Maxillary Metastasis of a Medullary Thyroid Carcinoma in a 21-year-old Woman 7 years After Thyroidectomy

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Metastasis of the oral cavity is a rare phenomenon and represents approximately 1% of all oral malignant tumors.† Tumor metastasis to the jaw most often involves the posterior mandible. Metastases to oral soft tissue sites represent less than 0.1% of oral tumors.2,5 As noted by Zachariades, the mandible is the site of involvement in 58.5% of metastatic tumors to the oral cavity and jaws, and the involvement rate for maxilla, oral soft tissues, and the major salivary glands is 11%, 25.8%, and 4.7%, respectively.4 The maximal incidence for metastatic tumors of head and neck occurs in the seventh decade ranging between 55.2 and 64.5 years with a mean age of 60 years.3,5 The incidence of oral metastases is higher in males compared with females (1.9 ratio).5 The most common symptoms associated with metastases to the jaws are pain, paresthesia, tooth mobility, and gingival enlargement. Metastases to oral cavity soft tissue are extremely rare.2 The primary sites for metastasis to the jaws and oral soft tissues are malignancies of the lung, breast, prostate, gastrointestinal tract, kidney, and liver.2,3 The prognosis of patients with metastasis to the oral cavity is poor with a median survival of approximately 6 months.3

Thyroid gland carcinoma is more common among females with a female-to-male ratio of 8:3.6 Thyroid gland carcinoma in people younger than 18 years is rare and the 10-year survival rate for these patients is about 40%.7 Three main histological types of thyroid cancer have been described: differentiated, medullary, and anaplastic. Medullary carcinoma is the term used to describe the type of thyroid gland malignancy composed of parafollicular cells.1 The frequency of medullary carcinoma is less than the differentiated forms and it has a tendency to act aggressively.1,8

We report an unusual case of medullary thyroid carcinoma (MTC) metastatic to the anterior maxilla 7 years after a thyroidectomy in a 21-year-old woman.

Case Report

A healthy, 1-month postpartum 21-year-old woman complained of an expansile, painless swelling in the anterior left maxilla, which had progressed in size over the last 2 months. The patient also complained of back pain, sweating, chills, dysphagia, and loss of appetite during the preceding 2 weeks. She had undergone vaginal delivery 3 weeks previously. Her past medical history was significant for thyroidectomy 7 years before at age 15, for what she
thought was a goiter. Levothyroxine was subsequently prescribed, although the patient took the medication only for a short time.

Facial examination showed that the mass extended from midline of the maxilla to the left periorbital region. The oral swelling had caused disappearance of the left nasolabial fold due to fullness of the buccal vestibule and slight deviation of left nostril. Diminished sensation of the left upper part of her nose, lip, and nasofrontal area was present (Fig 1).

Intraoral examination noted a tender swelling of the left palate and mucobuccal fold with a variable consistency ranging from hard and firm to rubbery. The mass appeared darker in color than that of normal oral mucous membrane (Fig 2A). The left maxillary second and third teeth (teeth number 10 and 11 according to the universal system) had migrated and showed grade 2 mobility, with no evidence of caries (Fig 2B).

The neck showed a scar from prior thyroid surgery. There was no cervical lymphadenopathy.

A panoramic radiograph showed a relatively well-defined mixed radiolucency of $2 \times 3 \text{ cm}$. No evidence of dental caries, retained roots, or sinus involvement was observed. A poorly defined outline was seen around the upper left second and third teeth (Fig 3A). On computed tomographic scan assessment, a destructive mass in the left maxillary alveolar process was seen that projected into the subcutaneous and cutaneous tissue. Neighboring teeth were displaced by the mass. The paranasal sinuses were otherwise normal (Fig 3B).

In addition to benign and malignant neoplasms, the differential diagnosis included an aggressive central giant cell granuloma, due to color and invasiveness of the lesion and displacement of the teeth and pyogenic granuloma, due to her pregnancy within the last month. An incisional biopsy was performed.

The histopathology consisted of hypercellular small packets of short spindle cells in an amyloid vascular background. The pathology report was “undifferentiated carcinoma with left maxillary bone invasion.”

Immunohistochemistry analysis showed positive results for pan-cytokeratin, calcitonin, and TTF-1, all as ready-to-use reagents from NovoCastra (Leica Microsystems, Germany). However, the test was negative for thyroglobulin at concentration 1:100 (Dako Cytomation, Denmark) in tumor cells. The overall findings were diagnostic for metastatic medullary carcinoma of thyroid gland (Fig 4).

Further information obtained regarding her prior thyroidectomy informed us that she had been diagnosed with...
medullary carcinoma of the thyroid. She had no family history of thyroid disorders. She had undergone “central nodal dissection, total thyroidectomy” surgery and had levothyroxine administration for 1 year. She had been under the impression that an esthetic procedure had been performed for a goiter.

Based on previous and recent pathology reports and also consultation with an oncologist, a diagnosis of “metastatic medullary thyroid carcinoma to left maxillary gingiva with bone destruction” was confirmed. The patient was referred to an oncologist for chemotherapy, but was lost to follow-up.

**Discussion**

Metastases to oral cavity are uncommon, but should not be overlooked by clinicians. In about 20% of cases, the oral metastasis is the first clinical sign of the malignancy. Metastatic tumors to the jaws originate from distant body sites, excluding lesions that are the result of direct extension from neighboring sites or those due to local recurrence. There are diverse routes of metastasis to the jaws, including lymphatic, hematogenous, and, rarely, iatrogenic reasons. The hematogenous route is considered the most common mode for metastasis to jaw bones. The real incidence for tumor metastasis to jaw bones is unknown. This is due to the fact prior to positron-emission tomography scanning, the jaws are not routinely involved in the radiographic metastatic search nor in autopsies. It has been postulated that the incidence of jaw bone involvement to be less than other bones because the red marrow and blood vessels in the jaws tend to decrease with age. Based on several reports by different authors, approximately 1% of oral malignancies are of metastatic origin. Metastases to the oral soft tissues are much rarer, representing less than 0.1% of oral tumors. Common sources of metastases indicate a gender-associated variation. Breast, ovaries, and thyroid are considered as common sources in females, while lungs, prostate, kidney, and liver are more prevalent in males.

Evidence for the presence of tumors may be pain, swelling, mobility of tooth, delay in healing of extraction socket, and pathological fractures or paresthesia. In the present case, swelling, migration, and...
mobility of teeth and paresthesia of relatively large area were seen. Metastatic tumors arising in or otherwise involving the oral soft tissues may frequently be confused with pyogenic granuloma, peripheral giant granuloma, peripheral fibroma, and periodontal abscesses,\textsuperscript{1,2} as these lesions are rarely ulcerated. Because the patient had recently been pregnant, 1 of the considerations for differential diagnosis was pyogenic granuloma. Radiographic findings in metastatic tumors to the jaw structure may range from the absence of any manifestation to a lytic or opaque lesion with ill-defined margins.\textsuperscript{2,9} In our case, the radiolucency was more well-defined.

There are 3 histologic categories of thyroid cancers: differentiated, medullary, and anaplastic. MTC has an intermediate prognosis between the relatively good prognosis of most differentiated forms and the dismal prognosis of anaplastic thyroid carcinoma. MTC can be sporadic or can occur as a hereditary form in up to 25\% of cases. The hereditary MTC syndromes, multiple endocrine neoplasia (MEN) type 2, affects approximately 1 in 30,000 individuals and consists of subcategories MEN 2A (Sipple’s syndrome), familial MTC, and MEN 2B.\textsuperscript{12} Hereditary forms can be diagnosed with a positive family history and/or other manifestation of MEN syndrome. Sporadic MTC, unlike hereditary forms, is usually diagnosed late with regional metastasis. That is because of the difficulty in diagnosis due to different morphologies.\textsuperscript{13}

Systemic chemotherapy has limited success rate in treatment of the metastatic MTC cases. There are some recommended chemotherapy regimens for the treatment of MTC, including cyclophosphamide, dacarbazine, and vincristine or dacarbazine, and fluorouracil or bleomycin, doxorubicin, and cisplatin, which have produced some partial responses.\textsuperscript{14}

New strategies to treat metastatic MTC cases are radioimmunotherapy and vaccine-based therapies. Compounds have been introduced that block kinases that are involved in the pathogenesis or progression of cancer. Recently, several kinase inhibitors have been under evaluation that may have important clinical advantages.\textsuperscript{15} However, it is important to consider the oral region as a metastatic source for thyroid gland malignancies.

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References