

Anaplastic Transformation of Papillary Thyroid Carcinoma in Metastatic Lymph Nodes: A case report

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Abstract

Anaplastic thyroid cancer is a rare and has an extremely poor prognosis. It is known that most of anaplastic transformation occurs in primary lesions, but rarely in metastatic lesions. We report 67-year-old female patient who received surgery, but whose postoperative pathological examination revealed anaplastic transformation in metastatic cervical lymph nodes.

Anaplastic Transformation of Papillary Thyroid Carcinoma in Metastatic Lymph Nodes: A case report

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Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy

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Abstract

Introduction: Anaplastic thyroid cancer is a rare cancer that is found in about 1% of thyroid malignant tumors and has an extremely poor prognosis. It is known that most of anaplastic transformation occurs in primary lesions, but rarely occurs in cervical lymph node lesions.

Case presentation: We report a case of 67-year-old female patient who underwent preoperative examination to diagnose papillary thyroid carcinoma and underwent surgery, but whose postoperative pathological examination revealed anaplastic transformation of metastatic cervical lymph nodes. Although postoperative radiation therapy was performed, rapid neck skin metastases, multiple lung metastases, and pleural effusion were observed, leading to an unfortunate outcome.

Conclusion: It is important to be aware that papillary thyroid carcinoma could develop anaplastic transformation at metastatic cervical lymph nodes.

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

Introduction

Anaplastic thyroid cancer (ATC) is a rare cancer that is found in about 1% of thyroid malignant tumors and has an extremely poor prognosis. Generally, papillary thyroid carcinoma (PTC) grows slowly, but when it exhibits a rapid growth, it is necessary to bear in mind the anaplastic transformation. It is known that most of anaplastic transformation occurs in primary lesions, but rarely occurs in cervical lymph node lesions or distant metastasis lesions.

We have experienced cases in which metastatic cervical lymph nodes have undergone anaplastic transformation. In this manuscript, we report our experience with courses and outcomes of a patient demonstrating papillary carcinoma in primary lesion but showing anaplastic transformation in the metastatic cervical lymph nodes with rapid recurrence after surgery.

Case presentation

A 67-year-old female patient presented to our hospital with a history of neck swelling for 1 year and hoarseness for 1 month. The swelling was situated in supraclavicular fossa of the right neck. Right vocal cord paralysis was noted in laryngoscopy. Cervical ultrasonography revealed a lymph node which having a major axis 80mm, elastic rigidity and poor movability in the right clavicle fossa, and neoplastic lesion measured 3 x 3 cm in the left lobe of the thyroid gland. Her serum level of thyroid hormones was normal, while white blood cell was $>10000 /\mu\text{L}$ and anti-thyroglobulin antibody was 214 IU/L. Cervical computed tomography (CT) showed lymph nodes swelling with central necrosis, compression of the right common carotid artery, and invasion to the right internal jugular vein with collapse. Multiple nodular lesions with calcification were also found in the left lobe of the thyroid. Right cervical lymph node was detected by F-18 fluorodeoxyglucose positron emission tomography but no distant metastases. The maximum standardized uptake value was calculated to be 40.5 in cervical lymph node. (figure 1) Fine needle aspiration cytology was performed on the right cervical lymph node and diagnosed as PTC.

With a pre-operative diagnosis of clinical T1bN1bM0 PTC, en-bloc total thyroidectomy and right D2b dissection were performed. The right cervical lymph node was firmly adherent to the surrounding tissue, so the following tissues were resected concurrently; right anterior scalene muscle, right phrenic nerve, right vagus nerve, right internal jugular vein. The operation time was 4 hours and 26 minutes, and the blood loss was 373 ml. Postoperative histological result showed multiple white nodules with calcification in both lobes of the thyroid. The atypical epithelium showing nuclear enlargement was follicular and papillary, and the nucleus was frosted glass with a nuclear groove and intranuclear inclusion bodies, which was a finding of papillary thyroid cancer. On the other hand, the cervical lymph nodes measured $80 \times 50 \times 50$ mm, and metastasis of papillary thyroid cancer was observed. In addition, nuclear enlargement and proliferation of spindle-shaped cells with strong irregular karyotype were observed, which was in agreement with ATC. (figure 2) Based on the above, the final pathological diagnosis was anaplastic transformation of metastatic cervical lymph nodes (pT4bN1bMx, Ex2, R0, pStage IVB).

External radiation therapy was started on 20th days after surgery. WBC and CRP were elevated at the time of 32 Gy irradiation on the 45th days after surgery, and same time, fever and cervical skin metastasis were observed. Chest CT showed multiple lung metastases, right pleural dissemination, and right cancerous pleural effusion. External radiation therapy was discontinued due to rapid deterioration of the condition, and BSC policy was decided. In spite of treatment, she expired due to primary illness on 57th days after surgery.

Discussion

ATC, which accounts for about 1 to 4% of thyroid cancers, often develops with rapidly increasing painful cervical mass, and worsens to a fatal condition in a short period of time [1]. It is a disease which is expected to be cured only in a very exceptional case such as a case where it is accidentally found in a tissue after excision. In 70 to 80% of cases, radical surgery is difficult due to peripheral invasion and distant metastasis. For this reason, most cases relapse shortly after the initial treatment, and the life expectancy is about 4 months. Patients die from asphyxiation and hemorrhage due to tumor growth in cervical region in addition

to the debilitating effects of systemic disseminated metastasis, therefore they cause unbearable to patients, families, and even medical staff. Unfortunately, treatment and prognosis have not improved significantly in the past decades.

The proportion of cases in which ATC remains in the thyroid gland (stage IVA) is reported to be 6-13 % [2-6]. Even if ATC has developed into the surrounding tissues (stage IVB), invasion into the tracheal, laryngeal, esophageal, recurrent laryngeal nerve, and anterior cervical muscles allows definitive surgery by combined resection and reconstruction [7]. Haymart et al. [8] reviewed the prognosis of 2,742 ATC patients using the National Cancer Database and showed that the median survival of stage IVA patients was 4.3 months (95% CI 3.1-7.4) with surgery alone, and less than 9.3 months, 6.4 months, 11.2 months in patients with postoperative radiation, chemotherapy, or both as adjuvant therapy. Yoshida et al. [9] reported that the prognosis after radical surgery of 25 cases of ATC accidentally found in postoperative pathological examination, and reported that the 1 year overall survival rate was 50% when treatment was completed only by surgery, which was significantly different from 87% when postoperative radiotherapy or adjuvant chemotherapy was added after surgery. However, all of these are retrospective study, and the type of drug to be administered and the method of administration are unknown, and a bias cannot be denied in which patients who can expect long-term prognosis are selected and adjuvant therapy is added.

Kim et al. [3] analyzed prognosis of 121 multi-center cases and reported that most long-term survivors had been received postoperative radiation therapy after surgery. Sugitani et al. [6] also report from the results of 677 cases of ATC research consortium that postoperative radiation therapy after surgery resulted in an insignificant but prolonged prognosis at stage IVA (6.2 vs. 13.0 months $p = 0.078$). On the other hand, Chen et al. [10] reported from the analysis of 261 cases of the Surveillance, Epidemiology, and End Results (SEER) database that there was no difference in prognosis between the administration and non-administration of radiation therapy after surgery at stage IVA. In addition, Sugitani et al. [6] analyzed clinical characteristics, and considered leukocytosis (10000 / μ L or more), acute exacerbation (within 1 month), distant metastases, and large tumors (5cm or more) as clinical poor prognostic factors, and proposed to proceed with treatment in consideration of these factors. In the case reported by the present inventors, although acute exacerbation was not observed, since the tumor diameter was as large as 55mm and the tumor was in the stage IVB, it was an unfortunate result despite complete excision and postoperative radiotherapy.

Anaplastic transformation occurs not only from the primary lesion but also from the metastatic lymph nodes or distant sites. Sugitani et al. [6] reported that ATC are classified into 4 types : common type, incidental type, anaplastic change at the neck type, and anaplastic change at the distant site type, and that the common type is 80.8%, the incidental type is 4.3%, the anaplastic change at the neck type is 14.0%, and the anaplastic change at the distant site type is 0.9%. This present case corresponds to the anaplastic change at the neck type described above. Although it is a well-known fact that the prognosis is not good in a case where anaplastic transformation is observed in a metastatic lymph nodes or distant sites in PTC [12,13]. According to Ito et al. [14], radical resection of lymph nodes is expected to have a long-term prognosis.

In molecular biology, the mechanism of the onset of anaplastic transformation has been variously reported to involve BRAF and N-RAS mutation, but has not yet been elucidated [15,16]. Elliott et al.[17] reported that EGFR, Platelet-Derived Growth Factor Receptor (PDGFR), and HER-2 are overexpressed in ATC with PTC, and there is a possibility that they play some role in anaplastic transformation, and an application to targeted therapy marker for ATC patients. In addition, Wiseman et al. [18] reported that 63 elements were examined in the tissue microarray structure of 12 cases of ATC with PTC, and 8 elements, i.e., thyroglobulin, Bcl-2, MIB-1, E-cadherin, p53, β -catenin, topoisomerase II- α , and VEGF, were found to be significantly changed, and were also searched for , which was described to be useful as a potential target for molecular biology diagnosis, prognosis, and targeted therapy. However, none of these results fall within speculation. Further molecular biological studies are expected to proceed in the future.

Conclusions

In conclusion, here we reported a case of anaplastic transformation in metastatic cervical lymph nodes of

PTC. Despite being recieved with postoperative radiation therapy, neck skin metastasis and multiple lung metastasis appeared, and the disease rapidly worsened, resulting in an unfortunate outcome. It is important to be aware that papillary thyroid carcinoma could develop anaplastic transformation at metastatic cervical lymph nodes.

Conflict of interest

The authors declare no conflict of interest.

ETHICAL APPROVAL

Written informed consent was obtained from the patient to report the case, and the manuscript was approved at the Ethics Committee of Kawasaki Medical School Hospital.

CONSENT STATEMENT

Published with written consent of the patient

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