Nasopharyngeal carcinoma with inguinal lymph node metastasis: A case report

ZHIBIN LIN[1,2], SHILIANG LI[2], DONGHONG YANG[3], TONGYUAN DENG[3], HAIWEN LI[3] and YONGCUN WANG[4]

[1]Department of Oncology, People's Hospital of Yangjiang, Yangjiang, Guangdong 529500, P.R. China; [2]The First Clinical Medical School, Guangdong Medical University, Zhanjiang, Guangdong 524000, P.R. China; [3]Department of Head and Neck Oncology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong 524000, P.R. China; [4]Department of Pulmonary Oncology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, Guangdong 524000, P.R. China

Received December 14, 2025; Accepted July 17, 2026

DOI: 10.3892/etm.2026.13257

Abstract. Nasopharyngeal carcinoma (NPC) usually metastasizes to cervical lymph nodes, whereas inguinal lymph node metastases (ILNM) are rare, with only a small number of cases reported. ILNs are an uncommon site of secondary involvement, a phenomenon attributed to their unique anatomical and immunological features. The current study reported a case of NPC in which baseline positron emission tomography/CT showed metastasis from the left pharyngeal recess to the left cervical levels II-III. Mildly increased metabolic activity was observed in levels II-III of the right cervical chain, the left supraclavicular area and the bilateral inguinal area, initially interpreted as reactive hyperplasia. The patient was diagnosed with NPC (T2N1M0, stage IIA, 8th edition of the American Joint Committee on Cancer). At 5 months after the completion of induction chemotherapy and concurrent chemoradiotherapy, the bilateral ILNs showed interval enlargement and biopsy confirmed metastatic NPC. The patient was classified as stage IVB based on biopsy results, prompting appropriate treatment for this advanced stage. This rare case underscores the importance of considering ILNM as a possible metastatic site in NPC, requiring clinicians to perform timely evaluations and lymph node biopsies to prevent clinical understaging due to unrecognized occult metastatic disease, particularly during the early stages of diagnosis.

Correspondence to: Dr Haiwen Li, Department of Head and Neck Oncology, Affiliated Hospital of Guangdong Medical University, 57 South Renmin Avenue, Xiashan, Zhanjiang, Guangdong 524000, P.R. China
E-mail: 505147279@qq.com

Dr Yongcun Wang, Department of Pulmonary Oncology, Affiliated Hospital of Guangdong Medical University, 57 South Renmin Avenue, Xiashan, Zhanjiang, Guangdong 524000, P.R. China
E-mail: wycdiyi@163.com

Key words: nasopharyngeal carcinoma, inguinal lymph node metastasis, case report, occult metastases, fine needle aspiration biopsy

Introduction

Nasopharyngeal carcinoma (NPC) occurs worldwide, but shows a particularly high incidence in the Western Pacific region and is one of the most common malignant tumors in China and Southeast Asia (1). In China, NPC also exhibits a distinct geographic distribution, with Guangdong province being a high-incidence area (2). NPC arises from epithelial cells that line the surface of the nasopharynx and its aggressive nature is characterized by early dissemination to regional lymph nodes. About 40% of patients present with cervical lymphadenopathy at initial diagnosis (3), and 60 to 90% develop cervical lymph node metastases during the disease course, with an orderly progression along the lymphatic network and a relatively low incidence of skip metastasis. The nodal regions most frequently affected are the retropharyngeal lymph nodes and the level II cervical lymph nodes (4,5). In addition, distant metastases are common, most commonly affecting the bones, lungs, liver and distant lymph nodes (6). Due to the anatomical inaccessibility of the nasopharynx and the nonspecific nature of early symptoms, most patients are diagnosed at an advanced stage, indicating a poor prognosis. In an intensity-modulated radiotherapy-treated validation cohort, the American Joint Committee on Cancer (AJCC) 8th edition staging system demonstrated stage-dependent prognostic discrimination, with 5-year overall survival rates ranging from >90% for stage IIA to ~70% for stage IV disease (7). This underscores the critical importance of early and accurate diagnosis. NPC inguinal lymph node metastasis (ILNM) is rare and has been scarcely reported in the literature, with an incidence of ~0.9% (8). The current study presents a case of NPC with ILNM encountered in clinical practice.

Case report

A 67-year-old woman from Guangdong first presented to the Affiliated Hospital of Guangdong Medical University (Zhanjiang, China) in July 2022 with a history since April

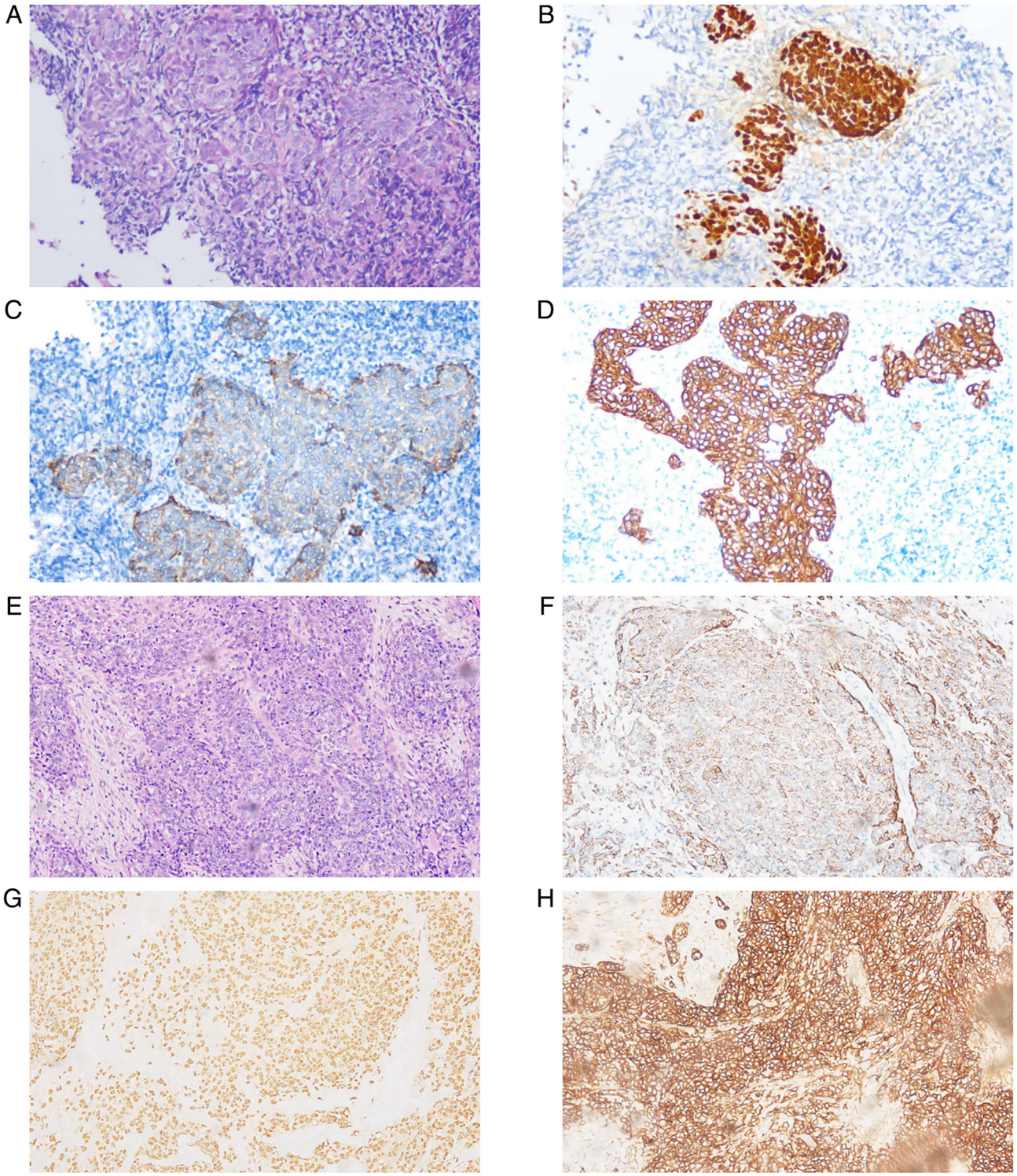

Figure 1. Histopathological analyses of primary and metastatic lesions (magnification, x200). Pathological diagnosis: Primary nasopharyngeal non-keratinizing carcinoma. (A) Tumor cells, arranged in nests within desmoplastic stroma, exhibited vesicular nuclei with prominent nucleoli and abundant cytoplasm (hematoxylin and eosin staining). (B) EBER *in situ* hybridization was positive. (C) EGFR showed weak positivity and Ki-67 positivity was 20-30%. (D) Neoplastic cells were CK immunoreactive. Left inguinal lymph node tissue: (E) Tumor cells in a nested or sheet-like distribution were seen in the fibrous connective tissue, with vesicular nuclei, pronounced nucleoli and numerous nuclear divisions (hematoxylin and eosin staining); the morphology of the inguinal lymph node and its immunohistochemical profile were consistent with non-keratinizing carcinoma, with positive staining for (F) CK5/6, (G) EBER by *in situ* hybridization and (H) EGFR. EBER, Epstein-Barr virus-encoded small RNA; CK, cytokeratin; EGFR, epidermal growth factor receptor.

2022 of enlarged left cervical lymph nodes, intermittent headaches, dizziness, occasional nasal bleeding, tinnitus and hearing loss in the left ear. The patient had no significant medical history, including no history of gynecological disorders, pelvic inflammatory disease, or prior pelvic or lower extremity surgery. The patient also denied smoking and alcohol consumption. Physical examination showed a Karnofsky performance status score (9) of 90, with a hard,

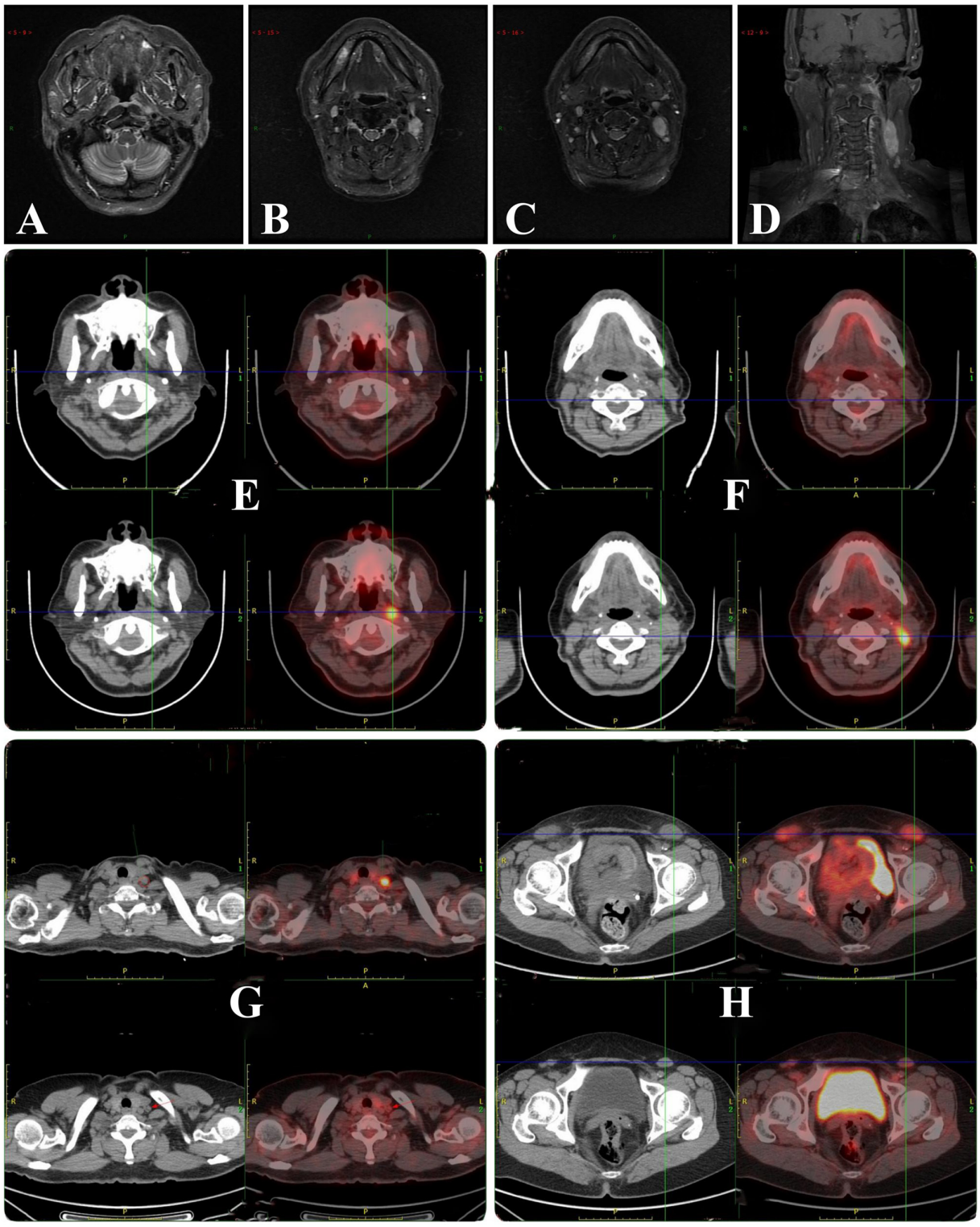

Figure 2. Imaging scans. Initial (A-D) MRI and (E-H) PET/CT scans are presented, with the PET/CT scans compared between pre-treatment (below) and post-treatment (above). (A) Nasopharyngeal mucosa thickening, enlarged lymph nodes in the left cervical lymph node regions: (B and D) RPN, levels II and III were considered possible meta-static tumors. (C and D) Left cervical level II lymph nodes showing extranodal extension (+). In the RPN of the (E) nasopharynx and (F) left neck lymph nodes levels II and III, there was no evidence of metastasis or recurrence. (G) Several left supraclavicular lymph nodes showed interval enlargement on follow-up PET/CT, with the largest measuring ~1.2 cm x1.0 cm and markedly increased glucose metabolism (SUVmax=11.8), in contrast to no abnormal uptake on baseline imaging. (H) Bilateral multiple enlarged inguinal lymph nodes showed interval progression, with the largest measuring ~3.5 cm x2.1 cm and markedly increased glucose metabolism (SUVmax=6.2), compared with a prior SUVmax of 2.5 on baseline imaging. PET, positron emission tomography; SUVmax, maximum standardized uptake volume; RPN, retropharyngeal lymph nodes.

fixed lymph node measuring 2.0x2.0 cm at level II of the left cervical chain, without tenderness. Baseline complete blood count and hepatic/renal function tests were within normal limits. Nasal endoscopy revealed a shallow left pharyngeal crypt and thickening of the mucosa. A biopsy confirmed non-keratinizing carcinoma (Fig. 1). Magnetic resonance

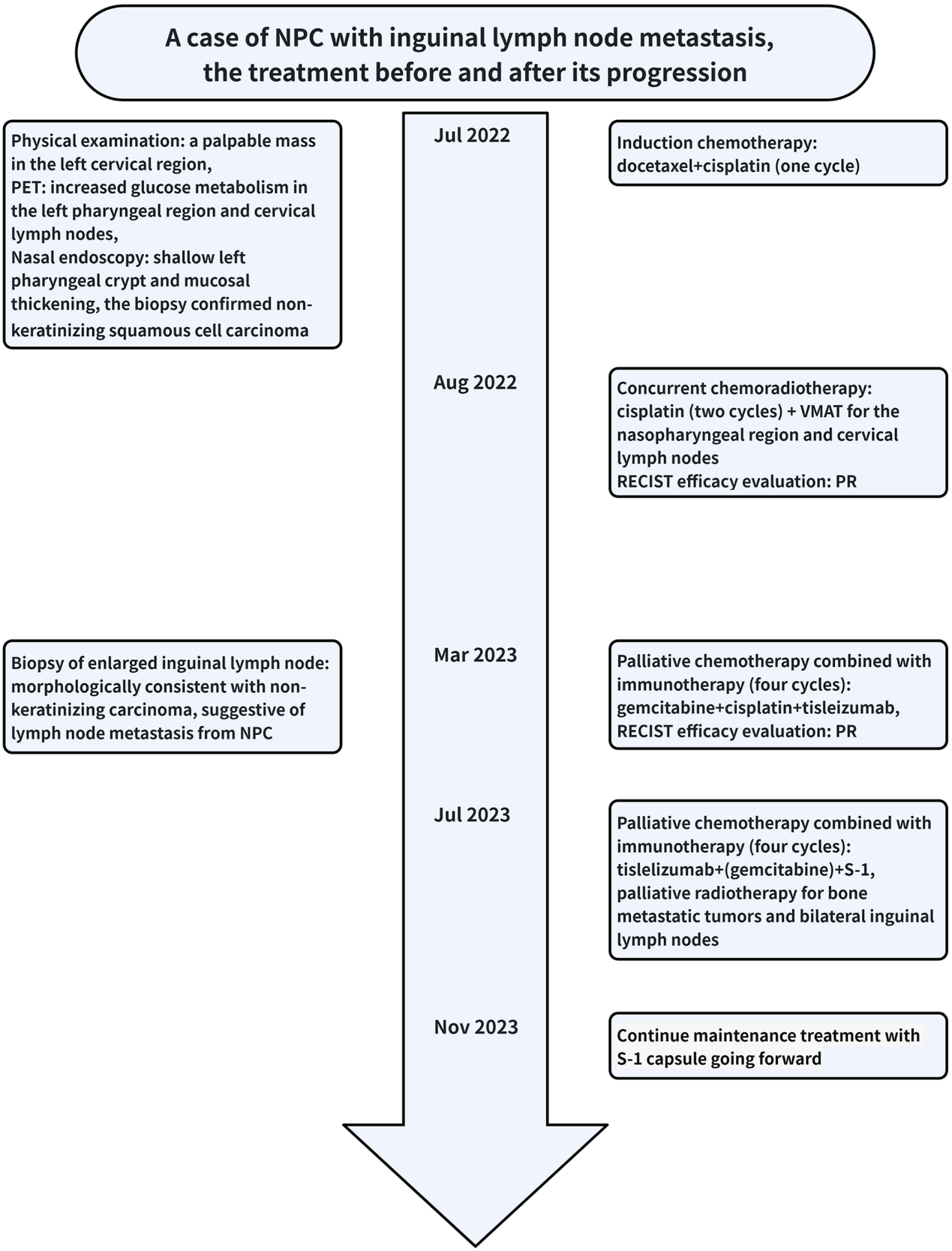

Figure 3. Treatment timeline. NPC, nasopharyngeal carcinoma; PET, positron emission tomography; VMAT, volumetric modulated arc therapy; RECIST, Response Evaluation Criteria in Solid Tumors; PR, partial response; S-1, a combination of tegafur, gimeracil and oteracil potassium.

imaging (MRI) indicated mucosal thickening in the left pharyngeal region, with invasion into adjacent muscles, suggesting NPC. Enlarged lymph nodes were observed in the left retropharyngeal, level IIb and level III regions (Fig. 2). Positron emission tomography (PET)/CT performed in July 2022 showed increased glucose metabolism in the left

pharyngeal area and cervical lymph nodes, indicating probable metastasis, but without liver, lung or bone involvement. Reactive hyperplasia was considered for some right cervical regions, left supraclavicular lymph nodes (SCLNs) and ILNs. Baseline plasma Epstein-Barr virus (EBV) DNA assay was negative. The patient was diagnosed with non-keratinizing carcinoma of the nasopharynx [T2N1M0, stage IIA, 8th edition of the AJCC staging system]. In July 2022, the patient received induction chemotherapy with docetaxel 75 mg/m^2 and cisplatin 75 mg/m^2. However, due to the development of grade IV leukopenia and neutropenia following chemotherapy, only 1 cycle of treatment was completed. Subsequently, the patient received radical concurrent chemoradiotherapy (CCRT) using volumetric modulated arc therapy, with prescribed doses of 69.96 Gy/33 fractions to the planning gross tumor volume of the nasopharynx and left cervical lymph nodes, 60.06 Gy/33 fractions to planning target volume 1 (PTV1) and 54.12 Gy/33 fractions to PTV2. Concurrent chemotherapy with cisplatin 80 mg/m^2, every 3 weeks (Q3W) was administered for 2 cycles. Post-CCRT MRI in September 2022 showed a complete response in the primary tumor and partial response in the cervical lymph nodes.

In March 2023, the patient returned with low back pain and bilateral inguinal lymphadenopathy. PET/CT showed multiple hypermetabolic lesions in the left supraclavicular, mediastinal, retroperitoneal, bilateral iliac and inguinal regions, as well as widespread bone involvement, consistent with metastases (Fig. 2). Inguinal fine-needle aspiration biopsy (FNAB) confirmed metastatic non-keratinizing carcinoma; the histopathological features were identical to those of the primary nasopharyngeal lesion, supporting the diagnosis of regional lymph node metastasis (Fig. 1) (Data S1). The patient was restaged as (rT0N3M1, stage IVB, AJCC 8th edition) and received 4 cycles of tislelizumab plus gemcitabine/cisplatin, achieving a partial response. Due to renal impairment related to cisplatin, cisplatin was switched to oral S-1 (a combination of tegafur, gimeracil and oteracil potassium) at a dose of 40 mg/m^2 twice daily on days 1-14, Q3W, for 2 additional cycles. The patient also underwent palliative radiotherapy to the thoracolumbar spine (30 Gy/10 fractions) in August 2023 and bilateral inguinal nodes (66 Gy/33 fractions) in October 2023; the latter was discontinued after 27 fractions due to myelosuppression. Maintenance S-1 continued, but the patient's overall condition subsequently declined, and management was shifted to primarily palliative and supportive care, with irregular follow-ups performed; the entire clinical course is summarized in Fig. 3 (last follow-up in March 2024).

Discussion

The patient of the present study initially presented with non-keratinizing NPC (T2N1M0, stage IIA, AJCC 8th edition staging system) and received standard CCRT, yet subsequently developed inguinal and bone metastases. This case highlights the mechanisms of distant nodal spread in NPC and the diagnostic challenges they pose.

At initial diagnosis, the patient's PET/CT scan indicated positive lymph nodes only in the left upper neck, without significant enlargement in the lower neck or retroperitoneum. Although the ILN were enlarged, their low metabolic activity on PET/CT led to the diagnosis of reactive hyperplasia. ILNs are important regional lymphatic stations involved in immune surveillance and lymphatic drainage from the lower extremities, perineum, external genitalia and the distal anal canal. Based on these drainage patterns, ILNM are commonly associated with malignancies of the external genitalia, anal canal, vulva, penis, lower-extremity or trunk skin, and, less commonly, low rectal adenocarcinoma (10,11). However, PET/CT showed no tumors in these areas. Reactive lymphadenopathy (LAD) may be due to infectious, immune-mediated or neoplastic causes, all of which warrant PET/CT evaluation to inform biopsy decisions. Similar diagnostic pitfalls have been reported: In one patient with NPC, ^{18}F-fluorodeoxyglucose PET/CT and MRI suggested bilateral cervical metastases, yet pathology revealed only reactive lymphoid hyperplasia; notably, ^{68}Ga-fibroblast activation protein inhibitor PET/CT showed no abnormal uptake in these nodes, suggesting that this novel tracer may aid in distinguishing reactive from metastatic LAD (12). It may be suggested that in patients with suspected reactive LAD, antitumor therapy can be initiated while closely monitoring the nodal response. If nodes show interval enlargement or progressive hypermetabolism on PET/CT, biopsy should be pursued without delay, as this indicates resistant malignant involvement rather than reactive hyperplasia. Even in the absence of regression, biopsy remains prudent to rule out occult metastatic disease, as reactive nodes may also persist after chemotherapy.

Distant metastasis of NPC to the ILNs is rare. Although the 'seed and soil' hypothesis (13) provides a general framework for organ-specific dissemination, imaging findings in this patient are more plausibly consistent with retrograde lymphatic spread through the supraclavicular-thoracic duct-retroperitoneal axis, rather than selective introduction into the inguinal microenvironment. In the present case, the left SCLN, initially interpreted as reactive hyperplasia on baseline PET/CT, was later highly suggestive of metastasis on follow-up PET/CT (Fig. 2G). This progression provides critical information on the likely route of inguinal dissemination. According to the retrograde metastatic pathway, tumor cells that drain from the nasopharynx into the cervical lymphatic system can reach the thoracic duct through the SCLN. When normal antegrade flow to the venous angle is obstructed, either due to tumor burden or lymphatic damage, malignant cells can reflux retrograde through the lymphatic trunks, descending into the mediastinum, retroperitoneum, and finally the pelvic and inguinal regions (14,15). Of note, subphrenic lymph node involvement-including inguinal metastasis-has been identified as an independent adverse prognostic factor in NPC (hazard ratio: 1.72, 95% CI: 1.02-2.90, P=0.038) (8). Clinically, the present case serves as a cautionary reminder: In patients with NPC and SCLN involvement, a high index of suspicion for occult subphrenic metastases should be maintained, even when inguinal lymphadenopathy exhibits only mild hypermetabolic activity on PET/CT. Persistent or progressive enlargement of the supraclavicular or inguinal nodes, regardless of low maximum standardized uptake values, warrants timely FNAB to rule out occult tumor spread. Early identification of this retrograde route may prompt more intensive initial systemic therapy and prevent the clinical understaging observed in this patient.

In addition, tumor cells can disrupt normal lymphatic structures, leading to remodeling of the lymphatic vessels. Lymphatic vessels lack the tight junctions and surrounding basement membrane layers commonly found in blood vessels, making them more fragile than blood vessels and thus weakening the barrier against tumor cell spread (16). Extracapsular invasion (Fig. 2C and D) observed in the cervical lymph nodes of the patient was associated with an increased risk of local recurrence or distant metastasis.

The N classification is an important prognostic factor for NPC, particularly with regard to distant metastasis-free survival. In the 8th edition of the AJCC staging system, stage N is based on the size and location of the nodes, although the number of metastatic lymph nodes more precisely reflects tumor burden (17). The N1 category is highly heterogeneous: Certain patients with N1 disease have outcomes comparable to those with N0 disease, whereas others experience markedly worse prognoses due to adverse nodal characteristics (18). Patients such as the one described in the present study, who exhibit extranodal extension of the cervical lymph nodes, cannot be classified as low-risk patients along with the stage N0, confirming that such a nodal phenotype warrants close surveillance for occult spread beyond initial imaging.

Longitudinal plasma EBV-DNA monitoring revealed an undetectable level at baseline (<500 copies/ml), with a transient mild elevation during the course that subsequently resolved, and a marked surge to 9.91×10^5 copies/ml in September 2023, long after widespread metastases had been confirmed. Other serial measurements remained negative or borderline. Although EBV-DNA is well established as a sensitive marker for NPC surveillance (19-21), this trajectory illustrates that low-level or transient elevations do not exclude metastasis, particularly via lymphatic spread, and thus should not delay biopsy of suspicious nodes.

In summary, the patient was initially diagnosed with T2N1M0; however, the presence of high-risk factors for distant metastases was not recognized. The absence of timely ILN biopsy led to clinical understaging of the disease. This underestimation of tumor burden resulted in the delivery of suboptimal initial therapy (definitive chemoradiotherapy alone, without systemic immunotherapy or intensified regimen), which ultimately contributed to early disease progression rather than sustained remission. In retrospect, the inguinal lesions represented occult metastases that were not appreciable on baseline PET/CT due to their low metabolic activity. In newly diagnosed patients with inguinal LAD, it is crucial to definitively determine their nature. PET/CT and FNAB can aid in diagnosis and help avoid missing occult metastases.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

ZBL drafted and revised the initial manuscript, collected the clinical data, organized and analyzed all patient data, screened and organized the medical images, and performed the literature review. SLL obtained medical images (including MRI, PET-CT and pathological images), and prepared and organized the figures. DHY and TYD participated in the overall clinical management of the patient throughout the disease course. HWL participated in the diagnosis and treatment planning of the patient, contributed to the overall clinical management, and contributed to the conception of the case report. YCW analyzed and interpreted the clinical, pathological and imaging data, and contributed to the conception of the case report. All authors have read and approved the final manuscript. YCW and HWL confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was reviewed and approved by the Clinical Research Ethics Committee of the Affiliated Hospital of Guangdong Medical University (approval no. YJKT-2026-018-01; Zhanjiang, China).

Patient consent for publication

Patient characteristics have been anonymized according to ethical standards. The patient provided written informed consent for the publication of any associated images or patient data.

Competing interests

The authors declare that they have no competing interests.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I and Jemal A: Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 74: 229-263, 2024.
2. Chen YP, Chan ATC, Le QT, Blanchard P, Sun Y and Ma J: Nasopharyngeal carcinoma. Lancet 394: 64-80, 2019.
3. Lee HM, Okuda KS, González FE and Patel V: Current perspectives on nasopharyngeal carcinoma. Adv Exp Med Biol 1164: 11-34, 2019.
4. Wang X, Hu C, Ying H, He X, Zhu G, Kong L and Ding J: Patterns of lymph node metastasis from nasopharyngeal carcinoma based on the 2013 updated consensus guidelines for neck node levels. Radiother Oncol 115: 41-45, 2015.
5. Ho FCH, Tham IWK, Earnest A, Lee KM and Lu JJ: Patterns of regional lymph node metastasis of nasopharyngeal carcinoma: A meta-analysis of clinical evidence. BMC Cancer 12: 98, 2012.
6. Qu W, Li S, Zhang M and Qiao Q: Pattern and prognosis of distant metastases in nasopharyngeal carcinoma: A large-population retrospective analysis. Cancer Med 9: 6147-6158, 2020.
7. Pan JJ, Ng WT, Zong JF, Chan LL, O'Sullivan B, Lin SJ, Sze HC, Chen YB, Choi HC, Guo QJ, *et al*: Proposal for the 8th edition of the AJCC/UICC staging system for nasopharyngeal cancer in the era of intensity-modulated radiotherapy. Cancer 122: 546-558, 2016.
8. Zhang XF, Zhang Y, Liang XW, Chen JL, Zhi SF, Yin WJ, Wang MY, Dong EL and Chen DP: Subphrenic lymph node metastasis predicts poorer prognosis for nasopharyngeal carcinoma patients with metachronous metastasis. Front Oncol 11: 726179, 2021.

9. Kan Y, Yang S, Wu X, Wang S, Li X, Zhang F, Wang P and Zhao J: The quality of life in nasopharyngeal carcinoma radiotherapy: A longitudinal study. Asia Pac J Oncol Nurs 10: 100251, 2023.
10. Swan MC, Furniss D and Cassell OCS: Surgical management of metastatic inguinal lymphadenopathy. BMJ 329: 1272-1276, 2004.
11. Wyatt J, Powell SG, Ahmed S, Arthur J, Altaf K, Ahmed S and Javed MA: Inguinal lymph node metastases from rectal adenocarcinoma: A systematic review. Tech Coloproctol 27: 969-978, 2023.
12. Shang Q, Zhao L, Pang Y, Yu Y and Chen H: 68Ga-FAPI PET/CT distinguishes the reactive lymph nodes from tumor metastatic lymph nodes in a patient with nasopharyngeal carcinoma. Clin Nucl Med 47: 367-368, 2022.
13. Fidler IJ and Poste G: The 'seed and soil' hypothesis revisited. Lancet Oncol 9: 808, 2008.
14. Zhang B, Zhang H, Chen Y, Xia W and Wang Y: Supraclavicular lymph node metastasis in esophageal carcinoma: A topic of ongoing controversy. Front Oncol 15: 1527625, 2025.
15. Fei Y, Lu Y, Yao Z, Yin K, Zhou D and Liu Z: Diagnostic value of multimodal lymphatic imaging techniques in thoracic duct outlet obstruction. Diagnostics (Basel) 15: 1288, 2025.
16. Lin M, Zhang XL, You R, Liu YP, Cai HM, Liu LZ, Liu XF, Zou X, Xie YL, Zou RH, *et al*: Evolutionary route of nasopharyngeal carcinoma metastasis and its clinical significance. Nat Commun 14: 610, 2023.
17. Xie C, Li H, Yan Y, Liang S, Li Y, Liu L, Cui C and Liu Y: A nomogram for predicting distant metastasis using nodal-related features among patients with nasopharyngeal carcinoma. Front Oncol 10: 616, 2020.
18. Peng WS, Xing X, Li YJ, Ding JH, Mo M, Xu TT, Zhou X and Hu CS: Prognostic nomograms for nasopharyngeal carcinoma with nodal features and potential indication for N staging system: Validation and comparison of seven N stage schemes. Oral Oncol 144: 106438, 2023.
19. Liu W, Chen G, Gong X, Wang Y, Zheng Y, Liao X, Liao W, Song L, Xu J and Zhang X: The diagnostic value of EBV-DNA and EBV-related antibodies detection for nasopharyngeal carcinoma: A meta-analysis. Cancer Cell Int 21: 164, 2021.
20. Chan KCA, Woo JKS, King A, Zee BCY, Lam WKJ, Chan SL, Chu SWI, Mak C, Tse IOL, Leung SYM, *et al*: Analysis of plasma Epstein-Barr virus DNA to screen for nasopharyngeal cancer. N Engl J Med 377: 513-522, 2017.
21. Chan DCT, Lam WKJ, Hui EP, Ma BBY, Chan CML, Lee VCT, Cheng SH, Gai W, Jiang P, Wong KCW, *et al*: Improved risk stratification of nasopharyngeal cancer by targeted sequencing of Epstein-Barr virus DNA in post-treatment plasma. Ann Oncol 33: 794-803, 2022.