

Multimodal Imaging Features of NUT carcinoma of the Submandibular Gland: A rare case report

Yanan Shi

Dongguan Tunwah Hospital, China

Da Shi

576867698@qq.com

Dongguan Tunwah Hospital, China

Dan Luo

Dongguan Tunwah Hospital, China

Yongzhou Xu

Phillips China Investment Co., Ltd.

Case Report

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Abstract

Rationale: NUT carcinoma (NC) is a rare and highly aggressive malignancy defined by rearrangements of the NUTM1 gene. Primary NC of the submandibular gland is exceptionally rare, with nonspecific imaging features that often lead to misdiagnosis as common salivary gland tumors and delayed treatment.

Patient concerns: A 32-year-old man presented with a painless mass in the left submandibular region that rapidly enlarged from 2 cm to approximately 4 cm within one month, accompanied by the development of ipsilateral pharyngeal and periauricular pain.

Diagnoses: Preoperative multimodal imaging—computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT)—revealed an ill-defined, invasive mass with heterogeneous enhancement and intense metabolic activity (SUVmax 18.4). The diagnosis was confirmed by histopathological examination and immunohistochemical analysis, which demonstrated diffuse nuclear positivity for NUT protein.

Interventions: The patient underwent radical surgical resection (left neck dissection), followed by adjuvant chemotherapy and radiotherapy.

Outcomes: No evidence of local recurrence or metastatic disease was observed on follow-up imaging at 9 months postoperatively.

Lessons: This case underscores that although the imaging features of submandibular gland NC are not pathognomonic, the combination of a rapidly growing invasive mass, heterogeneous enhancement, and marked hypermetabolism should raise clinical suspicion. Prompt biopsy with NUT immunohistochemical testing is essential for definitive diagnosis and early intervention, which is critical given the tumor's highly aggressive nature.

1. Introduction

Nuclear protein in testis (NUT) carcinoma, previously known as NUT midline carcinoma, is a rare and highly aggressive malignancy defined by rearrangements of the NUTM1 gene on chromosome 15q14 [1, 2]. It is associated with an extremely poor prognosis. To the best of our knowledge, based on a PubMed search using the query (“NUT carcinoma” [Title/Abstract] AND (“salivary gland” [Title/Abstract] OR “submandibular” [Title/Abstract] OR “parotid” [Title/Abstract] OR “sublingual” [Title/Abstract])), this case represents only the sixth reported instance of NUT carcinoma arising in the submandibular gland worldwide.

Owing to its exceptional rarity and nonspecific imaging features, NUT carcinoma is frequently misdiagnosed as more common salivary gland malignancies, which may result in a delay in appropriate treatment. Histologically, it typically presents as a poorly differentiated or undifferentiated squamous cell carcinoma [3]. A definitive diagnosis relies on immunohistochemical detection of the NUT protein, as other conventional markers lack specificity, thereby increasing the risk of diagnostic error [4]. Therefore, early recognition and accurate diagnosis are critical for improving patient outcomes.

In this report, we describe the case of a 32-year-old man with NUT carcinoma of the submandibular gland, supported by comprehensive preoperative multimodal imaging, including computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography/computed tomography (PET/CT), as well as

postoperative follow-up CT. We aim to highlight the characteristic imaging features of this rare entity and discuss its differential diagnosis in comparison with more common submandibular gland tumors.

2. Case Presentation

2.1. Clinical History

A 32-year-old man presented to our institution on November 2, 2024, with a painless mass in the left submandibular region that had been noticed one month earlier. The lesion had initially approximately 2 cm in diameter without associated discomfort. Over the following weeks, the mass progressively enlarged, and the patient developed left-sided pharyngeal pain, with the lesion increasing to approximately 4 cm in size and accompanied by ipsilateral periauricular pain.

On physical examination, a hard, poorly defined, and immobile mass measuring approximately 4.0×2.5 cm was palpated in the left submandibular region. No significant tenderness was noted.

2.2. Imaging Findings

Computed Tomography (CT):

CT revealed a soft-tissue mass measuring approximately $3.6 \times 2.9 \times 4.0$ cm within the left submandibular gland. On axial non-contrast images (Fig. 1A), the lesion appeared hypodense and relatively homogeneous with indistinct margins. Contrast-enhanced images showed heterogeneous enhancement, which was more pronounced at the periphery during the arterial phase (Fig. 1B), with relatively weak internal enhancement. The sagittal arterial phase image (Fig. 1D) revealed the presence of small intralesional vessels (black arrow in Fig. 1D). Slightly increased internal enhancement was noted on the axial and coronal venous phase images (Fig. 1C, F). Additionally, an enlarged lymph node measuring approximately 1.7×1.2 cm was observed in the ipsilateral carotid sheath (white arrow in Fig. 1E), showing heterogeneous enhancement and clear borders.

Magnetic Resonance Imaging (MRI):

On MRI, the mass measured approximately $3.6 \times 2.9 \times 4.0$ cm. It demonstrated signal intensity comparable to the contralateral gland on T1-weighted imaging (T1WI, Fig. 2A). On T2-weighted imaging (T2WI, Fig. 2B), it appeared heterogeneously hyperintense. On fat-suppressed T2WI (T2WI/FS, Fig. 2C), the lesion showed consistent high signal intensity with a linear hyperintense rim at the periphery. Axial enhanced T1WI subtraction image (Fig. 2D) and coronal enhanced T1WI (Fig. 2E) demonstrated marked and heterogeneous enhancement with a peripheral linear enhancing pattern. The sagittal enhanced T1WI (Fig. 2F) clearly showed the enlarged, heterogeneously enhancing lymph node in the ipsilateral carotid sheath (white arrow).

Positron Emission Tomography/CT (PET/CT):

PET/CT (Fig. 3) demonstrated a soft-tissue mass (red arrow) in the left submandibular gland, measuring approximately $3.6 \times 3.0 \times 3.9$ cm, with heterogeneous density and intense ^{18}F -fluorodeoxyglucose (FDG) uptake, with a maximum standardized uptake value (SUVmax) of 18.4. The enlarged lymph node in the carotid sheath (black arrow), measuring approximately $1.7 \times 1.2 \times 1.6$ cm, also showed intensely increased FDG uptake (SUVmax ≈ 13.1).

2.3. Pathological Diagnosis

Ultrasound-guided biopsy of the left submandibular mass indicated a poorly differentiated carcinoma. Immunohistochemical analysis demonstrated retained INI-1 expression and diffuse nuclear positivity for NUT protein, while Desmin was negative, confirming the diagnosis of NUT carcinoma (Fig. 4).

Figure 4A. (H&E staining, 20×): Nests and irregular sheets of epithelioid tumor cells with central coagulative necrosis.

Figure 4B. (H&E staining, 20×): Trabecular or sheet-like arrangements of epithelioid or basaloid tumor cells within a collagenous stroma, with noticeable apoptotic cells.

Figure 4C. (H&E staining, 40×): The tumor cells are monomorphic, round to polygonal, with indistinct cell borders and scant cytoplasm, partially clear. The nuclei are round or oval, often with intranuclear vacuoles and prominent nucleoli (black arrow).

Figure 4D. Immunohistochemistry: The tumor cells show positive nuclear expression of NUT.

2.4. Treatment and Follow-up (Timeline - Fig. 5)

On November 20, 2024, the patient underwent “Left Level I-V Neck Dissection”, “Left Supraclavicular Lymph Node Dissection”, and “Left Neck Vascular Exploration” under general anesthesia. The patient declined further next-generation sequencing (NGS) analysis. Adjuvant chemotherapy was initiated on December 10, 2024, consisting of reduced-dose nab-paclitaxel (225 mg/m²) plus carboplatin (AUC = 5). Postoperative radiotherapy commenced on January 9, 2025, followed by concurrent cisplatin chemotherapy (cycles 1–3) starting on January 17, 2025.

A follow-up MR plain and contrast-enhanced scan performed on August 1, 2025, revealed postoperative changes in the left submandibular region with soft tissue edema but no evidence of local recurrence or metastatic lymph nodes in the surrounding neck (Fig. 6).

T1WI (A) and T2WI (B) show the absence of the left submandibular gland and the mass, with disordered soft tissue architecture in the operative bed.

T2WI/FS (C) shows a patchy area of high signal intensity in the operative field, suggesting soft tissue edema.

Enhanced T1WI (D) shows no abnormal enhancing focus in the operative bed, indicating no signs of recurrence, and no metastatic lymph nodes in the surrounding area.

3. Discussion

First described in 1991, NUT carcinoma (NC) was initially recognized as a malignancy most frequently involving the head, neck, and mediastinum [5]. It is now known to arise in a broad spectrum of anatomical sites, leading the World Health Organization (WHO) to reclassify it simply as “NUT carcinoma” rather than “NUT midline carcinoma” [6]. NC can occur across a wide age range, with a reported median age between 18–23 years and no clear predilection for either sex [7–10]. Clinically, it often manifests as a rapidly enlarging mass, frequently accompanied by regional lymph node involvement at the time of diagnosis [11, 12], which is consistent with the clinical presentation in our patient.

The imaging features of head and neck NC are relatively nonspecific but typically include a large, ill-defined, and invasive soft-tissue mass with internal necrosis or hemorrhage, adjacent organ invasion, and regional nodal metastases [13]. On CT, it usually appears as a hypodense lesion, whereas MRI commonly demonstrates iso- to hypointensity on T1WI and hyperintensity on T2WI, with strong and heterogeneous enhancement following contrast administration [14]. In addition, PET/CT typically reveals markedly increased FDG uptake, with previously reported SUVmax values averaging approximately 12.0 (range 5.0–40.0) [15]. However, SUVmax alone is not sufficiently specific for differentiating NC from other aggressive salivary gland or head and neck tumors, underscoring the importance of comprehensive morphologic assessment and multimodal imaging evaluation [16]. The imaging findings observed in the present case are highly consistent with those previously reported in the literature. The main differential diagnoses and key distinguishing features are summarized in Table 1.

Table 1 Key Imaging Findings and Differential Diagnosis of NUT Carcinoma					
Diagnosis	Benign/Malignant	CT Features	MRI Features	PET/CT Features	Key Distinguishing Features from NC
NUT Carcinoma	Malignant	Irregular, ill-defined, invasive growth, heterogeneous enhancement	Heterogeneous signal, heterogeneous enhancement, neurovascular invasion	High FDG uptake (High SUV)	Highly aggressive, rapid progression, often young patients, confirmed by NUT testing
Pleomorphic Adenoma	Benign ^[17]	Well-defined, smooth, round/oval ^[18]	Homogeneous high T2 signal, mild-moderate enhancement ^[19,20]	Mild to marked uptake ^[21]	Slow growth, no invasion, typical benign appearance ^[17]
Adenoid Cystic Carcinoma	Malignant ^[22]	Ill-defined, perineural spread, neural foramen enlargement ^[23]	Perineural spread, marked enhancement ^[22]	Variable FDG uptake ^[24]	Propensity for perineural growth, indolent course, late lung metastases common ^[22,25]
Mucoepidermoid Carcinoma	Malignant ^[26]	Varies with grade: well-defined (low-grade) to ill-defined (high-grade), mucinous components ^[26]	High signal on T1/T2 (mucin), variable enhancement ^[27]	Uptake correlates with grade ^[28]	Presence of mucinous components, grade-dependent biological behavior ^[26]

From a pathological perspective, diffuse nuclear positivity for NUT protein on immunohistochemical staining is considered the diagnostic hallmark of NC. Therefore, this entity should be strongly suspected in case of rapidly progressing, poorly differentiated or undifferentiated carcinomas, particularly those composed of small round cells, in atypical locations such as the salivary glands. Approximately 75% of NC cases harbor a BRD4-NUTM1 fusion, while less common fusion partners, such as BRD3 and NSD3, have also been reported [29]. Although

standard next-generation sequencing (NGS) can identify the specific fusion partner and potentially guide targeted therapy [30], this analysis was declined by the patient in our case.

The management of NC requires a multidisciplinary approach. Radical surgical resection is recommended for localized disease. For advanced or metastatic cases, radiotherapy and cytotoxic chemotherapy (e.g., ifosfamide-based regimens) may be employed; however, treatment responses are generally limited and resistance frequently develops [31]. Recently, novel targeted strategies, including BET inhibitors and PROTAC degraders such as ARV-825, have demonstrated promising preclinical and early clinical activity and may represent potential therapeutic options in the future [32, 33]. Therefore, enrollment in clinical trials should be considered when standard treatments are ineffective or infeasible.

The prognosis of NC is extremely poor, with a reported median overall survival of approximately 6.5 months [34], and the majority of patients succumbing within 1–2 years of the diagnosis [35]. In contrast, our patient achieved a relatively prolonged survival of more than one year without evidence of local recurrence. This favorable outcome in our case may be attributed to the rapid tumor growth prompting early medical consultation, timely multimodal imaging, prompt biopsy with accurate pathological identification, and subsequent aggressive multimodal treatment including surgery, chemotherapy, and radiotherapy. This case therefore highlights the critical importance of early recognition, accurate diagnosis, and prompt intervention in improving clinical outcomes for this highly aggressive malignancy.

4. Conclusion

NUT carcinoma of the submandibular gland is exceedingly rare and highly aggressive. Although its imaging features are not pathognomonic, the presence of a rapidly enlarging, infiltrative mass with heterogeneous enhancement and high metabolic activity should raise clinical suspicion for this entity. When such findings are encountered—especially after common submandibular gland tumors have been reasonably excluded—NC should be considered in the differential diagnosis. Prompt biopsy with NUT immunohistochemical staining is essential for definitive diagnosis, enabling early, accurate identification and initiation of appropriate treatment, which may ultimately contribute to improved patient outcomes.

Abbreviations

NUT: Nuclear protein in testis

NUTM1: Nuclear Protein in Testis Family Member 1

NC: NUT carcinoma

CT: computed tomography

MRI: magnetic resonance imaging

PET/CT: positron emission tomography/computed tomography

FDG: ¹⁸F-fluorodeoxyglucose

SUVmax: maximum standardized uptake value

T1WI: T1-weighted imaging

T2WI: T2-weighted imaging

T2WI/FS: fat-suppressed T2-weighted imaging

H&E: hematoxylin and eosin

INI-1: Integrase Interactor 1

NGS: next-generation sequencing

AUC: area under the curve

BRD4: Bromodomain Containing 4

BRD3: Bromodomain Containing 3

NSD3: Nuclear Receptor Binding SET Domain Protein 3

BET: bromodomain and extra-terminal

PROTAC: proteolysis-targeting chimera

MIP: maximum intensity projection

WHO: World Health Organization

NC

NUT carcinoma

CT

computed tomography

MRI

magnetic resonance imaging

PET/CT

positron emission tomography/computed tomography.

Declarations

Ethics and consent to participate

This study was approved by the Ethics Committee of Dongguan Tungwah Hospital. All clinical operations complied with the ethical principles of the Declaration of Helsinki.

Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that there are no competing interests related to this manuscript.

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Author Contribution

Author Contributions—Drs Yanan Shi and Da Shi contributed equally to this work and are co-first authors. Dr Yanan Shi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Yanan Shi and Da Shi. Acquisition, analysis, or interpretation of data: All authors. Drafting of the manuscript: Yanan Shi. Critical review of the manuscript for important intellectual content: All authors. Radiological image acquisition and interpretation: Da Shi. Pathological analysis and interpretation: Dan Luo. Technical support and manuscript polishing: Yongzhou Xu. Supervision: Da Shi.

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Availability of data and materials

The original imaging, pathological and clinical follow-up data supporting this case report are stored in the electronic medical record system of Dongguan Tungwah Hospital. Reasonable data access requests can be submitted to the corresponding author upon valid institutional approval.

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Figures



Figure 1

description: Preoperative CT images of left submandibular NUT carcinoma and the enlarged lymph node.

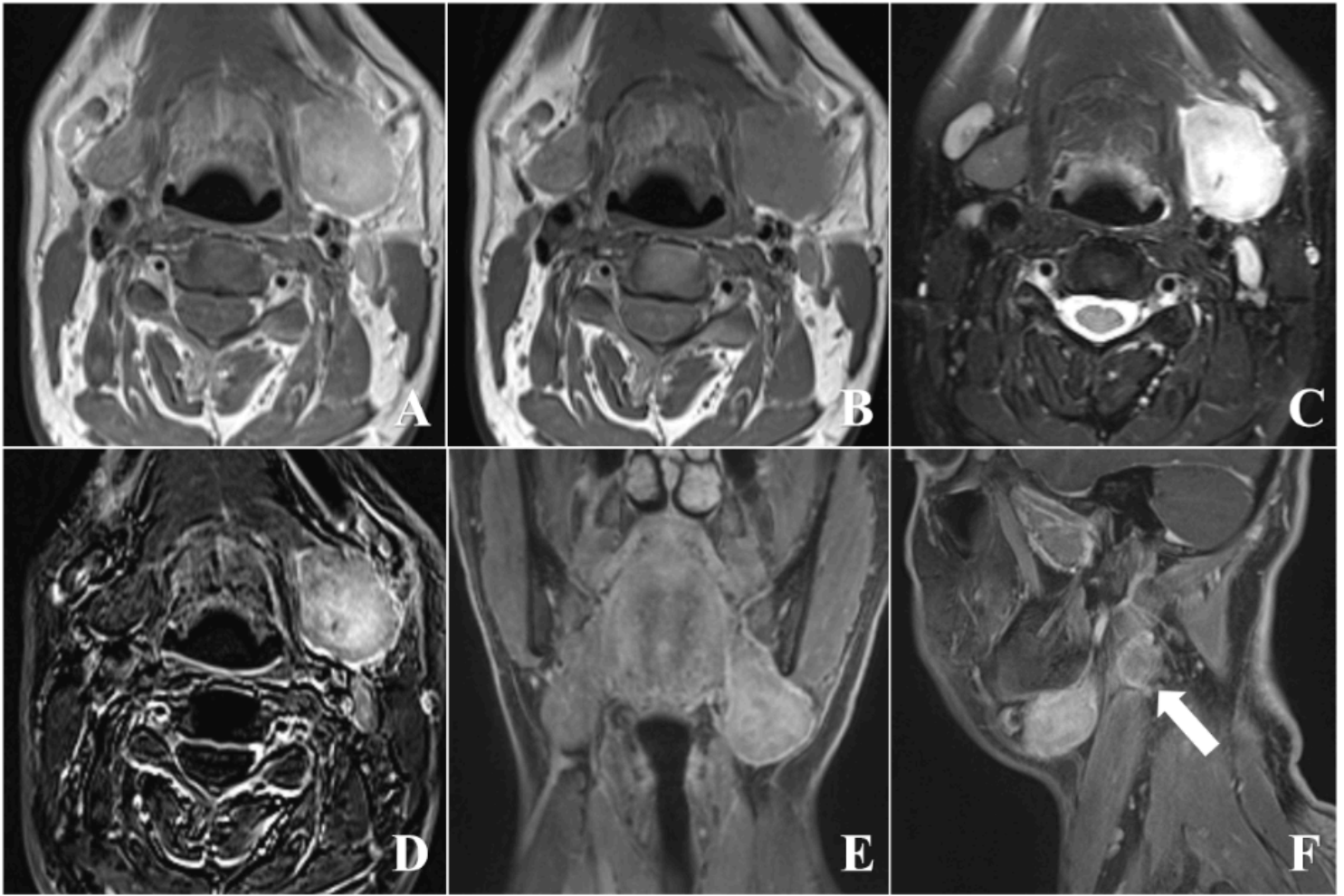


Figure 2

description: Preoperative MRI findings of left submandibular NUT carcinoma and the enlarged lymph node.

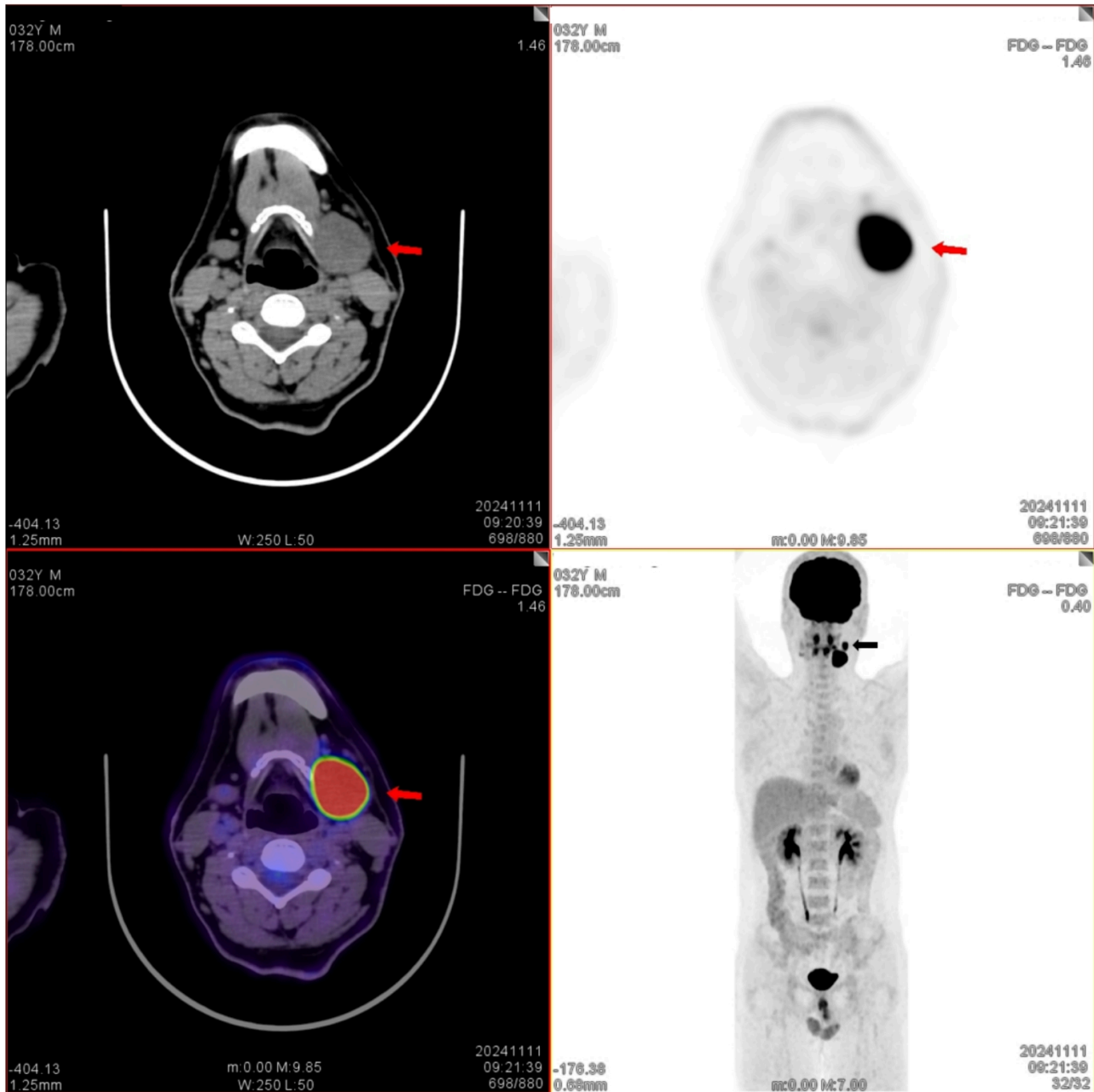


Figure 3

description: PET/CT images (Fused PET/CT and MIP) showing high FDG avidity in the mass and lymph node.

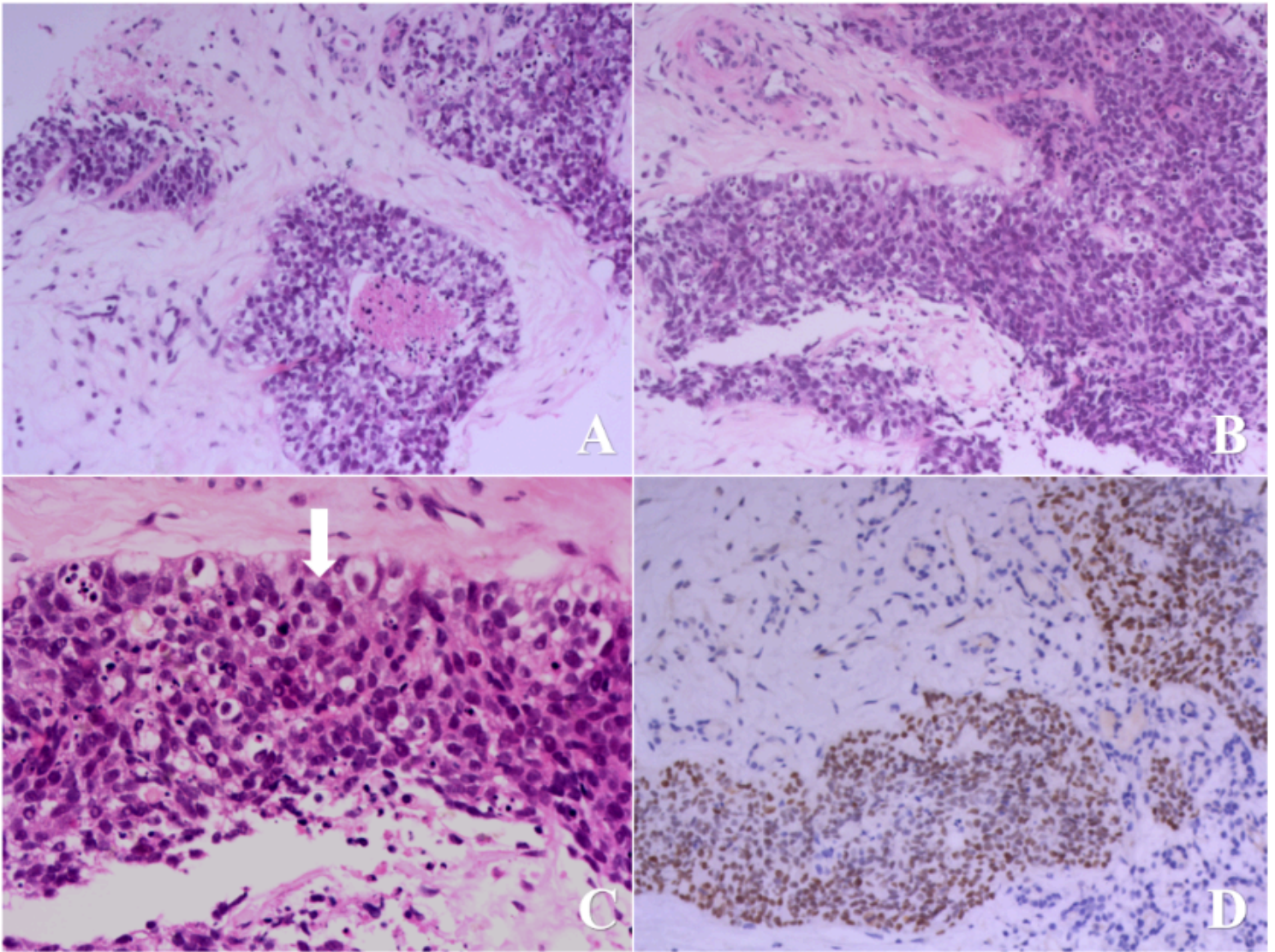


Figure 4

Pathological findings of the left submandibular mass biopsy.

Figure 4A.(H&E staining, 20×): Nests and irregular sheets of epithelioid tumor cells with central coagulative necrosis.

Figure 4B.(H&E staining, 20×): Trabecular or sheet-like arrangements of epithelioid or basaloid tumor cells within a collagenous stroma, with noticeable apoptotic cells.

Figure 4C.(H&E staining, 40×): The tumor cells are monomorphic, round to polygonal, with indistinct cell borders and scant cytoplasm, partially clear. The nuclei are round or oval, often with intranuclear vacuoles and prominent nucleoli (black arrow).

Figure 4D.Immunohistochemistry: The tumor cells show positive nuclear expression of NUT.

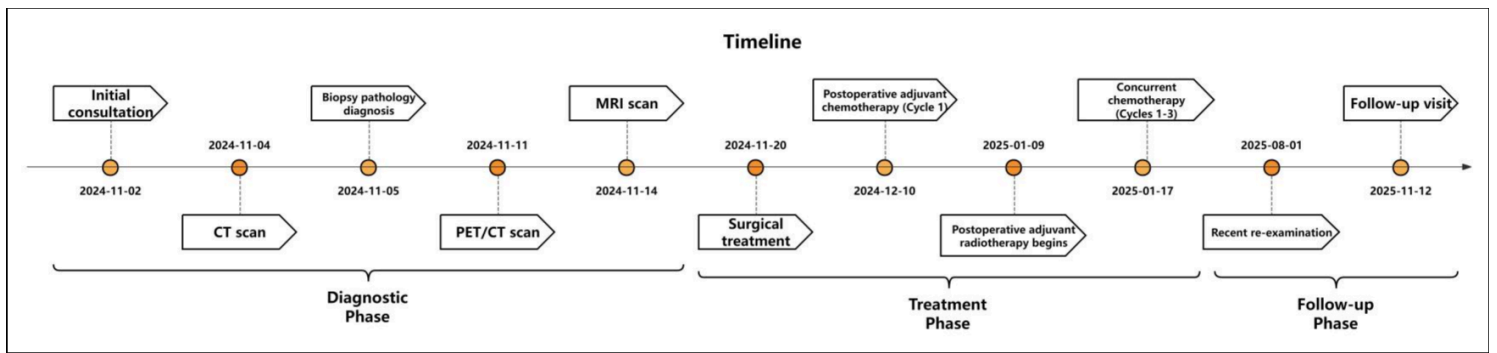


Figure 5

placeholder: Timeline illustrating the sequence of diagnosis, treatment, and follow-up.

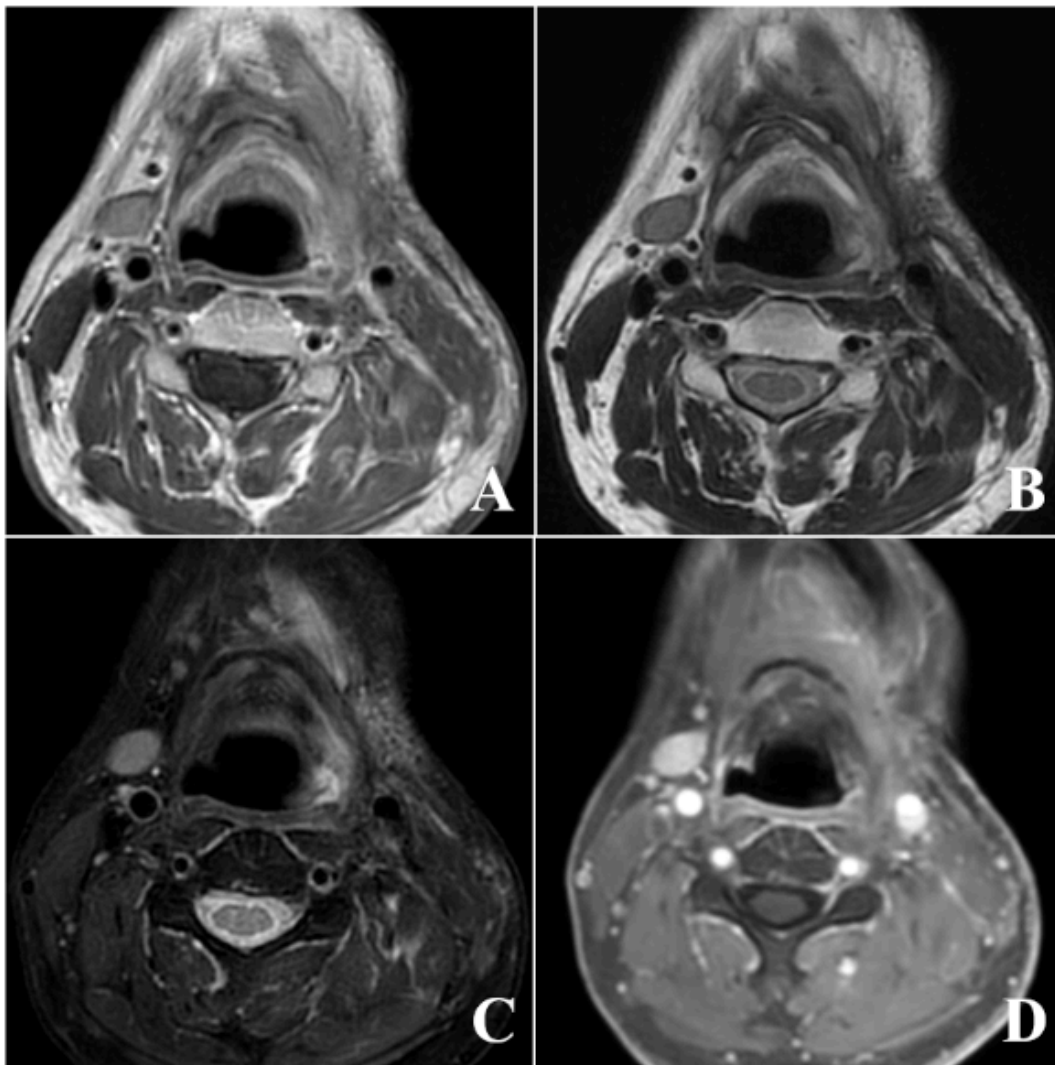


Figure 6

description: Follow-up MR images after surgery for left submandibular NUT carcinoma.

T1WI (A) and T2WI (B) show the absence of the left submandibular gland and the mass, with disordered soft tissue architecture in the operative bed.

T2WI/FS (C) shows a patchy area of high signal intensity in the operative field, suggesting soft tissue edema.

Enhanced T1WI (D) shows no abnormal enhancing focus in the operative bed, indicating no signs of recurrence, and no metastatic lymph nodes in the surrounding area.