

## Submandibular Lymph Node Metastasis as the Initial Presentation of an Occult Undifferentiated Nasopharyngeal Carcinoma: A Case Report

Jelloul Nouredine<sup>1\*</sup>, Soumaya Amaizo<sup>1</sup>, Arkoubi Zakkaria<sup>2</sup>, Hafi.Zakkaria<sup>2</sup>, Moad Mekkaoui<sup>2</sup>, Bencheikh Razika<sup>2</sup>, Benbouzid Anas<sup>2</sup>, Essakalli Leila<sup>2</sup>

<sup>1</sup>Resident Physician in Otolaryngology, Department of Otolaryngology, Head and Neck Surgery, Specialties Hospital, Faculty of Medicine, Mohammed V University, Morocco

<sup>2</sup>Professor of Otolaryngology, Department of Otolaryngology, Head and Neck Surgery, Specialties Hospital, Faculty of Medicine, Mohammed V University, Morocco

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\*Corresponding author: Jelloul Nouredine

Resident Physician in Otolaryngology, Department of Otolaryngology, Head and Neck Surgery, Specialties Hospital, Faculty of Medicine, Mohammed V University, Morocco

### Abstract

### Case Report

**Background:** Nasopharyngeal carcinoma (NPC), particularly the undifferentiated subtype (UCNT), is a head and neck malignancy strongly associated with Epstein-Barr virus and characterized by a high propensity for cervical lymph node metastasis. Rarely, patients present with cervical lymphadenopathy without an identifiable primary tumor, representing an occult form of NPC. **Case Presentation:** We report the case of a 64-year-old woman presenting with a progressively enlarging right submandibular mass. Clinical examination revealed a firm, painless lymph node measuring approximately 4 cm, associated with multiple right lateral cervical lymphadenopathies. Nasopharyngoscopy was normal. Contrast-enhanced CT and MRI demonstrated a 46 mm lesion in the right submandibular space infiltrating the submandibular gland and adjacent muscles, with associated lymphadenopathy. Histopathological examination of a lymph node biopsy, supported by immunohistochemistry, revealed metastatic undifferentiated carcinoma consistent with nasopharyngeal origin. Staging cervico-thoracic CT showed no distant metastases. The patient received concomitant chemoradiotherapy. **Conclusion:** This case highlights a rare presentation of occult UCNT in an older patient, revealed by submandibular lymph node metastasis. It emphasizes the importance of considering NPC in atypical presentations and supports the role of cervical lymph node biopsy and multimodal imaging in establishing the diagnosis and guiding treatment. Early recognition remains essential for optimal management.

**Keywords:** Occult Nasopharyngeal Carcinoma, Undifferentiated Carcinoma of Nasopharyngeal Type (UCNT), Submandibular Lymph Node Metastasis, Cervical Lymphadenopathy, Epstein-Barr Virus (EBV), Cervical lymph Node Biopsy, Diagnostic Challenge, Case Report.

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## INTRODUCTION

Nasopharyngeal carcinoma (NPC), particularly the undifferentiated subtype (UCNT), is a distinct head and neck malignancy with a high propensity for cervical lymphatic spread and a well-established association with Epstein-Barr virus (EBV) infection. Cervical lymph node metastasis is a common presenting feature and may even be the first clinical manifestation of disease, sometimes occurring in the absence of a detectable primary tumor [1–3].

At diagnosis, the primary nasopharyngeal lesion is identifiable on imaging, especially magnetic resonance imaging (MRI), in the majority of cases;

however, a small subset of patients (approximately 1–2%) present with cervical lymphadenopathy and elevated EBV markers despite a normal-appearing nasopharynx on endoscopy and imaging.<sup>4</sup> In such cases, repeated nasopharyngeal biopsies are sometimes pursued to uncover an occult primary, but this approach may increase procedure-related morbidity and delay definitive diagnosis [4].

The role of cervical lymph node biopsy in this setting has been debated. While historical concerns suggested that node excisional procedures might contribute to tumor cell dissemination and potentially worsen outcomes, recent large cohort studies have demonstrated that cervical lymph node biopsy (including

fine needle aspiration or excision) does not adversely impact overall survival compared with primary nasopharyngeal biopsy in NPC patients treated with modern multimodal therapy [5, 6]. Contemporary clinical practice guidelines, such as those from the National Comprehensive Cancer Network (NCCN) and the Chinese Society of Clinical Oncology (CSCO), recognize cervical lymph node biopsy as a useful diagnostic tool when nasopharyngeal sampling is inconclusive or not feasible [4-7].

Herein, we present a rare case of a 64-year-old woman, in whom a submandibular and lateral cervical lymph node metastasis revealed an occult UCNT of the nasopharynx, despite normal endoscopic and radiologic evaluation. The patient's advanced age and the atypical submandibular nodal involvement make this case particularly unusual. This report highlights the diagnostic challenge of occult primary NPC and underscores the clinical relevance of cervical lymph node biopsy and multimodal imaging in establishing the diagnosis.

## CASE PRESENTATION

A 64-year-old woman with no significant past medical history presented with a right submandibular swelling evolving over several weeks, progressively enlarging, painless, without associated inflammatory signs, and with preserved general condition.

Clinical examination revealed a firm, slightly mobile, painless right submandibular lymph node measuring approximately 4 cm in its largest diameter. In addition, multiple right lateral cervical lymph nodes of variable sizes were palpated. Complete ENT examination, including inspection of the oral cavity and oropharynx, did not reveal any suspicious lesion.

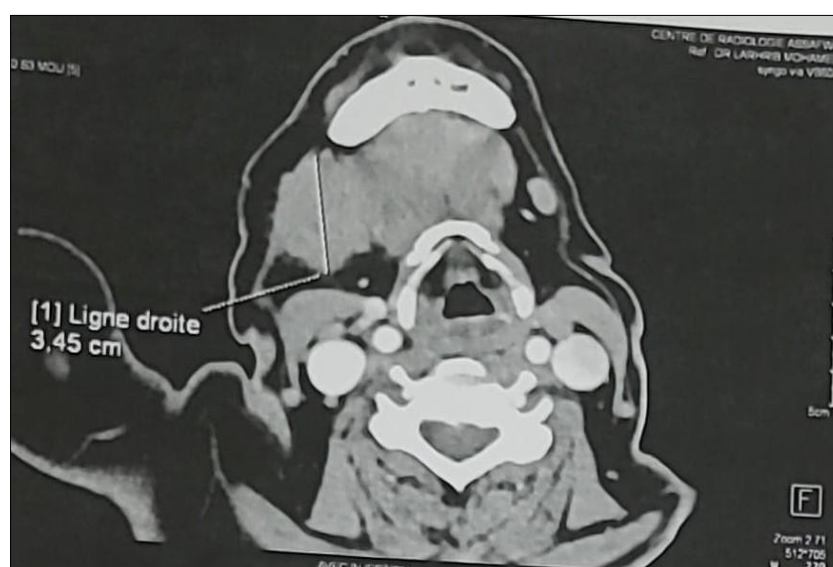
Nasopharyngoscopy showed a macroscopically normal nasopharynx.

Contrast-enhanced cervico-facial CT scan demonstrated a tissue lesion in the right submandibular space, showing heterogeneous contrast enhancement with irregular borders, infiltrating the right submandibular gland as well as adjacent muscles. Multiple right lateral cervical lymph nodes, some with central necrosis, were also noted. No abnormalities were identified in the nasopharynx.

Cervico-facial MRI confirmed a 46 mm lesion, isointense on T1 and hyperintense on T2, with diffusion restriction and low apparent diffusion coefficient (ADC) values, suggestive of a malignant process. The lesion was infiltrating the homolateral submandibular gland and adjacent muscles. A 3 cm right lateral cervical lymph node was also noted, along with several other nodes of variable sizes. The nasopharynx remained radiologically normal.

A lymph node biopsy was performed. Histopathology revealed a malignant undifferentiated proliferation, and immunohistochemical studies were consistent with a secondary lymph node localization of an UCNT, suggesting a nasopharyngeal origin.

Contrast-enhanced axial CT scan demonstrated a heterogeneous tissue lesion in the right submandibular space infiltrating the submandibular gland and adjacent muscles, with associated lateral cervical lymphadenopathy (Figure 1). Axial MRI confirmed a 46 mm lesion with isointense signal on T1, hyperintense signal on T2, and restricted diffusion on DWI, consistent with a malignant process (Figure 2).



**Figure 1:** Axial contrast-enhanced CT scan of the neck showing a heterogeneous tissue lesion in the right submandibular space infiltrating the right submandibular gland and adjacent muscles. Associated right lateral cervical lymphadenopathy is also visible



**Figure 2: Axial MRI of the neck showing the right submandibular lesion**

Cervico-thoracic CT scan for staging did not reveal any distant lesions, particularly in the thorax, and no additional suspicious lymph nodes were detected outside the right cervical and submandibular territories.

Based on these findings, the diagnosis of an occult nasopharyngeal carcinoma presenting as metastatic cervical lymphadenopathy, with an unusual submandibular localization, was established.

The patient was referred to oncology and received concomitant chemoradiotherapy targeting the nasopharynx and cervical lymph node regions.

## DISCUSSION

Undifferentiated nasopharyngeal carcinoma (UCNT) typically presents in younger adults, with a peak incidence between 40 and 50 years [1–3]. The presentation in a 64-year-old patient is therefore unusual, highlighting that UCNT can occasionally manifest in older individuals. Age-related rarity is particularly notable in the context of submandibular lymph node metastasis, as the majority of initial metastatic nodes are located in the upper lateral cervical chains [4].

Occult nasopharyngeal carcinoma, defined as metastatic disease with an undetectable primary lesion on nasopharyngoscopy and imaging, is reported in only 1–2% of cases [4]. In such situations, the diagnosis is challenging and often relies on cervical lymph node biopsy for histopathological and immunohistochemical confirmation. Our case underscores the importance of considering occult UCNT in older patients presenting with atypical cervical or submandibular

lymphadenopathy, even in the absence of nasopharyngeal abnormalities.

Historically, concerns existed regarding the safety of cervical lymph node biopsy in NPC. Excisional or needle biopsy was believed to potentially disseminate tumor cells, increasing the risk of distant metastases. Early studies suggested that lymph node puncture or excision could increase the rate of distant metastasis by over 20%. However, more recent evidence indicates that cervical lymph node biopsy, including fine needle aspiration (FNA), does not adversely affect overall survival, particularly in patients treated with modern chemoradiotherapy and intensity-modulated radiotherapy (IMRT) [507]. This supports current guideline recommendations, including the NCCN and ASCO guidelines, which advocate lymph node biopsy when nasopharyngeal sampling is inconclusive or infeasible [4–6].

Imaging plays a key role in characterizing both the primary lesion and nodal metastases. In our patient, contrast-enhanced CT revealed a heterogeneous submandibular mass infiltrating adjacent muscles, while MRI confirmed features consistent with malignancy, including T2 hyperintensity and restricted diffusion on DWI. These findings are consistent with previous studies reporting that MRI is superior to CT for delineating soft tissue involvement and nodal infiltration [8].

The treatment of UCNT with occult primary relies on definitive radiotherapy targeting the nasopharynx and cervical nodes, often combined with chemotherapy for locally advanced disease. Modern IMRT has improved local control and reduced toxicity

compared with conventional radiotherapy [9]. Our patient received concomitant chemoradiotherapy targeting the nasopharynx and involved cervical regions, in line with current standards.

In conclusion, this case highlights a rare presentation of UCNT in an older patient, revealed by a submandibular lymph node metastasis, reinforcing the need for a high index of suspicion, timely lymph node biopsy, and multimodal imaging to guide diagnosis and treatment.

## CONCLUSION

This case illustrates a rare presentation of undifferentiated nasopharyngeal carcinoma (UCNT) in an older patient, revealed by a submandibular lymph node metastasis with an occult primary tumor. It highlights the importance of maintaining a high index of suspicion for NPC even in atypical age groups and nodal locations. Cervical lymph node biopsy, combined with multimodal imaging, remains a crucial diagnostic tool, enabling timely and accurate diagnosis and guiding definitive treatment with modern chemoradiotherapy protocols. Clinicians should be aware that occult UCNT can present atypically, and early recognition can significantly impact patient management and outcomes.

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