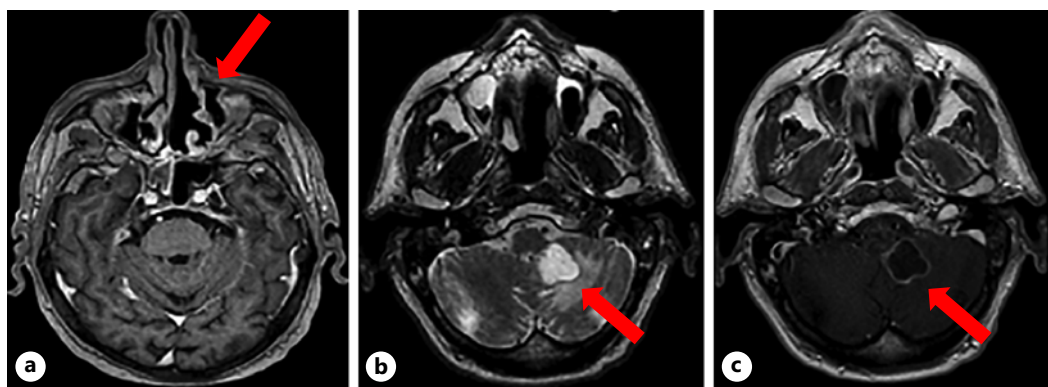


**Fig. 4.** **a** CT scan (axial view) shows response of the nasopharyngeal lesion. **b** CT scan (axial view) shows appearance of a left cerebellar tonsil lesion.

resulting in lesion reduction [14]. Wong et al. [15] presented the case of a patient with a solitary nasopharyngeal metastasis from a lung adenocarcinoma. This patient was treated with radiation therapy alone and remained disease free for 10 years. In the case reported by Hu et al. [16], a patient with previously treated squamous cell carcinoma of the lung developed nasopharyngeal metastases, which were treated with palliative excision to alleviate symptoms, followed by systemic chemotherapy. More recently, Iqneibi et al. [17] reported the case of a 54-year-old man diagnosed with lung adenocarcinoma and metastases to the nasopharynx and mediastinal and axillary lymph nodes. The patient underwent chemotherapy and radiation therapy experiencing disease progression and thus was further treated with immunotherapy.

Given the limited number of reports, there is no consensus about the appropriate management of nasopharyngeal metastases. Treatment of synchronous or metachronous oligometastatic disease in NSCLC requires a multidisciplinary approach. In 2019, the European Organization for Research and Treatment of Cancer-Lung Cancer Group (EORTC-LCG) defined oligometastatic disease as the presence of a maximum of 3 or 5 lesions in a maximum of 3 locations, excluding organs not amenable to ablative treatment, such as the pleura, peritoneum, leptomeninges, or sites of locoregional lymph node disease [18]. Several studies, that evaluated the use of local treatments, surgery, or radiation therapy, in patients with oligometastatic NSCLC disease have demonstrated their efficacy in terms of survival outcomes [19, 20]. Radiation therapy is a viable treatment option for oligometastatic disease, whether there is a single distant disease site or multiple lesions. Its use may be considered, under certain conditions, either in combination with systemic treatment or as a palliative measure to alleviate symptoms [21–23]. However, due to the complex characteristics of oligometastatic disease, the diversity among patients, and the absence of a standard treatment protocol, a multidisciplinary approach remains essential to determine the optimal course of treatment.

In the case presented here, the patient underwent radiation therapy for both his solitary bone lesion and his subsequent nasopharyngeal recurrence, with a good response and excellent treatment tolerance. However, given the multiple relapses, the case was thoroughly



**Fig. 5.** **a** MRI scan (axial view) confirms response of the nasopharyngeal lesion. **b** An MRI scan (axial view) confirms a left cerebellar tonsil lesion in T1-weighted images. **c** The same scan (axial view) confirms the left cerebellar tonsil lesion in T2-weighted images.

**Table 1.** Reported cases of lung cancer with metastasis to the nasopharynx from 1955 to 2023

| Year | Author  | Title   | Age | Gender | Treatment  | Ref  |
|------|---------|---|-----|--------|--|------|
| 1990 | Li      | A case of pulmonary adenocarcinoma in a young man with multiple metastasis to the nasopharynx and paranasal sinuses           | 36  | Male   | Radiotherapy<br>Chemotherapy   | [14] |
| 1998 | Wong    | Solitary nasopharyngeal metastasis from lung primary: a long-term survivor after radiotherapy                                 | 51  | Male   | Radiotherapy   | [15] |
| 2014 | Hu      | Lung squamous cell carcinoma metastasizing to the nasopharynx following bronchoscopy intervention therapies: a case report    | 61  | Male   | Pneumonectomy<br>Adjuvant chemotherapy<br>Radiotherapy<br>Chemotherapy | [16] |
| 2020 | Iqneibi | Metastatic pulmonary adenocarcinoma to the nasopharynx at first clinical presentation, a case report and review of literature | 54  | Male   | Radiotherapy<br>Chemotherapy<br>Immunotherapy                          | [17] |

discussed in a multidisciplinary group to assess the potential for systemic treatment. Following a detailed discussion with the patient regarding the risks and benefits of systemic treatment, it was decided to proceed exclusively with radiation therapy.

### Conclusion

Metastases to the nasopharynx from lung carcinoma are exceptionally uncommon, yet they should always be distinguished from primary head and neck tumors. It is crucial to be aware of associated symptoms, particularly in individuals with a personal history of cancer. Close clinical monitoring, along with radiological and endoscopic examinations and a biopsy, is essential for achieving a diagnosis, increasing the potential for effective treatment and improving clinical outcomes. Careful consideration of disease characteristics and patient factors makes a multidisciplinary team approach mandatory, especially

in case of oligometastatic disease. This collective effort ensures that treatment decisions are well informed, tailored to individual needs, and aimed at optimizing care and outcomes for patients.

### Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent to publish the details of this case report and any accompanying images was obtained from the patient. The study was conducted in accordance with the Declaration of Helsinki.

### Conflict of Interest Statement

Chiara Conti, Sabrina Nucera, Giuseppe Di Grazia, Fabio Motta, and Alfio Di Grazia have no conflicts of interest to declare. Federica Martorana declares the following conflict of interest in the last 3 years: honoraria, consultancies, and travel grants from Amgen, Gilead, GSK, Eli-Lilly, Novartis, Pfizer, and Roche. Paolo Vigneri declares the following conflict of interest in the last 3 years: honoraria, consultancies, and travel grants from Astra-Zeneca, Daiichi Sankyo, Eli-Lilly, Gilead, GSK, Istituto Gentili, MSD, Novartis, Pfizer, and Roche.

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### Author Contributions

Chiara Conti: conceptualization and writing – original draft. Sabrina Nucera: writing – original draft. Giuseppe Di Grazia: methodology. Federica Martorana: writing – review and editing and supervision. Fabio Motta: methodology and Writing. Paolo Vigneri: validation. Alfio M. Di Grazia: conceptualization and supervision. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

### Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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