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Case Report

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Anaplastic Transformation of Papillary Thyroid Carcinoma in Metastatic Lymph Nodes

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Abstract

Background: Anaplastic thyroid cancer (ATC) is a rare but highly aggressive malignancy, accounting for approximately 1–4% of all thyroid cancers and associated with extremely poor prognosis. Although anaplastic transformation most commonly arises within the primary thyroid tumor, transformation occurring in metastatic cervical lymph nodes is exceedingly uncommon. Early recognition of rapid clinical progression is essential, as timely diagnosis may influence management strategies.

Case Presentation: We report the case of a 67-year-old woman who presented with a year-long right neck swelling and recent onset of hoarseness. Imaging revealed an enlarged right cervical lymph node with central necrosis and a 3-cm thyroid mass. Fine needle aspiration identified papillary thyroid carcinoma (PTC). The patient underwent total thyroidectomy with right modified radical neck dissection. Histopathology demonstrated conventional PTC in the primary lesion, whereas the metastatic cervical lymph node exhibited spindle cell proliferation with marked nuclear atypia, consistent with anaplastic thyroid cancer. Postoperatively, external radiation therapy was initiated; however, rapid disease progression ensued, with the development of cervical skin metastasis, lung metastases, and pleural involvement. The patient died 57 days after surgery despite treatment.

Conclusion: This case highlights the rare occurrence of anaplastic transformation within metastatic cervical lymph nodes of PTC. Even with complete resection and postoperative radiation therapy, the disease course may be fulminant. Clinicians should remain vigilant for rapid morphological or clinical changes in metastatic lesions, as early detection of anaplastic transformation may improve diagnostic accuracy and inform treatment planning.

Keywords: Papillary thyroid carcinoma; Anaplastic transformation; Metastatic cervical lymph node; Poor prognosis; Multidisciplinary treatment

Introduction

Anaplastic thyroid cancer (ATC) is an uncommon but highly aggressive malignancy, accounting for approximately 1–4% of all thyroid cancers and conferring an extremely poor prognosis. Although papillary thyroid carcinoma (PTC) typically follows an indolent course, abrupt tumor enlargement should raise suspicion for anaplastic transformation. Most transformations arise within the primary tumor; however, anaplastic change within metastatic cervical lymph nodes or distant metastatic sites has been reported, albeit rarely.

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Here, we describe an unusual case of PTC with anaplastic transformation confined to metastatic cervical lymph nodes, which resulted in explosive postoperative recurrence and rapid clinical deterioration despite complete resection and adjuvant radiotherapy.

Case Presentation

A 67-year-old woman presented with a 1-year history of right supraclavicular swelling and a 1-month history of hoarseness. Laryngoscopy demonstrated right vocal cord paralysis. Ultrasonography revealed an 80-mm heterogeneous lymph node with irregular margins and internal vascularity in the right supraclavicular fossa, along with a 3 × 3-cm nodular lesion in the left thyroid lobe. Thyroid hormone levels were normal. Laboratory studies showed leukocytosis (>10,000/μL) and an elevated anti-thyroglobulin antibody level of 214 IU/L.

Contrast-enhanced computed tomography (CT) revealed a necrotic right cervical lymph node compressing the right common carotid artery and invading the right internal jugular vein, as well as multiple calcified nodules in the left thyroid lobe. FDG-PET demonstrated intense uptake in the right cervical lymph node (SUVmax 40.5) without distant metastases (Figure 1). Fine-needle aspiration cytology (FNA) of the lymph node yielded a diagnosis of PTC.

With a preoperative diagnosis of clinical T1bN1bM0 PTC, the patient underwent en-bloc total thyroidectomy and right modified radical neck dissection. Because the metastatic node was densely adherent to surrounding tissues, the right anterior scalene muscle, phrenic nerve, vagus nerve, and internal jugular vein were resected en bloc. The operative time was 4 hours 26 minutes, and blood loss was 373 mL.

Histopathological evaluation of the thyroid gland revealed multiple calcified nodules with classic features of PTC, including enlarged nuclei with grooves and intranuclear inclusions. In contrast, the metastatic 80 × 50 × 50-mm right cervical lymph node exhibited biphasic morphology: areas of metastatic PTC and regions composed of markedly atypical spindle cells with highly pleomorphic nuclei, consistent with ATC (Figure 2). The final pathological diagnosis was PTC with anaplastic transformation in a metastatic cervical lymph node (AJCC 8th edition: pT4bN1bMx, Ex2, R0; Stage IVB).

Postoperative external-beam radiation therapy (EBRT) was initiated on postoperative day 20. By postoperative day 45, at a cumulative dose of 32 Gy, the patient developed fever, worsening leukocytosis, and rapid cutaneous metastases in the neck. Chest CT subsequently demonstrated multiple lung metastases, right pleural dissemination, and malignant pleural effusion. Given her abrupt clinical decline, EBRT was discontinued, and best supportive care was initiated. The patient died of progressive disease on postoperative day 57.

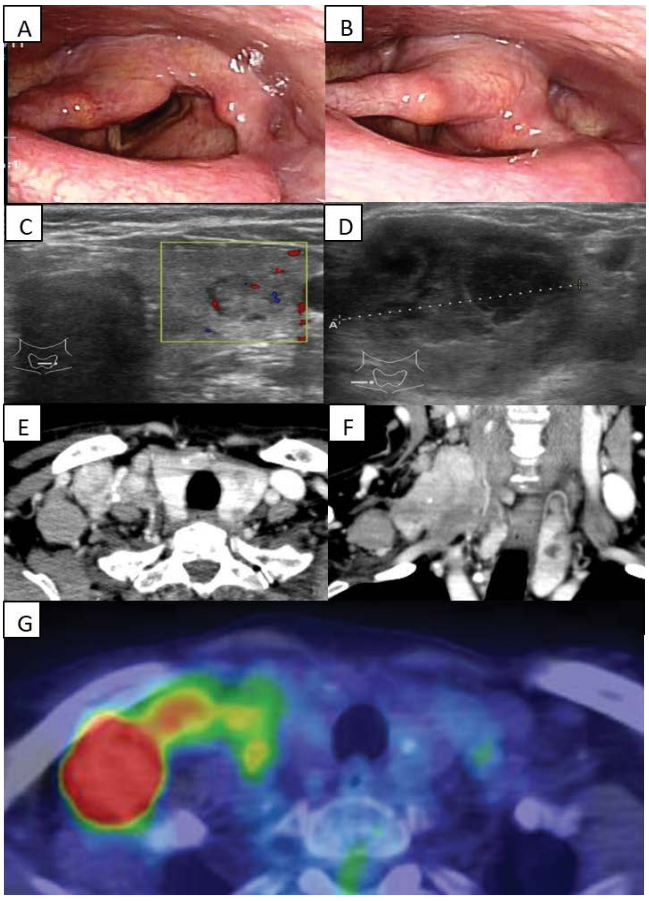

Figure 1: Endoscopic, cervical ultrasonographic, computed tomography, and positron emission tomography findings.

(A, B) Laryngoscopic images of the larynx. (A) Inspiratory phase of the glottis showing right vocal cord paralysis. (B) Expiratory phase of the glottis.

(C, D) Cervical ultrasonography images. (D) A lymph node measuring 28 mm in diameter with poorly defined margins and internal septations was observed in the right clavicular fossa.

(E, F) Contrast-enhanced cervical computed tomography (CT). (E) Multiple enlarged lymph nodes were identified in the right clavicular fossa, accompanied by retraction of the right common carotid artery and collapse of the right internal jugular vein.

(G) Positron emission tomography–CT revealed intense uptake in the right clavicular lymph nodes.

Discussion

Anaplastic thyroid carcinoma (ATC), accounting for approximately 1–4% of all thyroid cancers, typically manifests as a rapidly enlarging, painful cervical mass and progresses to a fatal condition within a short period of time [1]. Curative treatment is exceedingly rare and is generally limited to incidental ATC lesions discovered after complete excision. In 70–80% of patients, radical surgery is precluded by extensive local invasion or distant metastasis, leading to early relapse despite initial therapy, with a median survival of approximately 4 months [1]. Most patients ultimately die from airway compromise or catastrophic hemorrhage due to

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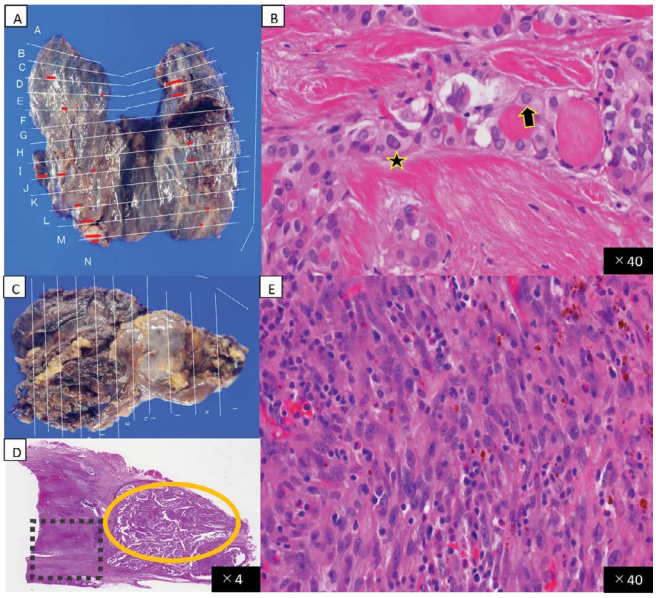

Figure 2: Pathological findings of the resected specimens.

(A, C) Macroscopic images of the surgically resected thyroid and cervical lymph nodes.

(B, D, E) Hematoxylin–eosin–stained sections of the thyroid and cervical lymph nodes. (A, B) Thyroid. (C, D, E) Cervical metastatic lymph nodes.

(B) Papillary thyroid carcinoma was diagnosed based on characteristic nuclear features, including glassy nuclei (arrow) and nuclear pseudo-inclusions (asterisk). Multiple intrathyroid metastases were also present.

(D) Papillary thyroid carcinoma (solid line) and anaplastic thyroid carcinoma (dashed line) were identified within the same lymph node. The interface between the papillary and anaplastic components was indistinct.

(E) Anaplastic thyroid carcinoma was diagnosed based on the presence of spindle-shaped tumor cells with nuclear enlargement and marked nuclear pleomorphism.

uncontrolled cervical tumor growth, in addition to systemic decline from widespread dissemination. Unfortunately, treatment outcomes have not significantly improved over recent decades.

The proportion of cases in which ATC remains confined to the thyroid gland (stage IVA) is reported to be 6–13% [2–6]. Even when the disease extends to adjacent structures (stage IVB), definitive resection may still be feasible if the invasion involves the trachea, larynx, esophagus, recurrent laryngeal nerve, or anterior neck muscles, provided that en bloc resection and reconstruction can be performed [7]. Haymart et al. [8], analyzing 2,742 patients in the National Cancer Database, reported that the median survival in stage IVA was 4.3 months (95% CI, 3.1–7.4) with surgery alone, and less than 9.3, 6.4, and 11.2 months with postoperative radiation, chemotherapy, or combined therapy, respectively. Yoshida et al. [9] examined 25 cases of incidentally detected postoperative ATC and reported that the 1-year overall survival was 50% with surgery alone, compared with 87% with adjuvant radiotherapy or chemotherapy. However, these retrospective studies inevitably suffer from selection bias, as adjuvant therapy tends to be offered to patients considered more likely to benefit.

Kim et al. [3] analyzed 121 multicenter cases and found that most long-term survivors had received postoperative radiotherapy. Similarly, Sugitani et al. [6], using data from the ATC research consortium (677 patients), demonstrated a nonsignificant but notable improvement in survival with postoperative radiotherapy for stage IVA disease (6.2 vs. 13.0 months, $p = 0.078$). In contrast, Chen et al. [10], using 261 cases from the SEER database, reported no significant difference in survival with or without adjuvant radiotherapy in stage IVA. Sugitani et al. [6] also identified four clinical features associated with poor prognosis—leukocytosis (≥10,000/μL), acute progression (within 1 month), distant metastasis, and a large tumor (≥5 cm)—and recommended incorporating these parameters into treatment decision-making. In our case, although acute exacerbation was not evident, the primary metastatic lymph node mass measured 55 mm, and the disease corresponded to stage IVB. Despite complete excision and postoperative radiotherapy, the disease progressed rapidly, resulting in a poor clinical outcome.

Anaplastic transformation may arise not only from the primary thyroid lesion but also, though uncommonly, from metastatic lymph nodes or distant metastatic deposits. Sugitani et al. [6] classified ATC into four subtypes: common type (80.8%), incidental type (4.3%), anaplastic change in cervical metastatic lymph nodes (14.0%), and anaplastic change at distant metastatic sites (0.9%). The present case falls into the third category. It is well recognized that anaplastic transformation arising from metastatic lymph nodes or distant metastases portends an extremely poor prognosis [12,13]. Nevertheless, Ito et al. [14] reported that radical lymph node dissection may contribute to prolonged survival in selected cases.

On a molecular level, the mechanisms underlying anaplastic transformation remain incompletely understood. Although BRAF and NRAS mutations have been implicated, these alterations do not fully explain the process and are not consistently observed [15,16]. Elliott et al. [17] demonstrated that EGFR, PDGFR, and HER-2 are overexpressed in ATC arising from PTC, suggesting their possible involvement in anaplastic transformation and their potential as therapeutic targets. Wiseman et al. [18] examined 63 molecular markers using tissue microarrays from 12 ATC-with-PTC cases, identifying significant alterations in eight markers—including thyroglobulin, Bcl-2, MIB-1, E-cadherin, p53, β-catenin, topoisomerase II-α, and VEGF—which may be relevant for diagnosis, prognosis, or targeted therapy development.

PAX-8 is a transcription factor crucial for differentiation of thyroid, renal, and Müllerian duct tissues and is often retained even after anaplastic transformation [19], whereas other thyroid-specific markers such as TTF-1 and thyroglobulin are frequently lost [20]. Therefore, PAX-8 immunostaining is valuable for confirming the diagnosis of ATC. In our case, PAX-8 expression was not assessed. Given the rapidly enlarging neck mass and the diagnostic difficulty associated with anaplastic transformation in metastatic sites, PAX-8 staining should have been included to strengthen diagnostic confirmation.

While several molecular alterations have been described, most remain speculative, and further studies are required to clarify the mechanisms underlying anaplastic transformation.

Conclusions

We report a rare case of PTC with anaplastic transformation confined to metastatic cervical lymph nodes. Despite complete tumor resection and early initiation of postoperative radiotherapy, the patient experienced explosive locoregional and distant recurrence, ultimately resulting in rapid mortality. Clinicians should recognize that even metastatic lymph nodes harboring PTC may undergo abrupt anaplastic transformation, necessitating vigilant surveillance and timely intervention.

Conflict of Interest

The authors declare no conflicts of interest.

Ethical Approval

Written informed consent for publication was obtained from the patient. This report was approved by the Ethics Committee of Kawasaki Medical School Hospital.

Consent Statement

Published with written consent of the patient.

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