Case Report

Occult Papillary Thyroid Carcinoma without Detection of the Primary Tumor on Preoperative Ultrasonography or Postoperative Pathological Examination: A Case Report

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Keywords

Ectopic thyroid cancer · Occult thyroid cancer · Papillary thyroid carcinoma · Symptomatic papillary thyroid microcarcinoma

Abstract

Herein, we report a case of an occult thyroid cancer that was not detected as a primary tumor on preoperative ultrasonography or postoperative pathological examination, although a diagnosis of papillary thyroid carcinoma metastasis was made owing to the presence of a mass in the right upper neck. Needle biopsy of the mass in the right upper neck revealed positive results for thyroglobulin and TTF-1 on immunostaining, and a papillary thyroid carcinoma was observed with papillary and follicular patterns. We suspected papillary thyroid carcinoma (T0N1bM0) or ectopic papillary thyroid carcinoma. Accordingly, we performed total thyroidectomy, central lymph node dissection, right lateral neck dissection, and resection of the superficial lobe of the right parotid. A postoperative pathological examination of 5-mm slices of the specimen revealed no primary tumor in the thyroid. However, a hyalinized image of the thyroid indicated that a micropapillary thyroid carcinoma might have spontaneously disappeared. As there was no normal thyroid tissue in the metastasis to the superior internal jugular lymph node, the tumor was unlikely to be an ectopic papillary thyroid carcinoma. Therefore, we made a diagnosis of a papillary thyroid carcinoma (pT0N1bM0). After surgery, we

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determined that the tumor belonged to a high-risk group of papillary thyroid carcinomas and a poor-prognosis group of symptomatic papillary thyroid microcarcinomas; accordingly, ablation was performed with 30 mCi iodine-131. There was no recurrence or metastasis 24 months after the first surgery.

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Introduction

Occult thyroid cancers are small carcinomas in the thyroid that are observed on a secondary examination after a primary diagnosis of lymph node or distant metastasis [1]. Occult thyroid carcinomas are commonly detected after patients show swelling in the cervical lymph nodes [2]. In fact, most occult thyroid carcinomas are small thyroid carcinomas that are ≤ 1 cm, and the prognosis is poor when metastatic lesions are evident [3]. There are few reports of occult papillary thyroid carcinomas that were not detected as primary tumors on preoperative ultrasonography or postoperative pathological examination. Herein, we report a case of an occult papillary thyroid carcinoma that was diagnosed after swelling was observed in the superior internal jugular lymph node, although the primary tumor in the thyroid could not be identified.

Case Presentation

A 66-year-old woman with no family history of thyroid disease presented with the main complaint of swelling in the right upper neck. She had a medical history of rheumatoid arthritis and cholelithiasis and was taking 5 mg/day prednisolone for rheumatoid arthritis; in addition, she had a smoking history of 20 cigarettes per day since the age of 20 years, but she had no history of alcohol consumption. She had noticed swelling of the right upper neck 1 year previously, and it had gradually worsened. Therefore, the patient was referred to our hospital for examination and treatment. During the initial examination, no tumor was observed in the oral cavity, nasal cavity, pharynx, or larynx. There was a palpable 45-mm mass just below the right parotid. The mass was elastic, hard, and movable, and the patient did not have any tenderness. There was no palpable swollen cervical lymph node other than the swelling in the right upper neck. The patient did not have any facial paralysis.

A blood test revealed no abnormalities in thyroid function (fT3; 3.25 pg/mL, fT4; 1.11 ng/mL, TSH; 0.53 μ U/mL). The thyroglobulin levels were slightly elevated (46.40 ng/mL). The squamous cell carcinoma-associated antigen (SCC) level was 0.3 ng/mL (≤ 1.5 ng/mL), and the carcinoembryonic antigen (CEA) level was 3.2 ng/mL (≤ 5.0 ng/mL). Cervical contrast-enhanced computed tomography (CT) (Fig. 1a) revealed a lobular mass with a relatively clear boundary in the inferior pole of the right parotid. The mass was accompanied by calcification, but no primary tumor was observed in the head and neck region including the thyroid. Cervical magnetic resonance imaging (MRI) (Fig. 1b, c) revealed a 31-mm lobular mass with a relatively clear boundary and with equal signal intensity on T1- and T2-weighted images. Gadolinium-enhanced T1-weighted MRI (Fig. 1d, e) revealed contrast enhancement within the tumor below the right parotid. No primary tumor was observed on MRI of the head and neck region including the thyroid. Fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT (Fig. 1f) revealed strong accumulation (maximum standardized uptake value of 25.9) in the tumor below the right parotid. No other findings indicated a primary lesion or metastasis.

Fig. 1. Imaging findings before surgery. **a** A cervical contrast-enhanced computed tomography (CT) scan (axial section) showing a lobular mass with a relatively clear boundary (blue arrow) in the inferior pole of the right parotid. **b** A cervical T1-weighted magnetic resonance imaging (MRI) scan (axial section) showing a lobular mass with a relatively clear boundary (blue arrow), with equal signal intensity on T1-weighted imaging, below the right parotid. **c** A cervical T2-weighted MRI scan (axial section) showing a lobular mass with a relatively clear boundary (blue arrow), with equal signal intensity on T2-weighted imaging, below the right parotid. **d** A gadolinium-enhanced T1-weighted MRI scan (axial section) showing the contrast effect inside the tumor (blue arrow) below the right parotid. **e** A gadolinium-enhanced T1-weighted MRI scan (coronal section) showing the boundary between the tumor (blue arrow) located below the right parotid and the parotid. **f** A fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT scan showing strong accumulation of FDG, with the maximum standardized uptake value of 25.9 (blue arrow) in the tumor below the right parotid.

Fine-needle aspiration cytology of the mass below the right parotid (Fig. 2a) revealed a papillary agglomerate comprising columnar epithelial cells with intranuclear cytoplasmic inclusions, indicating that the mass might be a metastasis from a papillary thyroid carcinoma. However, no tumor was observed on thyroid and neck ultrasonography. Therefore, to make a definitive diagnosis, we performed histological examination of the tumor below the right parotid via needle biopsy. Histological examination revealed a final diagnosis of a papillary thyroid carcinoma (Fig. 2b). Immunostaining revealed positive results for TTF-1 and thyroglobulin (Fig. 2c, d). Thus, the preoperative diagnosis indicated that the tumor belonged to a high-risk group of papillary thyroid carcinomas (cT0N1bM0) [4, 5] or ectopic papillary thyroid carcinoma. However, it was difficult to preoperatively discriminate between them. Therefore, after consulting the patient and her family, we decided to perform total thyroidectomy in addition to excision of the parotid mass.

The patient underwent total thyroidectomy, central lymph node dissection, right lateral neck dissection, and resection of the tumor in the right upper neck and the superficial lobe of

Fig. 2. Preoperative pathological examination findings. **a** Fine-needle aspiration cytology ($\times 400$) revealed columnar epithelial cells (red arrow) with clear intranuclear cytoplasmic inclusions in a papillary agglomerate, suggesting the possibility of metastasis of papillary thyroid carcinoma. **b** Histological examination on hematoxylin and eosin (H-E) staining ($\times 200$) revealed papillary tissue, and a diagnosis of papillary thyroid carcinoma was made. **c** Histological examination after staining for TTF-1 ($\times 200$) revealed that the nuclei were stained, and the cells were positive for TTF-1. **d** Histological examination after staining for thyroglobulin ($\times 200$) revealed that the cytoplasm was stained, and the cells were positive for thyroglobulin.

the parotid gland. On macroscopic observation, the right upper neck tumor was seen to invade the accessory nerve (Fig. 3a), which was concomitantly resected. The facial nerve was conserved. The recurrent laryngeal nerve was conserved on both sides.

Postoperative pathological examination revealed the largest mass to be $35 \times 30 \times 28$ mm in size, and this mass was a fusion of two superior internal jugular lymph nodes. A total of 23 lymph nodes were observed on neck dissection. On histological examination, metastasis of papillary thyroid carcinoma to the fused lymph nodes was observed, including two superior internal jugular lymph nodes. In addition, the right parotid gland was compressed due to the fused lymph node metastasis. Similar to the preoperative cytology and histology findings observed in papillary thyroid carcinomas, preoperative findings revealed lymph node metastases from papillary thyroid carcinoma. There was no ectopic thyroid tissue in the dissected metastatic or normal lymph nodes; the tumor was unlikely to be an ectopic papillary thyroid carcinoma. Although an adenomatous goiter was observed in the thyroid, examination of the 5-mm slices of the specimen did not reveal papillary carcinoma in the thyroid. However, a hyalinized image in the thyroid was detected; it revealed the possibility of spontaneous disappearance of the papillary thyroid microcarcinoma (Fig. 3b, c).

On the basis of the pathology results, we suspected that the tumor belonged to a high-risk group of papillary thyroid carcinomas (pT0N1bM0) and a poor-prognosis group of symptomatic papillary thyroid microcarcinomas, as proposed by Sugitani et al. [4]. Accordingly, we

Fig. 3. Intraoperative findings of the resected specimens and pathological findings after surgery. **a** During right lateral neck dissection, tumor invasion was observed into the right accessory nerve (blue arrow), which was resected concomitantly. **b** Macroscopically, a 2 × 2-mm tumor-like lesion (red arrow) on the dorsal and lateral edges of the middle lobe of the right thyroid. **c** A thyroid section stained with H-E (×20): Histologically, the mass-like lesion (blue arrow) resembles scars with fibrous connective tissues with hyaline. In addition, small thyroid follicles showing regression or atrophy are aggregated in some parts.

performed ablation with 30 mCi iodine-131 after surgery. Scintigraphy performed 6 months after ablation confirmed the complete disappearance of the tumor. In fact, there has been no recurrence or metastasis for the past 24 months after the first surgery.

Discussion/Conclusion

In the present case, it was difficult to preoperatively determine whether the mass in the right upper neck was a lymph node metastasis from papillary thyroid carcinoma or an ectopic papillary thyroid carcinoma. If the tumor is not present in normal thyroid tissue or in the

thyroglossal duct, the tumor is likely to be a metastatic lesion of thyroid cancer; in contrast, when the tumor is present in normal thyroid tissue or in the thyroglossal duct, it is likely to have developed from an ectopic thyroid tissue [5, 6]. In the current case, the postoperative pathological examination revealed 23 lymph nodes in the dissected lymph node specimen, of which 2 had metastasis. The two metastatic superior internal jugular lymph nodes were fused. The resected thyroid specimen was an adenomatous goiter, and fibrous tissue – as shown in Fig. 3c – was observed in the thyroid, but there were no findings of papillary cancer.

As it is difficult to prepare slices of pathological specimens thinner than 5 mm, the tumor was suspected to be a micropapillary thyroid carcinoma <5 mm or an ectopic papillary thyroid carcinoma. Therefore, the lesion in the two superior internal jugular lymph nodes, which was preoperatively identified as the only cancerous lesion, was further examined. As no normal thyroid tissue was observed in the metastatic lymph node, we finally made a diagnosis of cervical lymph node metastasis of a micropapillary thyroid carcinoma. Pathological evaluation is necessary to differentiate between lymph node metastasis of papillary thyroid carcinoma and ectopic papillary thyroid carcinoma [5, 6], and the present case required a pathological examination of the surgically resected specimens for obtaining a definitive diagnosis.

Among 5,400 patients with papillary thyroid carcinoma who underwent surgery as the first-line treatment between 1990 and 2004, only 17 patients (0.3%) had occult thyroid carcinoma [2]. Of the 17 patients, 16 had lateral cervical lymph node metastasis and 1 patient had mediastinal lymph node metastasis. Twelve patients (71%) had a single lymph node metastasis and 5 (29%) had multiple lymph node metastases. The size of the metastatic lymph nodes was >3 cm in 12 of the 17 patients (71%). To summarize the findings of that study [2], most cases of occult thyroid carcinoma were found after a single metastasis of ≥ 3 cm was identified in the lateral cervical lymph node. The present case was also identified after a metastasis of ≥ 3 cm was observed in the lateral cervical lymph node. In the previous study of 17 patients with occult thyroid carcinoma, 14 patients underwent thyroidectomy, and in 5 patients, even the pathological examination did not reveal any cancerous lesion in the thyroid [2]. In the present case, no cancerous lesion was observed on ultrasonography or pathological examination. In some cases of papillary thyroid microcarcinoma, tumor cell components are extremely reduced and may be replaced by connective tissue and hyalinized tissue, thereby causing regressive changes [7]. In fact, a total of 741 cases of spontaneous cancer disappearance have been reported between 1900 and 1987 [8–10]. Among these cases, kidney cancer, neuroblastoma, malignant melanoma, choriocarcinoma, and bladder cancer account for approximately 40% of the cases, with only 6 cases of spontaneous disappearance of thyroid cancer. In the present case, the hyalinized image – shown in Fig. 3c – may reveal the spontaneous disappearance of the micropapillary thyroid carcinoma.

The World Health Organization (WHO) pathological classification published in 1989 defined papillary thyroid carcinomas ≤ 1 cm as papillary thyroid microcarcinomas [11]. Moreover, Sugitani and Fujimoto [12] defined papillary thyroid carcinomas ≤ 1 cm that do not cause metastatic lesions or symptoms as asymptomatic papillary thyroid microcarcinomas, and papillary thyroid carcinomas ≤ 1 cm that cause metastatic lesions or symptoms as symptomatic papillary thyroid microcarcinomas. The present case was diagnosed as a symptomatic papillary thyroid microcarcinoma metastasizing to the superior internal jugular lymph nodes. Currently, active surveillance without surgery is recommended for asymptomatic papillary thyroid microcarcinomas owing to the highly favorable prognosis [13]. In contrast, the prognosis of symptomatic papillary thyroid microcarcinomas that cause metastasis or invasion can be poor [4].

In the study by Sugitani et al. [4], all 57 patients with symptomatic papillary thyroid microcarcinomas who underwent thyroid surgery between 1976 and 2006 had metastatic

lymph nodes ≥ 1 cm. Of the 57 patients, 8 had recurrent nerve paralysis caused by primary thyroid tumors or metastatic lymph nodes and 1 had distant metastasis. Among 56 patients, excluding the 1 patient with distant metastasis, 21 (38%) had recurrence and 8 (14%) died of primary disease. In particular, extracapsular invasion of the thyroid tumors, extranodal invasion of the metastatic lymph nodes, metastatic lymph nodes ≥ 20 mm, and tumors with anaplastic components were poor prognostic factors. The 10-year disease-specific mortality rate for patients who had any of those poor prognostic factors was 74%. In fact, there was no death owing to primary disease in any patient without these poor prognostic factors. Ito et al. [2] also reported poor prognosis in cases of metastatic lymph nodes with extranodal invasion.

In the current patient, the diameter of the metastatic lymph node was >30 mm, which is classified as a high-risk group of papillary thyroid carcinoma per the guidelines for the treatment of papillary thyroid carcinomas [14]. In addition, the metastatic lymph node, which is a lymph node ≥ 20 mm with extranodal invasion, is classified into a poor-prognosis group of symptomatic papillary thyroid microcarcinoma [4]. As the tumor was classified into a high-risk group of papillary thyroid carcinoma and a poor-prognosis group of symptomatic papillary thyroid microcarcinoma, we performed ablation with 30 mCi iodine-131 after surgery to prevent recurrence and metastasis. Accordingly, there was no recurrence or metastasis for 24 months after treatment. Nevertheless, careful follow-up is required to monitor the possibility of recurrence or metastasis as the present case was classified into a poor-prognosis group.

In conclusion, we report a case of occult thyroid carcinoma that required differentiation from ectopic papillary thyroid carcinoma, wherein neither ultrasonography nor pathological examination revealed a papillary carcinoma in the thyroid. Therefore, a pathological evaluation of the surgical specimen was required for making a definitive diagnosis. The prognosis of patients with asymptomatic papillary thyroid microcarcinomas is favorable, whereas the prognosis of those with symptomatic papillary thyroid microcarcinomas, as observed in the present case, is poor. Thus, as the tumor was classified into a poor-prognosis group, treatment that focused on avoiding recurrence and metastasis, such as total thyroidectomy and ablation, was required.

Statement of Ethics

This case study was conducted ethically in accordance with the World Medical Association's Declaration of Helsinki, and we obtained written informed consent from the patient to report this case.

Disclosure Statement

We have no potential conflicts of interest or financial relationships to disclose.

Funding Sources

We received no financial support for this study.

Author Contributions

Gai Yamashita drafted the manuscript. Takahito Kondo designed the study and revised the manuscript. Akira Okimura, Munehide Nakatsugawa, and Hiroshi Hirano performed the pathological analysis. Atsuo Takeda, Naiue Kikawada, Yusuke Aihara, and Yuujin Chiba treated the patient. Yasuo Ogawa and Kiyooki Tsukahara supervised the study.

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