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Case Report

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Thymic Neuroendocrine Tumor Presenting with Cervical Lymphadenopathy: A Case Report and Diagnostic Challenge

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Abstract

Background: *Thymic neuroendocrine tumors (NETs) are extremely rare and often present diagnostic and therapeutic challenges due to nonspecific symptoms and frequent late-stage diagnosis.*
Case Presentation: A 44-year-old male presented with painless cervical lymphadenopathy. Imaging and biopsy confirmed metastatic atypical carcinoid (NET G2) with the primary tumor localized to the thymus. The patient received capecitabine and temozolomide (CAPTEM) chemotherapy followed by bilateral neck dissection and mediastinal tumor resection.

Management and Outcome: *CAPTEM chemotherapy resulted in disease stabilization. Radical surgical resection was performed, achieving R0 status. Histopathology confirmed the diagnosis, and no intrathoracic lymph node involvement was found. The patient recovered well.*

Conclusion: *This case highlights the diagnostic complexity of thymic NETs and underscores the importance of a multidisciplinary approach integrating imaging, pathology, systemic therapy, and surgery.*

Keywords: Thymic neuroendocrine tumor, atypical carcinoid, cervical lymphadenopathy, capecitabine-temozolomide.

1. Introduction

Neuroendocrine tumors (NETs) comprise a heterogeneous and increasingly recognized group of neoplasms arising from neuroendocrine cells, which are ubiquitously distributed throughout the body, most frequently involving the gastrointestinal tract, pancreas, and lungs [1,2]. These neoplasms are characterized by their capacity to synthesize, store, and secrete various peptides, amines, and neuroendocrine markers, potentially leading to distinct clinical syndromes, such as carcinoid syndrome, or remaining clinically silent for extended periods [2,3]. Over recent decades, both the incidence and prevalence of NETs have risen markedly, attributable to improvements in diagnostic modalities and heightened clinical awareness [4]. Epidemiological data demonstrate that the age-adjusted incidence of NETs in the United States has increased from 1.09 per 100,000 in 1973 to more than 6.98 per 100,000 in recent years, underscoring the growing clinical relevance of these tumors [1].

The clinical manifestations of NETs are is remarkably heterogeneous, primarily influenced by the anatomical location, secretory activity, and extent of tumor. A substantial proportion of patients remain clinically silent until metastatic spread has occurred, at which

juncture nonspecific manifestations such as lymphadenopathy, unexplained weight loss, or various paraneoplastic syndromes may emerge. Metastatic NETs of unknown primary origin represent a significant diagnostic challenge due to their intrinsic rarity, considerable histopathological overlap with other neoplastic entities, and frequent lack of site-specific clinical signs [5,6].

NETs display a broad spectrum of biological behavior, ranging from well-differentiated, indolent neoplasms to poorly differentiated, highly aggressive carcinomas. The world health organization (WHO) classification has evolved to incorporate tumor grade, proliferative index, hereby establishing a standardized and clinically relevant framework to facilitate accurate diagnosis and guide therapeutic management[7]. Thymic and other extra-gastrointestinal NETs, including those arising in the mediastinum, are exceedingly rare and typically present at advanced stages, frequently with metastasis to lymph nodes, liver, bone, or, as in this report, the cervical region[8, 9].

Recent advancements in diagnostic strategies, notably the advent of somatostatin receptor-based positron emission tomography–computed tomography (PET-CT), refined histopathological analyses, and molecular profiling, have significantly improved localization and characterization of both primary and metastatic NETs [10]. Nevertheless, optimal management remains complex and necessitates a multidisciplinary approach involving oncology, pathology, radiology, surgery, and nuclear medicine.

Herein, we report a rare case of a metastatic neuroendocrine tumor presenting as cervical lymphadenopathy, with the primary site ultimately identified as the thymus. We discuss the diagnostic complexity and therapeutic considerations in light of recent developments in neuroendocrine tumor management.

2. Case Presentation

A 44-year-old male patient presented in September 2023 with a self-detected, asymptomatic mass located in the left cervical region. Initially, the patient did not pay attention to the mass until January 2024, when bilateral cervical lymphadenopathy was detected during a routine physical examination. The patient subsequently presented to the department of thoracic surgery at our hospital for further evaluation. On admission, clinical assessment demonstrated satisfactory nutritional status and general well-being, with no signs of jaundice, rash, or bleeding diathesis. Physical examination revealed multiple enlarged, freely mobile lymph nodes in the cervical and supraclavicular regions, with the largest measuring approximately 2 cm in diameter. No other abnormalities were detected on systemic examination.

On January 22, 2024, contrast-enhanced computed tomography (CT) revealed a mediastinal mass with bilateral supraclavicular and right cervical lymphadenopathy (Figure 1A-B). Concurrent PET-CT demonstrated abnormal radiotracer uptake in the enlarged supraclavicular and right cervical lymph nodes, indicating a high likelihood of malignancy. Ultrasound-guided core needle biopsy of the left cervical lymph node revealed metastatic neuroendocrine tumor, with histopathological features consistent with atypical carcinoid. Immunohistochemical analysis showed positivity for CD117, INSM1, and synaptophysin, with a Ki-67 proliferation index of approximately 30%. The tumor cells were negative for CD5, S-100, P40, TTF-1, P63, CK5/6, CK7, calretinin, and Epstein-Barr virus-encoded RNA. These findings support the diagnosis of metastatic, moderately differentiated neuroendocrine tumor.

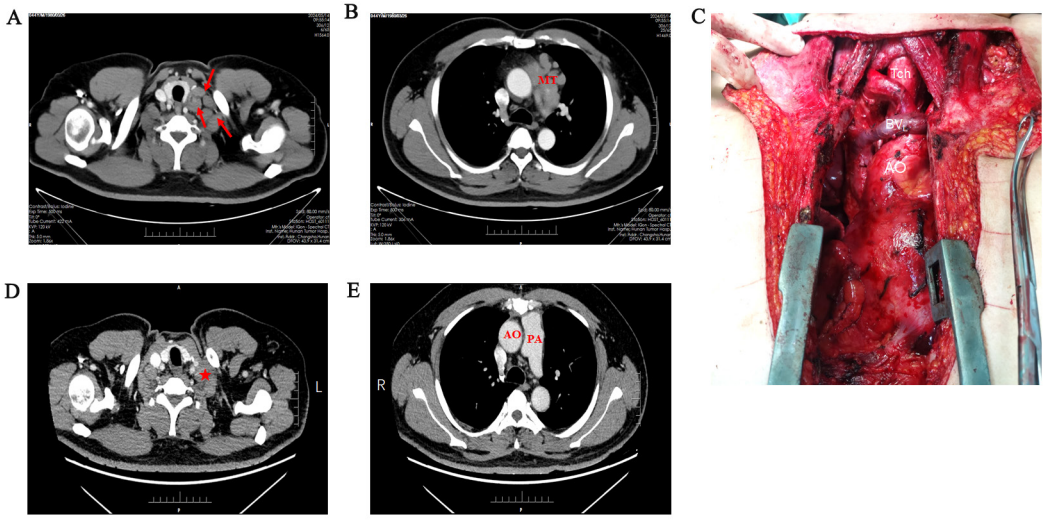

Figure 1: Preoperative and Postoperative CT Scan Images and Intraoperative Anatomical Illustration of the Patient

(A) Axial CT image at the trachea-thyroid level showed abnormal cervical lymph node clusters. Red arrows indicating enlarged lymph nodes. (B) Axial CT image at the carina level demonstrating a mediastinal tumor. MT: mediastinal tumor. (C)The surgery involved complete resection of the thymus containing the tumor and pericardial fat. Resection extended superiorly to the left brachiocephalic vein, inferiorly to the diaphragm, and laterally to the phrenic nerves, encompassing all perithymic and pericardial

fat. Tch: trachea. BVL: left brachiocephalic vein. AO: aorta. (D-E) postoperative CT scan images at the trachea-thyroid level showed

From February to April 2024, the patient underwent three cycles of chemotherapy with capecitabine and temozolomide (CAPTEM). Follow-up imaging revealed stable disease according to response evaluation criteria in solid tumors criteria. After multidisciplinary evaluation confirmed surgical eligibility and informed consent was obtained, the patient underwent median sternotomy with resection of the mediastinal mass and thymus, as well as bilateral cervical lymph node dissection, on May 22, 2024. Intraoperatively, involvement of the pericardium by tumor was observed, requiring partial pericardiectomy. The surgical procedure was completed uneventfully, achieving complete resection of the tumor and cervical lymph nodes (Figure 1C).

Histopathological examination of the resected specimens confirmed metastatic involvement in multiple enlarged and firm cervical lymph nodes, while no tumor infiltration was identified in the mediastinal lymph nodes, consistent with an R0 resection. Postoperative histopathological examination revealed a neoplastic lesion characterized by diffusely distributed tumor cells demonstrating focal infiltration and moderate nuclear atypia, along with frequent mitotic figures (Figure 2A). Numerous vascular tumor thrombi were identified (Figure 2B). Prominent fibrous septation and central necrosis were evident within the tumor mass (Figure 2C). In conjunction with immunohistochemical findings, these features were consistent with a grade 2 neuroendocrine tumor (NET G2). The patient had an uneventful postoperative recovery, with no significant discomfort. Follow-up CT scans demonstrated complete removal of the mediastinal tumor and involved lymph nodes, with clear visualization of the aorta and pulmonary artery (Figure 1D-E).

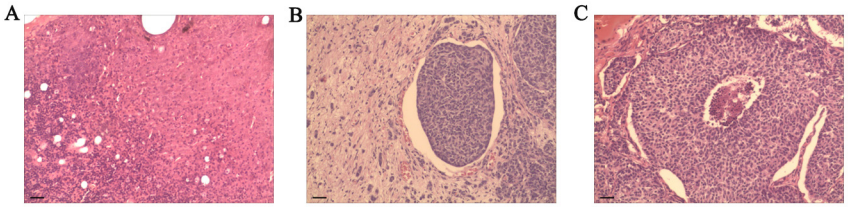

Figure 2: Postoperative Pathology of the Patient Diagnosed with Atypical Carcinoid (Neuroendocrine Tumor G2)

(A) Hematoxylin and eosin (H&E) image showed scattered infiltrates of tumor cells within the background tissue. Focal areas of solid tumor growth are observed, providing an overview of the spatial distribution of neoplastic cells. Bar :100µm (B) H&E staining reveals a well-circumscribed nest of tumor cells separated by fibrous stroma. Vascular tumor thrombi are identified. The tumor cells exhibit moderate nuclear atypia and granular chromatin. Bar: 50µm (C) H&E staining demonstrates solid nests of uniform tumor cells with moderate to high cellularity. The central of mass show central necrosis. The tumor cells display round to oval nuclei with characteristic salt-and-pepper chromatin, typical of an atypical carcinoid tumor. Bar: 50µm

3. Discussion

NETs of the thymus are exceedingly rare, accounting for less than 5% of all neuroendocrine carcinomas [9]. Thymic NETs, including atypical carcinoids, frequently present significant diagnostic and therapeutic challenges owing to their low incidence and propensity for late-stage detection, often accompanied by metastatic disease. The present case illustrates these complexities, as the patient initially manifested with cervical lymphadenopathy rather than classic thoracic symptoms, highlighting the potential for atypical presentations that may lead to diagnostic delays.

The clinical manifestations of thymic NETs are frequently nonspecific, often mimicking other mediastinal or lymphoproliferative disorders. Such ambiguity may contribute to diagnostic delays, as exemplified in this patient. Advances in imaging modalities, particularly PET-CT with radiolabeled somatostatin analogs, have substantially improved both the detection and localization of NETs, including those originating from the thymus [10,11]. In this case, PET-CT was pivotal in delineating the extent of disease and informing surgical planning. Furthermore, immunohistochemistry remains indispensable for establishing a definitive diagnosis and tumor grading, with markers such as CD117, INSM1, and Ki-67 providing critical prognostic information.

Given the rarity of thymic NETs, treatment strategies are often extrapolated from guidelines for NETs arising at other anatomical sites [5]. Complete surgical resection with negative margins (R0 resection) remains the cornerstone of management for localized and resectable disease, offering the best chance for prolonged disease-free survival [12]. In this patient, radical resection was accomplished through comprehensive lymphadenectomy and mediastinal tumor excision. The pivotal role of surgery is further underscored by the high risk of recurrence and limited efficacy of systemic therapies in advanced stages. Adjuvant therapies, such as chemotherapy with CAPTEM, may offer disease stabilization, particularly in cases with residual or metastatic disease, as demonstrated in this report.

Novel therapeutic modalities, including targeted therapies and peptide receptor radionuclide therapy, are being actively investigated for patients with advanced or recurrent NETs who have limited response to conventional treatments [13,14]. Early data suggest that these strategies may enhance disease control and survival outcomes, though further validation in prospective

clinical trials is warranted. The establishment of dedicated centers and multidisciplinary tumor boards is critical for optimizing individualized management strategies, particularly for rare entities such as thymic NETs.

Surgical management in this case involved partial pericardiectomy, necessitated by direct tumor invasion of the pericardium. Resection in proximity to vital mediastinal structures presents significant technical challenges; however, meticulous surgical planning enabled successful removal without major complications, such as recurrent laryngeal nerve injury. Preservation of normal postoperative vocal function attests to the importance of surgical expertise in achieving optimal outcomes. This case reinforces that, even in rare thoracic tumors involving critical anatomy, complete resection is feasible and can be accomplished safely in experienced centers.

Despite growing international expertise in the management of rare NETs, including thymic subtypes, there remains an unmet need for larger, multicenter clinical trials and the development of evidence-based, site-specific guidelines. In China, increasing attention is being paid to the formulation of dedicated protocols and the advancement of specialized care for these uncommon malignancies. This case underscores the importance of international collaboration and robust clinical research to enhance understanding and improve prognostic outcomes for patients with rare thymic NETs.

4. Conclusion

Thymic-origin neuroendocrine carcinoma remains a rare and challenging entity. Continued advancements in diagnostic imaging, molecular pathology, and therapeutic strategies are crucial. This case underscores the importance of a thorough and multidisciplinary approach to diagnosis and treatment, contributing to the growing body of knowledge and improving care for patients with this rare malignancy.

Nonstandard Abbreviations and Acronyms

NETs: thymic neuroendocrine tumors
CAPTEM: capecitabine and temozolomide
WHO: world health organization
PET-CT: positron emission tomography–computed tomography
CT: computed tomography
NET G2: grade 2 neuroendocrine tumor

Declarations

All participants provided written informed consent for the use of their data and images in this publication.

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Conflicts of Interest

None.

Authors Contribution Statement

KQ, WW, DY collected and assembled the data. XX drafted the manuscript. KQ and JT revised the manuscript. KQ conceived and designed the study. All authors read and approved the final version of the manuscript.

Availability of Data and Material

The datasets from the current study are available from the corresponding author upon reasonable request.

References

1. Dasari, A., Shen, C., Halperin, D., Zhao, B., Zhou, S., Xu, Y., ... & Yao, J. C. (2017). Trends in the incidence, prevalence, and survival outcomes in patients with neuroendocrine tumors in the United States. *JAMA oncology, 3*(10), 1335-1342.
2. Yao, J. C., Hassan, M., Phan, A., Dagohoy, C., Leary, C., Mares, J. E., ... & Evans, D. B. (2008). One hundred years after "carcinoid": epidemiology of and prognostic factors for neuroendocrine tumors in 35,825 cases in the United States. *Journal of clinical oncology, 26*(18), 3063-3072.
3. Caplin, M. E., Baudin, E., Ferolla, P., Filosso, P., Garcia-Yuste, M., Lim, E., ... & Zheng-Pei, Z. (2015). Pulmonary neuroendocrine (carcinoid) tumors: European Neuroendocrine Tumor Society expert consensus and recommendations for best practice for typical and atypical pulmonary carcinoids. *Annals of Oncology, 26*(8), 1604-1620.
4. Pavel, M., Öberg, K., Falconi, M., Krenning, E. P., Sundin, A., Perren, A., ... & ESMO Guidelines Committee. (2020). Gastroenteropancreatic neuroendocrine neoplasms: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology, 31*(7), 844-860.
5. Pavel, M., O"Toole, D., Costa, F., Capdevila, J., Gross, D., Kianmanesh, R., ... & all other Vienna Consensus Conference participants. (2016). ENETS consensus guidelines update for the management of distant metastatic disease of intestinal, pancreatic, bronchial neuroendocrine neoplasms (NEN) and NEN of unknown primary site. *Neuroendocrinology, 103*(2), 172-185.
6. Oronsky, B., Ma, P. C., Morgensztern, D., & Carter, C. A. (2017). Nothing but NET: a review of neuroendocrine tumors and carcinomas. *Neoplasia, 19*(12), 991-1002.
7. Rindi, G., Falconi, M., Klersy, C., Albarello, L., Boninsegna, L., Buchler, M. W., ... & Wiedenmann, B. (2012). TNM staging of neoplasms of the endocrine pancreas: results from a large international cohort study. *Journal of the National Cancer Institute, 104*(10), 764-777.
8. Bohnenberger, H., Dinter, H., König, A., & Ströbel, P. (2017). Neuroendocrine tumors of the thymus and mediastinum. *Journal of thoracic disease, 9*(Suppl 15), S1448.
9. Wang, Y. Z., Mayhall, G., Anthony, L. B., Campeau, R. J., Boudreaux, P. J., & Woltering, E. A. (2012). Cervical and upper mediastinal lymph node metastasis from gastrointestinal and pancreatic neuroendocrine tumors: true incidence and management. *Journal of the American College of Surgeons, 214*(6), 1017-1022.
10. Ambrosini, V., Campana, D., Bodei, L., Nanni, C., Castellucci,

P., Allegri, V., ... & Fanti, S. (2010). 68Ga-DOTANOC PET/CT clinical impact in patients with neuroendocrine tumors. *Journal of Nuclear Medicine, 51*(5), 669-673.
11. Hope, T. A., Bergsland, E. K., Bozkurt, M. F., Graham, M., Heaney, A. P., Herrmann, K., ... & Strosberg, J. R. (2018). Appropriate use criteria for somatostatin receptor PET imaging in neuroendocrine tumors. *Journal of Nuclear Medicine, 59*(1), 66-74.
12. Gaur, P., Leary, C., & Yao, J. C. (2010). Thymic neuroendocrine tumors: a SEER database analysis of 160 patients. *Annals of surgery, 251*(6), 1117-1121.
13. Strosberg, J., El-Haddad, G., Wolin, E., Hendifar, A., Yao, J., Chasen, B., ... & Krenning, E. (2017). Phase 3 trial of 177Lu-Dotatate for midgut neuroendocrine tumors. *New England Journal of Medicine, 376*(2), 125-135.
14. Öberg, K., Knigge, U., Kwekkeboom, D., Perren, A., & ESMO Guidelines Working Group. (2012). Neuroendocrine gastro-entero-pancreatic tumors: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology, 23*, vii124-vii130.