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Case Report

Papillary Thyroid Cancer Presenting with Incidental Skin Lesion: Critical Management of Distant Metastasis

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Abstract

Papillary thyroid cancer can usually metastasize to neck lymph nodes. Distant metastases are generally seen as solid organ metastases, in contrast, skin metastasis can rarely be seen. We present a case with papillary thyroid cancer diagnosed with skin metastasis as first clinical sign of distant organ metastasis.

A 63-year-old male patient admitted with a skin lesion in the left lateral neck. He had undergone subtotal thyroidectomy 14 years ago without relevant history of malignancy. Follicular variant papillary thyroid cancer was detected in the excisional biopsy performed from the cutaneous lesion. A 12 × 10 × 8 mm hyperechoic nodule in the left lobe was detected in USG and evaluated as Bethesta-III in fine needle aspiration biopsy. Bilateral multiple lung metastases were detected on thorax CT, trucut-biopsied from largest nodule and confirmed as metastasis. Carcinoma was not detected in total thyroidectomy, and post-operative multiple RAI therapies were applied.

Patients without history of thyroid cancer rarely present with skin metastases and thyroid cancer should not be overlooked in differential diagnosis. Despite meticulous evaluation of the thyroidectomy specimen, tumor may not be detected in the gland. Skin metastasis in papillary thyroid cancer should be evaluated as distant metastasis and investigations for other metastases should be done, and the treatment should be planned in a multidisciplinary manner.

Keywords: Endocrine malignancy, papillary thyroid carcinoma, skin metastasis

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Thyroid carcinoma is the most common endocrine malignancy. Although rare, distant metastasis may develop in 20% of the patients during long-term follow-up. The spread of metastasis is through lymphatics, usually to the lymph nodes in the neck. The most common site of visseral metastasis is the lung, followed by bone, liver, and brain. [1] However, it is a rare condition to be diagnosed with skin metastasis without a previous diagnosis of thyroid cancer. [2] There may even be skin metastasis defined without any identified primary tumor in thyroid gland.[3] Skin metastases are only reported in 43 cases between 1964 and 1996, with an incidence rate below 0.1%, and the most common pathology was papillary carcinoma (41%), followed by follicular carcinoma (28%), anaplastic carcinoma (15%), and medullary carcinoma (15%).[4] In this study, we presented a case with distant skin metastasis without primary tumor detected in thyroid gland.

Case Report

A 63-year-old man referred to the plastic surgeon after noticing a lesion on the left side of his neck which was gradually enlarged in 5 months.

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There was neither relevant family history nor history of radiotherapy. He had subtotal thyroidectomy 14 years ago because of multinodullary goiter. The pre-operative fine needle aspiration biopsy (FNAB) from 3 cm nodule in the left lobe was benign before that operation, and malignancy was not detected in the histopathological examination postoperatively. Eventually, the patient was clinically euthyroid without any hormone therapy taken.

In the hospital, the patient was admitted, an excisional biopsy was taken from the skin lesion including the subcutaneous tissue, from which the diagnosis of papillary thyroid cancer metastasis was made. The specimens were once more consulted to experienced pathologists in our hospital. The histopathological sections consisted of eosinophilic atypical cells with large, pleomorphic, vesicular, and irregular shaped nuclei and the immunohistochemical examination was positive for CK7, CK19, thyroid transcription factor-1 (TTF-1), thyroglobulin, Galektin-3, HBME-1, and E-cadherin. CK-19, HBME-1, and Galectin-3 immunoreactivity in neoplastic cells were concordant with the metastasis of the follicular variant of thyroid papillary carcinoma (Fig. 1).

The ultrasound disclosed a predominant cystic nodule with a solid component of 15 × 13 × 9 mm in the right lobe and a hyperechoic solid nodule of 12 × 10 × 8 mm surrounded by a peripheral thin hypoechoic rim in the left lobe. There was no pathological lymph node in the neck. The biopsy to the nodule on the left thyroid lobe resulted as AUS/FLUS (Bethesda III). Since a cutaneous metastasis was found, thorax computed tomography (CT) was planned, and multiple metastases were detected in lungs, the biggest at right inferior lobe (25 mm). These nodules showed increased fluorodeoxyglucose uptake (SUVmax: 9.3) in positron emission tomography-CT. Trucut biopsy of biggest nodule in lung was pathologically coherent with papillary carcinoma metastasis.

The case was preopereatively discussed in multidisciplinary endocrine council and the management of therapy was planned.

Total thyroidectomy was done without prophylactic central dissection, since clinically suspicious enlarged lymph nodes were not detected in physical examination, as well as in ultrasonographic examination and intraoperatively (Figs. 2 and 3). 3 µm sections were prepared from 3 mm serial tissue blocks of thyroid specimen and stained with hematoxylin and eosin. The pathological examination was benign adenomatous hyperplasia without evidence of cancer. Paient's consent was taken for using clinical data for further studies. Two months postoperatively, 200 mCI I-131 RAI was applied. During the follow-up with CT, lung metastases was shown to be persisting, and two more 200 mCI I-131 RAI therapy were given consecutively. After the

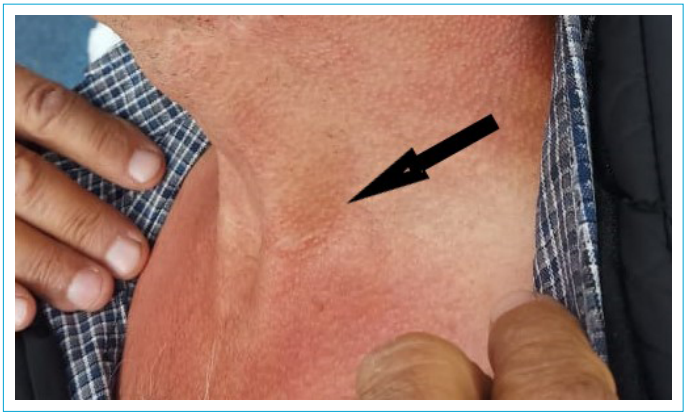

Figure 2. The photograph of the incision and the neck after the last operation – lateral view.

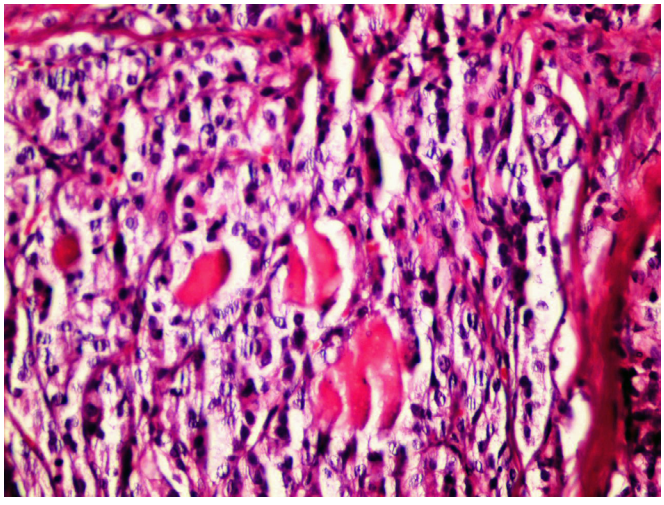

Figure 1. Microscopic view of skin metastasis of papillary thyroid cancer oncocytic variant (H&E ×40).

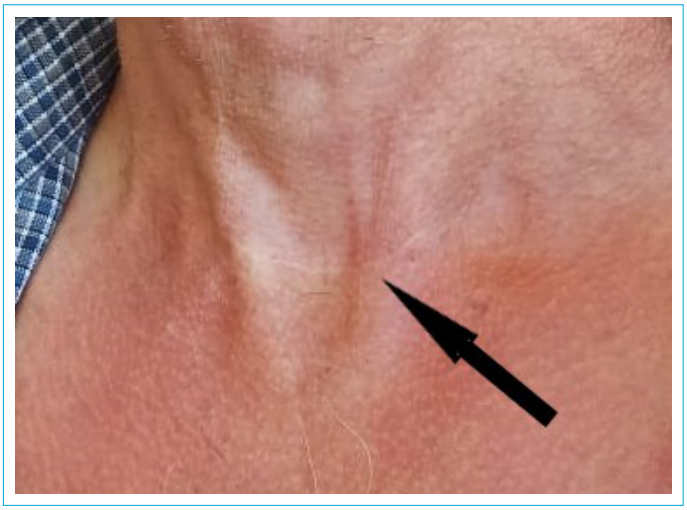

Figure 3. The photograph of the incision and the neck after the last operation – front view.

third therapy, the scintigraphy showed active lung lesions, mostly in the right inferior posterobasal segment. He was discharged with active surveillance.

Discussion

Papillary thyroid cancer is the most common cancer of thyroid gland and tends to metastasize to regional lymph nodes instead of distant metastasis. Skin metastasis of papillary thyroid carcinoma is an extraordinary manifestation, and almost all skin metastases of papillary cancer were reported in head-and-neck areas.[5] Even though it is unusual and rare to diagnose papillary thyroid cancer with skin metastases, the skin metastasis may be the first presentation site of cancer.[6]

Lissak et al. reported that in two cases presenting with solitary skin metastasis without any lesions detected by preoperative thyroid US, thyroid cancer foci below 1 cm could be detected in the examination of the whole thyroid gland postoperatively.[1] The authors reported that preoperative US may not recognize a tumor if the thyroid gland is in micronodular formation, and the thyroid gland removed by operation needs to be examined in consecutive sections. Although pre-operative US can detect small thyroid lesions as small as 2 mm and have an important role in differentiating between malignant and benign lesions, small tumors may often be overlooked.[7] Occasionally, the primary tumor in thyroid may not be detected in the pathological examination of occult papillary thyroid carcinoma presented with pre-operative neck lymph node metastasis or distant organs.[8]

Its mechanism may be explained by a few hypotheses. The first hypothesis is that the primary microscopic tumor within the thyroid may be overlooked. The other possibility is spontaneous tumor regression.[3] In our case, standard histopathological examination was performed after the previous surgery of subtotal thyroidectomy, and the primary tumor might be overlooked at this stage. After the second thyroidectomy, the small microscopic tumor might still have been overlooked, although the whole specimen was routinely examined histologically. Histological sections of 3 μm thickness were prepared from typical 3 mm thick tissue blocks as in the previous cases in which all thyroid were examined.[3] In fact, only 0.1% of the tissue was prepared for hematoxylin eosin and examined microscopically. Although all thyroid tissue is examined, routine histopathological examination may not detect microcarcinomas smaller than 3 mm in diameter.[3] However, papillary microcarcinomas smaller than 3 mm also have the potential to develop metastasis.[9]

Spontaneous tumor regression or diminution is defined as spontaneous regression of malignant neoplasm as a result of the host response, a common phenomenon affecting 10–35% of cutaneous melanomas. The histological feature of melanoma regression is fibrosis, often associated with lymphocytes and macrophages.[10] Fibrous foci were also detected in metastatic cases where no primary tumor was detected in the thyroid. This may be related to tumor regression.[3]

This is the first case presenting with cutaneous and lung metastases without primary focus in thyroid. This patient underwent the left subtotal thyroidectomy 14 years ago. There was no malignancy in the post-operative histopathological examination of the thyroid and no additional treatment was performed. After the second thyroidectomy, although all thyroid series were examined by serial sections, no primary malignant focus was detected in the thyroid and not any fibrous foci within the thyroid was detected. It also comes to mind that the patient might have a missed microscopic papillary thyroid cancer diagnosis in the pathological examination of the former thyroidectomy.

In the literature, it is reported that patients with skin metastases usually present 2–20 years after papillary thyroid cancer diagnosis.[11] Even though both the disease free survival and overall survival rates of papillary thyroid cancer are high, the average survival period is really low in PTC with skin metastases which is thought to be a disseminated disease regardless considering the metastases through adjacent tissues as in our case. In case series reported, the average survival of patients with cutaneous metastases is 19 months after the first diagnosis in five lethal cases.[1]

The majority of thyroid cancer metastases to the skin tends to localize in the head-and-neck area and may be related with rich dermal capillary network capturing the tumor cells and forming a metastatic lesion though circulation. Since the skin metastasis develops through the capillary beds, it usually occurs in the scalp. Scalp metastases of thyroid carcinoma are derived from the circulating malignant cells along external carotid artery. The tumor cells may also be transmitted through vertebral venous system leading to distant organ metastases.[12]

However, still, unlikely from our case, skin metastasis after FNA biopsy and thyroidectomies gave rise to discussion on two more hypotheses for possible skin metastasis mechanisms. These mechanisms for skin metastasis are explained by the contamination during surgery after the eruption of thyroid nodules and implantation after FNAB.[12,13]

The morphology of the cutaneous metastases may be variable to the limits of mimicking other lesions such as infections or alopecia. The initial presentation of the metastatic disease of papillary thyroid cancer can be lesions in thy-

roidectomy scar, scalp, and nodules in the neck. Definitive identification of metastatic nodules of thyroid carcinoma in different sites of the body requires a biopsy with immunohistochemistry stainings. Microscopic evaluation expresses TTF-1 (a DNA-binding nuclear protein expressed in the follicular cells of thyroid and present in 93% of tumor cells) and thyroglobulin (a glycoprotein expressed from the follicular thyroid epithelial cells and found in 5% of papillary thyroid cancers).[14] Furthermore, the expression of cytokeratin-7 (a Type II keratin found in follicular cells) and paired box gene-8 (a nephric-lineage transcription factor for the organogenesis of thyroid, kidneys, and the Mullerian system) is not rare.[15]

In cases diagnosed with skin lesion, locoregional imaging methods for thyroid, and neck in addition, should be performed, definitely followed by other distant metastasis screenings, and the treatment should be decided according to the extent of the disease.

Conclusion

Although skin metastasis is very rare in patients without a history of thyroid cancer, the possibility of thyroid cancer metastasis should not be ignored in the differential diagnosis of metastatic skin lesions. If defined, the specimen of thyroid gland should be carefully examined by the pathologist to exclude micropapillary thyroid cancer. Skin metastasis of thyroid gland defines the disseminated disease, and the treatment algorithm should be managed in multidisciplinary approach.

Disclosures

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