CASE REPORT

High-grade Neuroendocrine Carcinoma Presenting with Cervical Lymphadenopathy in a Teenager: A Rare Case

Ashfaque Ansari[1], Mahendra Katre[2], Lovee Gupta[3]

Received on: 09 May 2024; *Accepted on*: 24 June 2025; *Published on*: xx xx xxxx

Abstract

Background: Neuroendocrine tumors (NETs) are rare malignancies arising from neuroendocrine cells, with head and neck neuroendocrine neoplasms comprising a small percentage of cases. We present a unique case of a 19-year-old male initially suspected to have tubercular lymphadenopathy, later diagnosed with high-grade poorly differentiated neuroendocrine carcinoma (NEC).

Case description: The patient presented with a persistent painful right-sided cervical swelling and discharging sinus, evolving over 8 months. Imaging revealed a mass in the pharyngeal mucosal space with metastasis to a submandibular lymph node. Surgical debulking and neck dissection were performed, confirming high-grade NEC with a Ki67 index of 75%.

Conclusion: The case underscores the diagnostic challenges and management complexities of high-grade head and neck NECs. Treatment involved intensity-modulated radiation therapy with image-guided radiation therapy, targeting the primary tumor and involved lymph nodes. Prognosis for high-grade NETs is generally poor, emphasizing the need for multidisciplinary care and further research into optimal treatment strategies.

Clinical significance: This case emphasizes the importance of accurate diagnosis and tailored management in rare head and neck NECs. Selecting appropriate imaging modalities, considering tumor characteristics, is crucial for guiding treatment decisions and improving patient outcomes. Collaborative efforts among multidisciplinary teams and ongoing research are essential for refining strategies for NET management.

Keywords: Case report, Head and neck, ISMN1, Neck swelling, Neuroendocrine tumor, Rare entity.

Otorhinolaryngology Clinics: An International Journal (2025): 10.5005/jp-journals-10003-1665

Background

Neuroendocrine tumors (NETs) encompass a heterogeneous group of tumors arising from amine-producing neuroendocrine cells anywhere in the body.[1–3] The incidence of NETs is 2 per lakh, and they account for 0.5% of all malignancies with a female preponderance.[2,3] While the gastrointestinal tract is a common site for neuroendocrine neoplasms, they can also develop in the lungs and pancreas. In the head and neck region, neuroendocrine neoplasms are uncommon, accounting for only 0.3% of all head and neck cancers, with squamous cell carcinoma being the predominant tumor type; moreover, they can present initially as cervical lymphadenopathy because of the nonsecretory nature of tumor being more common in this anatomical location; therefore, high index of suspicion and meticulous management is required.[4,5]

This case report aims to discuss a distinctive case involving a 19-year-old male who presented with painful cervical lymphadenopathy accompanied by a discharging sinus on the right side that had been persistent for 8 months. Initial assessments indicated a possible tubercular cause; however, further imaging and histopathological analyses unveiled an uncommon diagnosis of high-grade poorly differentiated neuroendocrine carcinoma (NEC). This case sheds light on the diagnostic and management complexities associated with this infrequent type of tumor.

Case Presentation

A 19-year-old male presented with a right-sided persistent painful cervical swelling associated with a discharging sinus, which was insidious in onset, measuring around 4 × 4 × 5 cm and slowly growing over the course of 8 months. Routine ear, nose, and throat (ENT) examination revealed grade II tonsillar hypertrophy and a deviated nasal septum on the right side. The patient reported chronic complaints of nasal obstruction and mouth breathing, although they were not significantly debilitating.

Ultrasonography of the swelling revealed necrotic matted cervical lymphadenopathy, raising suspicion of a tubercular etiology. Therefore, for confirmation, fine needle aspiration cytology was performed, which showed atypical cells and was negative for acid-fast bacilli. Moreover, subsequent biopsy results were inconclusive.

[1]Department of ENT, MGM Medical College, Aurangabad, Maharashtra, India

[2]Department of Head Neck Surgery, Government Cancer Hospital, Aurangabad, Maharashtra, India

[3]Department of ENT, Mahatma Gandhi Mission Medical College and Hospital, Aurangabad, Maharashtra, India

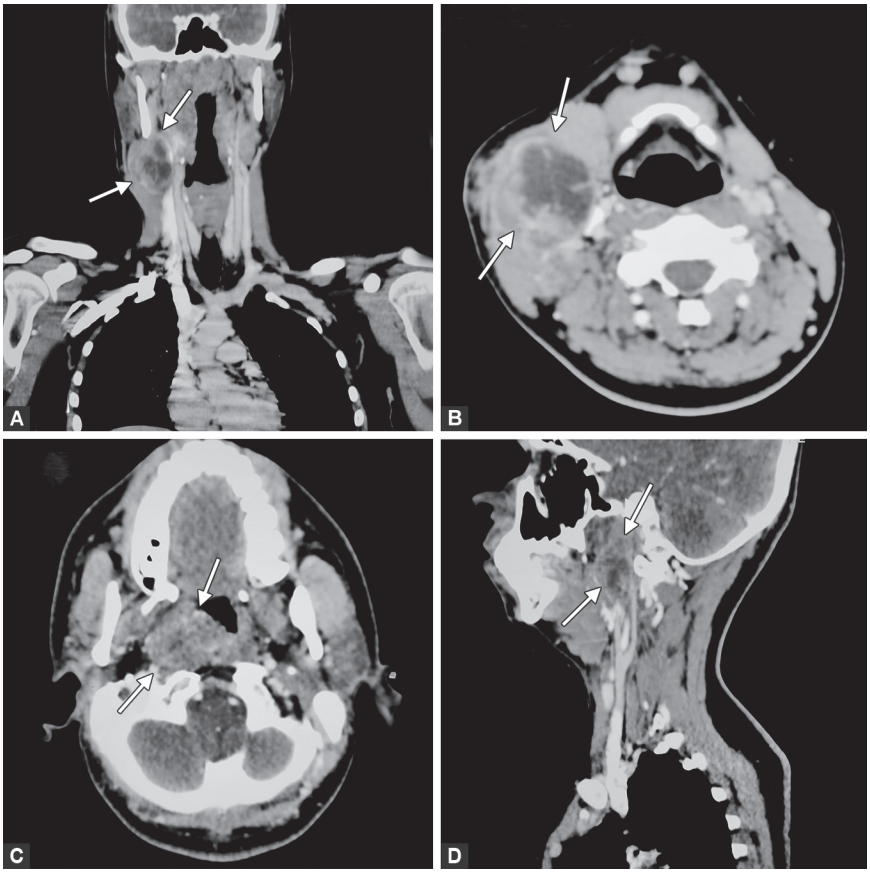
Corresponding Author: Lovee Gupta, Department of ENT, Mahatma Gandhi Mission Medical College and Hospital, Aurangabad, Maharashtra, India, Phone: +91 9644446622, e-mail: gupta.lovee@gmail.com

How to cite this article: Ansari A, Katre M, Gupta L. High-grade Neuroendocrine Carcinoma Presenting with Cervical Lymphadenopathy in a Teenager: A Rare Case. Int J Otorhinolaryngol Clin 2025;x(x):xx–xx.

Source of support: Nil

Conflict of interest: None

Patient consent statement: The author(s) have obtained written informed consent from the patient for publication of the case report details and related images.



Figs 1A to D: Contrast-enhanced CT scan of neck and thorax – (A) Coronal cut showing mass of matted lymph nodes abutting the internal jugular vein (IJV) with no obvious thrombosis; (B) Axial cut showing a mass of matted lymph nodes; (C) Axial cut showing heterogeneously enhancing mass lesion centered around the right fossa of Rosenmuller causing obstruction of the right choana; (D) Sagittal cut showing mass in the nasopharynx, causing significant narrowing of the airway

Hence, a contrast-enhanced CT scan was performed, which revealed an ill-defined, heterogeneously enhancing mass measuring approximately 31 × 1.3 × 3 cm in the pharyngeal mucosal space on the right side, centered over the fossa of Rosenmuller. The mass extended posteriorly into the prevertebral space. Additionally, it extended into the right carotid space with an angle of contact of less than 90 degrees. There was no obvious extension into the right parapharyngeal space, while medially, the mass caused significant narrowing of the nasopharyngeal airway by approximately 50%. Superiorly, no intracranial extension was observed, while inferiorly, the mass extended into the tonsillar fossa. These features suggested a neoplastic etiology, with possible differential diagnoses, including nasopharyngeal carcinoma or nasopharyngeal rhabdomyosarcoma. Enlarged peripherally enhancing nodes of Rouviere were noted bilaterally, along with conglomerated lymph nodes forming a mass on the right side measuring approximately 3.9 × 3.7 × 4.8 cm, causing significant compression of the ipsilateral internal jugular vein without obvious thrombosis. Additionally, multiple subcentimeter-sized reactive homogeneously enhancing lymph nodes were observed in bilateral levels IA, B, I, and III (Fig. 1).

Furthermore, on diagnostic nasal endoscopy, a mass was seen arising from the right fossa of Rosenmuller, causing significant choanal obstruction. Moreover, the endoscopic evaluation revealed mucosal irregularity and friability of the mass, with contact bleeding observed on manipulation. The mass appeared to extend into the nasopharyngeal roof, contributing to a reduction in airway patency (Fig. 2). There was no visible extension into the oropharynx or hypopharynx, and the contralateral nasal cavity appeared unremarkable. These findings further supported the suspicion of a neoplastic process, warranting histopathological confirmation.

Therefore, a treatment plan was devised that involved surgical debulking of the tumor with neck dissection. Initially, the tumor was debrided endoscopically, following which modified radical neck dissection type II was performed. This entailed utilizing a modified Schobinger incision and removing lymph nodes from levels 1 to 5, along with the sternocleidomastoid muscle. Special care was taken to spare the spinal accessory nerve and internal jugular vein (Fig. 3). Subsequently, the entire sample was sent for histopathological analysis. Postoperative events were uneventful, and the patient recovered with mild marginal mandibular nerve palsy (Fig. 4).

Histopathological analysis of the excised mass from the neck revealed a well-circumscribed, solid cystic nodal mass measuring 8 × 4 × 33 cm, accompanied by 14 identified lymph nodes, with one showing metastasis. The excised sample from the nasopharynx exhibited features consistent with poorly differentiated carcinoma, characterized by round to oval tumor cells with pleomorphic nuclei and eosinophilic cytoplasm. Overall, the findings suggested a diagnosis of poorly differentiated carcinoma with metastasis to a single right submandibular lymph node, without extra-nodal extension. This prompted further immunohistochemistry studies, which revealed tumor cells positive for insulinoma-associated protein 1 (INSM1), NSE (focal), and CD56 (rare), with a

high Ki67 proliferation index of approximately 75%. The tumor cells were negative for several markers, including chromogranin, synaptophysin, and S100, indicating a high-grade and poorly differentiated NEC, PDNEC grade III (Fig. 5).

Following which a whole-body fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) was performed, a series of 3 mm computed tomography (CT) cuts with contrast were obtained which revealed that there is an ill-defined soft tissue density lesion involving the bilateral nasopharyngeal region, extending to various structures such as the posterior pharyngeal wall, pharyngeal mucosal space, fossa of Rosenmuller, torus tubarius, and the base of the skull. This area shows a likelihood of being a metabolically active primary malignancy (Fig. 6). There was also uptake in the contralateral level 1b lymph node, suggestive of metastatic deposits. The delineation of treatment volumes was as follows:

- Gross tumor volume (GTV): Comprised of the primary nasopharynx tumor and involved lymph nodes.
- Clinical target volume (CTV): Included GTV, microscopic infiltration, and anatomic structures at risk with a 10 mm margin.
- Planning target volume (PTV): Expanded from CTV to account for systemic and random setup errors, as well as physiological motion, with an additional 5 mm margin.

The treatment plan involved the following three differential volumes:

- Planning target volume high-risk (Gross Disease): 70 Gy delivered in 33 fractions.
- Planning target volume high-risk subclinical: 59.4 Gy delivered in 33 fractions.
- Planning target volume low-risk subclinical: 54 Gy delivered in 30 fractions.

The treatment volume encompassed the entire nasopharynx, anterior 2/3 of the clivus, skull base (foramen ovale and rotundum bilaterally), pterygoid fossae, parapharyngeal space, and pterygopalatine fossae. Lymph node groups at higher risk for regional metastases, including bilateral retropharyngeal lymph nodes and bilateral IB-level V lymph nodes, were also included in the target volume.

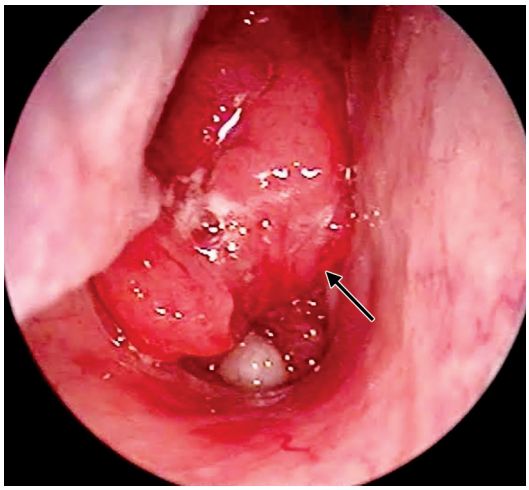


Fig. 2: Endoscopic view showing a friable mass arising from the right fossa of Rosenmuller, causing choanal obstruction and narrowing of the nasopharyngeal airway

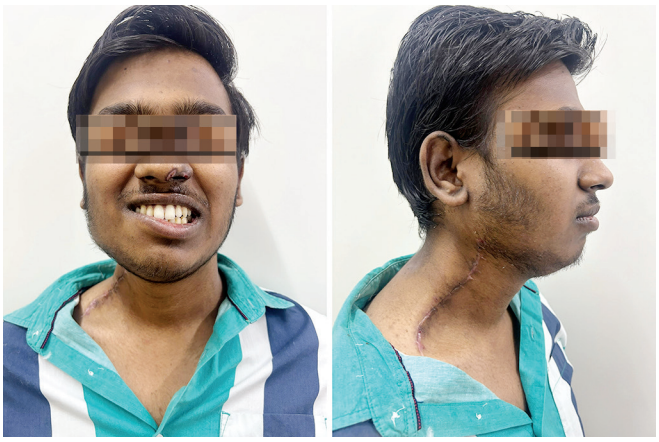


Fig. 4: Postoperative outcome showing mild marginal mandibular nerve palsy. Recovery was otherwise uneventful

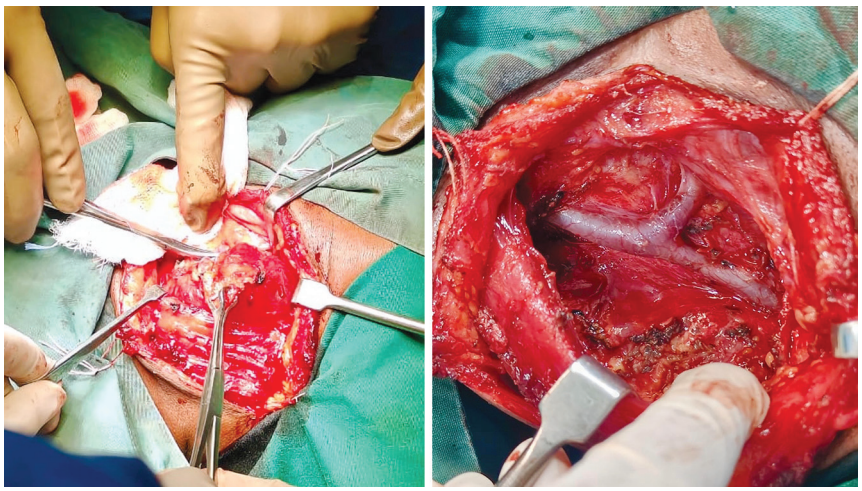
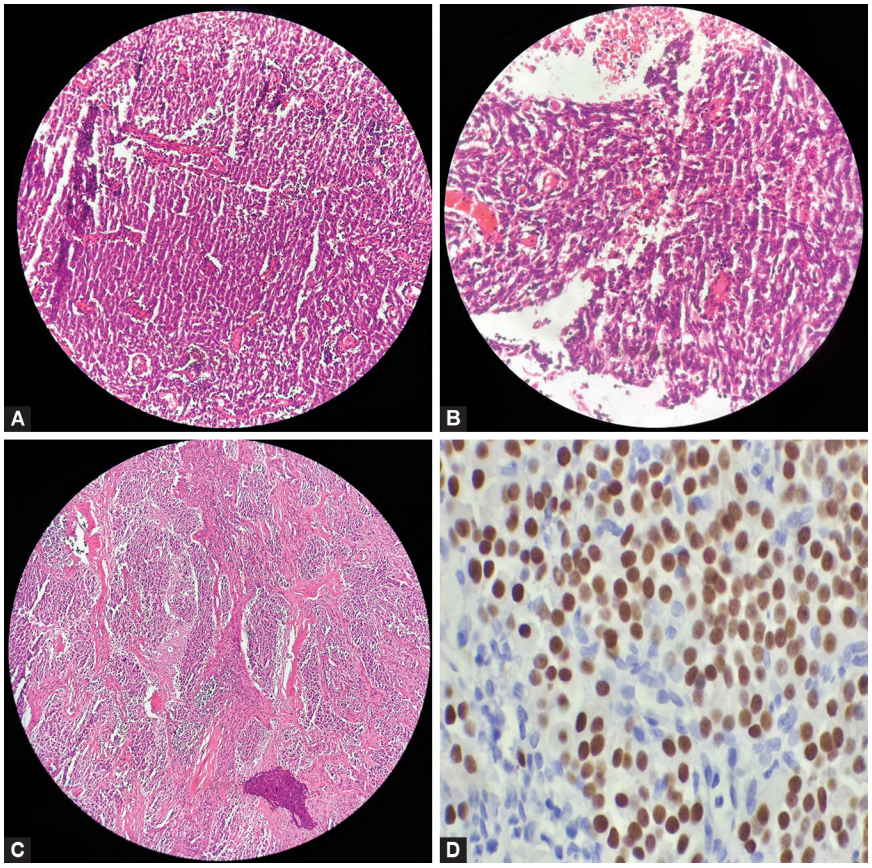
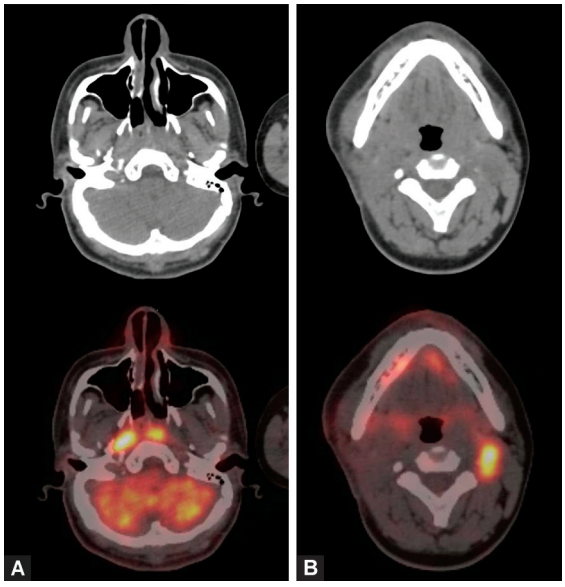


Fig. 3: Intraoperative photos: The left image shows dissection of the neck mass, and the right image displays postmodified radical neck dissection (type II) with the IJV preserved



Figs 5A to D: Hematoxylin and eosin-stained slides showing (A) Tumor in 10× magnification; (B) Tumor at 40× magnification; (C) Tumor in lymph node at 10× magnification; (D) Immunohistochemistry study showing tumor positive for INSM1 marker



Figs 6A and B: Whole-body FDG-18 PET-CT: (A) Showing increased FDG tracer uptake in the nasopharyngeal region, suggesting the possibility of metabolically active primary tumor; (B) Contralateral increased nodal uptake in the submandibular region, suggestive of metastatic deposit

The treatment technique employed was intensity-modulated radiation therapy with image-guided radiation therapy to ensure accurate delivery of the prescribed doses to the target volumes while sparing surrounding healthy tissues.

This comprehensive treatment approach aimed to effectively target the disease while minimizing potential side effects, providing the patient with the best possible outcome.

Discussion

The World Health Organization has recently released classification criteria for head and neck tumors, categorizing neuroendocrine neoplasms into well-differentiated NETs and poorly differentiated NECs. Well-differentiated NETs are further classified into three grades (G1–G3) based on factors like mitotic activity, Ki67 index, and presence of necrosis, while poorly differentiated NECs are high-grade tumors divided into small cell NEC or large cell NEC based on their morphology. Regardless of their origin, neuroendocrine neoplasm cells typically express synaptophysin and chromogranin A.[6]

High-grade poorly differentiated NETs of the head and neck region represent a rare subset of malignancies characterized by their aggressive behavior and neuroendocrine differentiation. In this discussion, we focus on the clinical characteristics, diagnostic challenges, treatment modalities, and prognostic implications of high-grade NETs in the head and neck region.

High-grade NETs of the head and neck typically present with nonspecific symptoms such as neck mass, pain, dysphagia, hoarseness, or respiratory distress, depending on the site and extent of the tumor. Patients may also exhibit signs of neuroendocrine

hormone hypersecretion, such as flushing, diarrhea, or carcinoid syndrome, although this is less common in head and neck NETs compared to gastrointestinal or pulmonary counterparts. Due to their aggressive nature, these tumors often present at an advanced stage with local invasion and regional or distant metastasis. Like in our case, where the presenting complaint was cervical lymphadenopathy due to distant metastasis.[7]

The diagnosis of high-grade NETs in the head and neck region can be challenging due to their rarity and diverse histological features. Initial imaging studies, including CT and MRI, may reveal a mass lesion with heterogeneous enhancement and infiltration into adjacent structures. However, these findings are nonspecific and may overlap with other head and neck malignancies, such as squamous cell carcinoma or lymphoma. Definitive diagnosis relies on histopathological examination, which may require multiple biopsies or surgical excision for accurate subtyping and grading. Furthermore, 68-Gallium/64-Copper DOTATATE PET-CT identifies NETs that impact the management of patients who have negative anatomic imaging and endoscopy studies but have carcinoid-like symptoms and or are biochemically positive for NETs, but their use is limited in grade I and grade II well-differentiated tumors that have somatostatin receptors on the tumor cells. For faster-growing, grade III poorly differentiated tumors, 18-FDG PET scan is preferred, as in our case. Selecting the right imaging modalities for NETs, considering tumor grade, differentiation, and metabolic activity, is pivotal for guiding management decisions and enhancing patient care.[8]

The management of high-grade NETs in the head and neck region is multimodal and typically involves a combination of surgery, radiation therapy, and systemic therapy. Surgical resection with clear margins remains the cornerstone of treatment for localized disease, aiming to achieve complete tumor excision while preserving critical neurovascular structures and functional integrity. Adjuvant radiation therapy is often recommended to reduce the risk of local recurrence, especially in cases with high-risk features such as positive margins or extracapsular extension. Systemic therapy options include platinum-based chemotherapy regimens, peptide receptor radionuclide therapy, targeted agents, somatostatin analogs, and immunotherapy, although the optimal approach remains to be defined.[9]

The prognosis of high-grade NETs in the head and neck region is generally poor, with a high propensity for locoregional recurrence and distant metastasis. Prognostic factors associated with worse outcomes include advanced stage at diagnosis, high-grade histology, lymphovascular invasion, and presence of distant metastasis. Molecular biomarkers such as Ki67 proliferation index and expression of neuroendocrine markers are also relevant. Traditional general neuroendocrine markers include synaptophysin and chromogranin A, with synaptophysin typically being more sensitive and chromogranin A more specific. Insulinoma-associated protein 1 has recently gained recognition as an additional general neuroendocrine marker, which may also provide valuable prognostic information and guide therapeutic decisions.[10]

Given the rarity of high-grade NETs in the head and neck region, collaborative efforts are needed to improve our understanding of their pathogenesis, molecular drivers, and treatment responses. Prospective clinical trials evaluating novel therapeutic agents, biomarkers, and personalized treatment strategies are warranted to address the unmet needs of patients with this aggressive malignancy. Furthermore, multidisciplinary tumor boards involving experts in head and neck oncology, pathology, radiology, and molecular genetics are essential for optimizing patient care and advancing research in this field.

Clinical Significance

This case highlights the complex diagnostic journey and management of a high-grade NEC in a young patient presenting with a painful neck swelling. Overall, the selection of appropriate imaging modalities for NETs, taking into account factors such as tumor grade, differentiation status, and metabolic activity, plays a crucial role in guiding clinical management decisions and improving patient care in these complex and challenging malignancies. Collaborative efforts among multidisciplinary teams and ongoing research are essential to further refine imaging strategies and treatment approaches for NETs across the spectrum of grades and histological subtypes. This patient-centered approach, supported by evidence-based practices and interdisciplinary teamwork, is crucial for delivering personalized and effective care to individuals facing the complexities of neuroendocrine malignancies.

Acknowledgments

The authors extend their heartfelt thanks to the dedicated healthcare professionals involved in the care of the patient in this case report. Special appreciation to the multidisciplinary team, patient, and family for their collaboration and support. Gratitude also to our institution for enabling comprehensive care delivery.

Orcid

Ashfaque Ansari https://orcid.org/0000-0002-0509-3133
Lovee Gupta https://orcid.org/0009-0001-8953-0352

References

1. Kulkarni RS, Anand AS, Parikh SK, et al. Clinical and epidemiological profile of neuroendocrine tumors: An experience from a regional cancer center from Western India. South Asian J Cancer 2019;8(3):198–202. DOI: 10.4103/sajc.sajc_364_18.
2. Mitra S, Roy SG, Sur PK. Adrenocortical carcinoma with skeletal metastases in a postmenopausal woman. Indian J Med Paediatr Oncol 2009;30(1):24–27. DOI: 10.4103/0971-5851.56332.
3. Taal BG, Visser O. Epidemiology of neuroendocrine tumours. Neuroendocrinology 2004;80(Suppl 1):3–7. DOI: 10.1159/000080731.
4. Pointer KB, Ko HC, Brower JV, et al. Small cell carcinoma of the head and neck: An analysis of the National Cancer Database. Oral Oncology 2017;69:92–98. DOI: 10.1016/j.oraloncology.2017.04.009.
5. Bellizzi AM. Immunohistochemistry in the diagnosis and classification of neuroendocrine neoplasms: What can brown do for you? Hum Pathol 2020;96:8–33. DOI: 10.1016/j.humpath.2019.12.002.
6. Rindi G, Mete O, Uccella S, et al. Overview of the 2022 WHO Classification of Neuroendocrine Neoplasms. Endocr Pathol 2022;33(1):115–154. DOI: 10.1007/s12022-022-09708-2.
7. Subedi N, Prestwich R, Chowdhury F, et al. Neuroendocrine tumours of the head and neck: Anatomical, functional and molecular imaging and contemporary management. Cancer Imaging 2013;13(3):407–422. DOI: 10.1102/1470-7330.2013.0034.
8. Akay S, Pollard JH, Eddin AS, et al. PET/CT imaging in treatment planning and surveillance of sinonasal neoplasms. Cancers (Basel) 2023;15(15):3759. DOI: 10.3390/cancers15153759.
9. Lo Nigro C, Denaro N, Merlotti A, et al. Head and neck cancer: Improving outcomes with a multidisciplinary approach. Cancer Manag Res 2017;9:363–371. DOI: 10.2147/CMAR.S115761.
10. La Rosa S. Diagnostic, prognostic, and predictive role of Ki67 proliferative index in neuroendocrine and endocrine neoplasms: Past, present, and future. Endocr Pathol 2023;34(1):79–97. DOI: 10.1007/s12022-023-09755-3.