CASE REPORT

Metastatic Cervical Carcinoma to the Thyroid Gland: A Case Report and Review of the Literature

Elena Karapanagiotou, Muhammad Wasif Saif, Dimitra Rondoyianni, Sofia Markaki, Maria Kiagia, Kosmas Pantazopoulos, Ifigenia Tzannou, Kostas Syrigos

*A Oncology Unit, Third Department of Medicine, Athens School of Medicine, Sotiria General Hospital, Athens, Greece; †Yale Cancer Center, Yale University School of Medicine, New Haven, Connecticut; ‡Department of Pathology, Evangelismos General Hospital, Athens, Greece; §Department of Pathology, Alexandra General Hospital, Athens, Greece

Although metastases within the thyroid gland are rare, they are not as infrequent as generally believed. Asymptomatic breast, lung, and renal cell carcinomas may metastasize to the thyroid. When they become symptomatic, diagnosis relies upon fine needle aspiration cytology. We report the case of a squamous cell cervical cancer that presented metastatic lesions to the thyroid gland four years after the initial diagnosis. The procedures used to confirm the diagnosis, stage, and subsequently manage the patient are described. We present both a review of the necessary clinical investigation and the therapeutic options open to these patients. We conclude that patients who present swelling or palpable nodules in the thyroid side and have a history of a previous malignancy must be considered for metastatic disease.

INTRODUCTION

Metastases to the thyroid gland have been described as early as the 1930s [1]. Since then, several reports have demonstrated a discrepancy in the incidence, depending on the perseverance with which the thyroid nodules were investigated. In general, it is estimated that only 1.1 percent of all clinically detectable thyroid cancers are of metastatic origin [2]. Nevertheless, a single post-mortem study suggests that secondary tumors in the thyroid gland might be up to 10 times as common as primary thyroid cancer [3]. Other autopsy studies describe thyroid metastatic lesions in as many as 24 percent of patients with disseminated disease; although in most cases, there is no evidence of clinical manifestations from thyroid infiltration [4]. With regard to the origin of the metastatic thyroid lesions, the most common primary sites are cancers of the kidney, breast, lung, and gastrointestinal system, and melanoma. The mean interval from the diagnosis of the primary tumor to the development of the thy-
roid metastasis is 14 months, the range varying according to the histological type [5]. We present the case of a patient with cervical carcinoma who developed thyroid metastases four years after the curative treatment of the primary tumor.

CASE REPORT

A 68-year-old woman was admitted to our department after complaining of a persistent cough over the course of a week, hemoptysis, and a temperature that would peak at 37.8°C (100°F) over the last two months. She had noticed a painless swelling in the region of the thyroid gland and a palpable mass in the right side of her neck. Four years ago, the patient had been diagnosed with squamous cell carcinoma of the cervix stage IIIB, moderately differentiated, for which she had received external beam radiotherapy to the pelvis and brachytherapy. Upon physical examination, an irregular, hard-fixed mass measuring 8.6 cm was felt in the right lateral region of the neck, along with a firm thyroid enlargement. Chest auscultation revealed altered breath sounds in the left lung, with rales and rhonchi. Her blood cell count and serum biochemistry were normal, and the rate of sedimentation was 65 mm the first hour. The patient underwent a CT scan of the neck, thorax, abdomen, and pelvis that revealed a large irregular mass 9 cm in diameter in the right lateral region of the neck, enlargement of the thyroid gland, enlarged mediastinal and paraaortic nodes, and multiple patchy airspace infiltrates, without evidence of local recurrence. A bone scan was negative for metastases. Fiberoptic bronchoscopy revealed edematous and erythematous mucosa of the upper bronchus of the right lower lobe and erythematous edematous mucosa with probable subserosa infiltration of the lingual bronchus. Sputum cytology after bronchoscopy washing and brushing was positive for undifferentiated carcinoma. Since the cytology report could not establish a definite diagnosis, a biopsy of the thyroid gland was performed, which showed non-keratinizing squamous cell carcinoma compatible with primary squamous cell carcinoma of the cervix. The pathologist also reviewed slides of the cervical biopsy from four years previous and confirmed that the thyroid tumor was histologically identical to the initially documented cervical carcinoma.

The patient received six cycles of systematic chemotherapy with cisplatin and gemcitabine, with partial response. Subsequently, she received radiation therapy to the right side of the neck and the thyroid, with further decrease of the lymph nodes and thyroid mass. Five months after the completion of radiotherapy, the patient developed progressive disease and succumbed four months later. The overall survival after diagnosis of the thyroid metastasis was 16 months.

DISCUSSION

Metastases to the thyroid may occur with high frequency in patients with widespread metastatic lesions. When the thyroid lesions become symptomatic, patients usually present with thyroid enlargement and palpable nodules, cough, hoarseness, dysphagia, and dyspnea. Thyroid implication to other solid malignancies may arise either by direct spread from adjacent tissues or by lymphatic and hematogenous spread, which is not surprising, considering the thyroid gland is one of body’s most abundantly arterialized organs [6].

Up to 70 percent of patients with cervical cancer who present nodal metastases and/or locally advanced disease will relapse. Cervical cancer gives distant metastases via the lymphatic spread, from the satellite nodes to the paraaortic and supraclavicular nodes. The route of the hematogenous spread is presumed to occur via the blood stream to the caval venous system through the lung parenchyma and systematic circulation. In patients who develop distant metastases, the most frequently observed metastatic sites are the lung (21 percent), the para-aortic lymph nodes (11 percent), the abdominal cavity (8 percent), and the supraclavicular lymph nodes (7 percent). Bone metastases occur in only 16 percent of pa-
tients. Metastatic carcinoma of the thyroid gland from cancer of the cervix is very rare. Upon reviewing the English literature, only five cases of cervical carcinoma are described as having metastasized to the thyroid gland [7-11].

The involvement of the thyroid gland usually becomes apparent some years after the diagnosis of the primary malignancy and is a feature of tumor dissemination, which is indicative of a poor prognosis. In the context of widespread metastatic disease, the clinical manifestation of thyroid lesions is usually of no importance. In fact, surgical statistics reveal that lesions of metastatic origin represent only 8.5 percent of all removed malignant neoplasms. It is unknown whether secondary tumors of the thyroid are more common in an already abnormal thyroid gland. Two studies have been performed with contradictory results as one group of researchers maintains that thyroid metastases are associated with underlying thyroid abnormalities, while the other failed to establish such a correlation [12,13].

Explaining the nature of thyroid nodules (whether malignant or benign) can become a difficult diagnostic task, especially if they occur many years after the initial tumor. A differential diagnosis must be made of multinodular goiter and benign thyroid nodules. If the malignant phenotype is confirmed, it must be clarified as to whether it is a primary or secondary neoplastic lesion. Since both entities have the same clinical signs and symptoms (if any), diagnosis relies upon fine needle aspiration cytology (FNAC), a simple, inexpensive, and safe procedure with high negative diagnostic value. In most cases, confirming the cytological origin of the neoplastic cells can be based on morphology and immunocytochemical staining; negative staining with anti-thyroglobulin and anti-calcitonin antibodies would exclude the thyroid as primary origin of the neoplastic cells. On the contrary, thyroid follicular neoplasms tend to maintain some cytoplasmic granularity and, as a result, usually stain positively for thyroglobulin. In the pathology examination, the presence of multiple deposits within the thyroid gland makes the diagnosis of a metastatic tumor more probable. Furthermore, a predominantly interstitial pattern of penetration, with deformation and dissemination of the follicles by the neoplastic cells, is more compatible with metastatic origin of the carcinogenic cells. On the contrary, primary thyroid neoplasms usually infiltrate the follicles. Despite all the above techniques, occasionally it may be difficult to determine from cytology whether the neoplastic cells originate from the thyroid gland, especially in cases of anaplastic carcinoma or the unusual clear cell variant of follicular carcinoma. In any case, diagnostic re-evaluation of the primary tumor and search for other metastatic sites are mandatory to establish metastatic derivation of thyroid nodules [14,15].

The management of patients with metastatic thyroid lesions is determined by the primary tumor type, the presence of other metastatic sites, the patient’s symptoms and the patient’s performance status. Aggressive surgical treatment of an isolated thyroid metastasis, which is most often from renal cell carcinoma, could be curative. The regional application of radiotherapy in symptomatic patients may achieve sufficient improvement of the quality of life and constitutes an acceptable alternative approach. Finally, the location of other metastatic sites will determine the manner of systemic management. Since the presence of metastases in the thyroid gland is indicative of disseminated disease, the prognosis of these patients is poor, regardless of the primary tumor site and therapeutic approaches. The time between presentation of thyroid metastasis and death ranged from three to 45 months in one study of 79 patients [16].

In conclusion, patients who present unilateral swelling or palpable nodules in the thyroid and have a history of a previous malignancy must be considered for metastatic disease, despite the fact that in most cases thyroid lesions are occult and do not pose a clinical problem. FNAC provides a quick, easy, and reliable way of diagnosis, while biopsy of the lesion and histopathological examination is the most appropriate tool for
the final diagnosis. Although detection of metastases to the thyroid gland is often indicative of a poor prognosis, aggressive medical treatment such as radiotherapy and systemic chemotherapy may be effective in offering a better quality of life.

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