Skin Metastasis as the Initial Manifestation of Poorly Differentiated Thyroid Carcinoma

Dear Editor,

Poorly differentiated thyroid carcinoma (PDTC) is a rare and clinically aggressive thyroid cancer of follicular cell origin. This thyroid tumor can also arise from Hürthle cell or papillary thyroid carcinoma (1). PDTC accounts for 4-7% of all thyroid cancers and it is twice as common in men of a mean age of 55.7 years (1,2). According to the World Health Organization (WHO) definition, PDTC has 2 histomorphologic subtypes: insular and noninsular (1). However, based on clinical features, PDTC has a morphologically and behaviorally intermediate position between well differentiated (follicular and papillary) and undifferentiated (anaplastic) thyroid carcinoma (3,4). Notably, PDTC often presents in an advanced stage and has a propensity for local recurrence, tending to metastasize to regional lymph nodes, the lungs, and bone (1). Accordingly, this thyroid tumor has a rapid and fatal outcome despite appropriate treatment (3).

Skin metastases are a rare phenomenon in PDTC, representing 0.7-2.0% of all cutaneous malignant neoplasms (5). Skin metastasis from thyroid carcinoma is rare and occasionally represents the initial manifestation of an occult thyroid carcinoma (5,6). To the best of our knowledge, only a few cases of cutaneous metastasis from PDTC have been reported in the English-language literature until 2012. Herein, we report on an additional case of PDTC with metastasis to the skin as a presenting sign of thyroid cancer.

A 78-year-old man presented with multiple skin nodules on the scalp, forehead, and chin. The patient presented with a progressive mass on the right side of the thyroid lobe that had developed 3 months previously. The patient had a history of odinophagia, weight loss, and decreased appetite. He had been a smoker for 40 years, but had no familial history of thyroid disease or exposure to radiation. On examination, multiple erythematous and tender nodules were found on the scalp, forehead, and chin (Figure 1). Thyroid examination revealed both sides of the thyroid gland were enlarged, as well as fixed and firm nodules in the right thyroid lobe without any evidence of thyrotoxicosis or hypothyroidism. Additionally, there was a palpable cervical lymphadenopathy on the right side. Routine hematological and biochemical thyroid hormones profile tests were within normal ranges. X-ray of the chest showed multiple foci of calcification on both lungs, but skull X-ray, abdomen ultrasonography, and brain computered tomography (CT) were normal.

A thyroid scan revealed a cold nodule in the right lobe of the thyroid gland. A fine needle aspiration of the thyroid nodule was performed, and stained with Papanicolaou stain. Cytology smears revealed a mainly bloody background with few atypical cells indicating a neoplastic process. One of the scalp lesions was excised due to the clinical diagnosis of metastatic skin tumor and adenexal tumor, and submitted for histopathological examination. Histology of the lesion showed normal epidermis with presence of grenz zone between tumoral cells (Figure 2), as well as neoplastic cells arranged in nests within the delicate vascular stroma with minimal nuclear pleomorphic and small, but distinct nucleoli and clear cytoplasms. Additionally, solid nests, trabeculae, and a cribriform arrangement of cells with micro follicle formation and a wide area of necrosis were seen. These findings were consistent with poorly differentiated carcinoma (insular carcinoma). On the other hand, immunohistochemical tests were positive for thyroid transcription factor 1 (TTF-1) and thyroglobulin staining.

Although the surgery was a difficult task because of the extensive thyroid metastases of tumor cells, a right-sided thyroid lobectomy and modified radical neck dissection was performed. The patient was dis-

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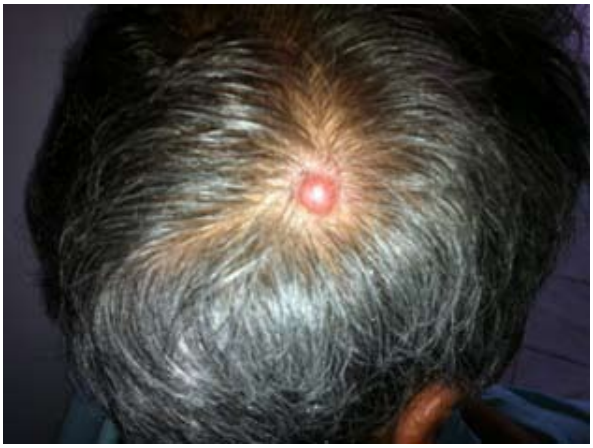

Figure 1. Erythematous nodular skin lesion on the scalp skin, completely raised.

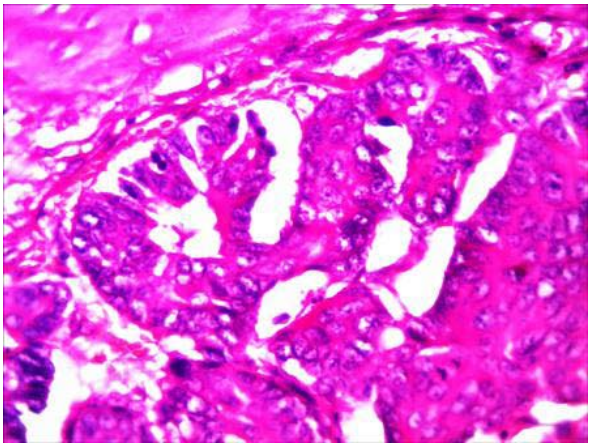

Figure 2. Metastatic poorly differentiated thyroid carcinoma; epidermis is intact with presence of a grenz zone between tumoral cells and the epidermis H&E; x 400

charged from the hospital and referred to the oncology department for palliative treatment. Follow-up was continued for 4 months after the primary diagnosis of skin metastases, but he died due to the widespread metastases of tumor cells**.**

Thyroid carcinoma metastases to the skin are a rare clinical entity, particularly as a presenting feature of underlying malignancy (5,6). In a recent study that included 3848 patients with metastatic carcinoma, no thyroid neoplasms were observed (7). Dahl *et al.* reviewed English-language literature since 1964 onwards and found 43 cases of thyroid carcinoma with cutaneous metastases among the 39 patients for whom histological findings of the tumor were reported (7). Papillary neoplasm was most common (41%), followed by follicular (28%), anaplastic (15%), and medullary carcinoma (15%). In that study, thyroid cancer was diagnosed before cutaneous metastasis in most cases, with a single case where cutaneous metastasis preceded the diagnosis of the primary thyroid cancer (7).

Thyroid metastatic skin lesions are typically present as slowly growing erythematous or purple nodules that are tender, may be itchy, and can ulcerate (6,8). Studies have shown that the scalp is the most common site, being involved in approximately two thirds of thyroid carcinoma cases (8,9).

Immonoperoxidase methods have been used to demonstrate that thyroglobulin, a 670 kd glycoprotein synthesized in the cytoplasm of follicular thyroid epithelial cells, is present in normal thyroid glands, goiters, thyroiditis, and some thyroid carcinomas. Thyroglobulin is detectable in all cases of follicular carcinoma and 95% of papillary carcinoma but is absent in anaplastic thyroid carcinoma (7).

Thyroid transcription factor-1 (TTF–1) is a nuclear protein expressed in follicular cells of the thyroid gland and also in lung and brain cells. This factor is a good marker of thyroid differentiation and detection of origin in metastatic carcinomas (1). The sensitivity for thyroglobulin and TTF–1 alone for thyroid tumor is 90.5% and 92.9%, respectively, and combined monitoring of the two increases the sensitivity for detection of thyroid carcinoma (10). Survival after the diagnosis of PDTC shows a poor outcome. The mean 5-year survival of affected patients is 71.6% and the 10- year survival rate is 46.3% (4). In our patient, skin metastases stained positive for TTF–1 and thyroglobulin. The tumor was aggressive and led to death 4 months after the initial diagnosis and treatment.

In conclusion, we report on one more case of PDTC in an old man with multiple skin metastases.

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