Secondary Lymphoma Involving Metastatic Follicular Thyroid Carcinoma to the Skull: A Unique Example of Tumor-to-Tumor Metastasis

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Abstract Tumor-to-tumor metastases to the skull, presenting as a scalp mass, and thyroid follicular carcinoma presenting in that location are extremely rare. We present the case of a patient with recently diagnosed retroperitoneal diffuse large B-cell lymphoma and an 8-year history of a non-tender large scalp-based mass. The scalp mass was an osteolytic enhancing lesion on imaging studies and diagnosed as metastatic thyroid carcinoma to the skull. The patient had no pre-existing history of thyroid cancer. This metastatic carcinoma was also secondarily involved with diffuse large B-cell lymphoma. This case illustrates a unique and previously unreported example of tumor-to-tumor metastasis in which both malignancies represent metastatic tumors to the skull with soft tissue extension presenting as a large scalp mass.

Keywords: Thyroid follicular carcinoma · Thyroid carcinoma · Skull metastasis · Non-Hodgkin’s lymphoma · Large cell lymphoma · Tumor-to-tumor metastasis

Introduction

There are over 30,000 new cases of thyroid cancer each year, representing approximately 2.5% of cancer diagnoses [1]. Although the overall prognosis of thyroid cancer is good, the presence of metastasis greatly increases risk of cancer-related death. The most common site of metastasis from thyroid cancer is lung, followed by bone [2]. Metastasis to the skull is rare and reported in 1.8–5.8% of cases in the literature [2–4]. Metastasis to the thyroid gland, including secondary involvement by lymphoma, is also rare. Although thyroid tumors have been known to be recipients of tumor-to-tumor metastases, less than ten cases have been reported in the literature [5]. We present a patient with an unusual presentation of tumor-to-tumor metastasis involving metastatic follicular carcinoma and metastatic large B-cell lymphoma. The patient had recently been diagnosed with diffuse large B-cell lymphoma in a retroperitoneal lymph node biopsy. The follicular carcinoma component was very well-differentiated, mimicked benign thyroid follicles and was discovered incidentally, without prior history of thyroid cancer, during work up of changing size of a scalp mass, apparently indolent for 8 years.

Case Presentation

The patient is a 55 year-old woman with a history of beta thalassemia trait who presented with 20-pound weight loss and abdominal pain along with nausea, vomiting, loss of appetite, and back pain. On physical examination, no abdominal tenderness or palpable masses were noted. She was also noted to have a lobulated, non-tender mass on her right parietal scalp that measured 15 × 15 × 12 cm reportedly present for approximately 8 years. The mass started out the size of an olive and was stable until 2 years ago, when it began to grow. She reported no pain associated with the scalp mass or any neurological symptoms.
An abdominal computed tomogram (CT) showed a 15 cm retroperitoneal mass and mesenteric lymphadenopathy. A subsequent head CT of the scalp mass showed a fairly homogeneously enhancing mass with destruction of the calvarium and intracranial extension with mass effect on the frontal and parietal lobes. Scattered spicules of radiating calcification and band-like nodular areas of non-enhancement were also noted within the mass. The mass had well-defined borders and a brain magnetic resonance image (MRI) showed the mass to be primarily extradural (Fig. 1a and b).

Her complete blood count was notable only for a mild anemia; other parameters were normal. The patient underwent a CT-guided biopsy of the abdominal mass, which showed diffuse large B-cell lymphoma. A biopsy of the scalp mass was also performed that showed diffuse large B-cell lymphoma intimately intermixed with normal appearing thyroid follicles (Fig. 2a and b).

Subsequently, a neck CT scan was performed and showed a large calcified thyroid nodule in the left lobe. Her serum thyroglobulin concentration was elevated to >10,000 μg/l (>10,000 ng/ml) and her serum thyroid stimulating hormone was within normal limits. A fine needle aspiration of the thyroid gland was diagnosed as a follicular lesion. A positron emission tomography (PET) scan showed moderately intense focal uptake in the left thyroid lobe. Total body I-131 radionuclide imaging showed increased radioiodine accumulation in the thyroid gland as well as the scalp mass. Radioiodine accumulation was also seen in a left neck lymph node. Although a focus of radioiodine accumulation was seen in the right pelvis, no significant ovarian pathology was noted on the pelvic CT and no uptake was seen on the PET scan in this region. The patient was started on chemotherapy and rituximab.

Despite an early response with shrinkage of the abdominal and scalp masses, repeat staging after five cycles at 4 months showed progression of the abdominal lymphoma with new and enlarging abdominal masses and a repeat biopsy showed loss of CD20 expression. The disease progression was associated with left sciatic area pain. Salvage chemotherapy with rituximab was initiated. However, her lymphoma continued to progress, leading to loss of both legs. After two cycles, the decision was made to stop chemotherapy. At the time of last available follow up, 6 months after initial presentation, the patient was alive with disease.

**Pathology**

Sections of the biopsy from the skull lesion showed variably-sized thyroid follicles containing colloid and lined by bland follicular epithelium. The nuclei showed no evidence of enlargement, grooves, or pseudoinclusions and no psammoma bodies or giant cells were seen. Capsular/vascular invasion could not be evaluated due to the limitations of the specimen. The follicular cells stained positive for thyroid transcription factor 1 (TTF-1), thyroglobulin, pancytokeratin, and cytokeratin 7 by immunohistochemistry and showed no reactivity for cytokeratin 20 (Fig. 2c and d). In addition, large, irregular, malignant lymphoid cells, some with single prominent nucleoli, were evident infiltrating between the follicles. By flow cytometry, 94% of the lymphoid cells were CD19 positive B-cells that also expressed CD20, CD10, and were surface kappa light chain immunoglobulin restricted. No expression of CD5 or CD23 was detected. Malignant lymphoid cells with similar morphology and immunophenotype were seen in the biopsy of the abdominal mass. In
addition, a ‘starry sky’ pattern was focally noted with increased numbers of tingible body macrophages. These cells also showed positive immunohistochemical staining for Bcl-2, Bcl-6, and no immunostaining for TdT, cyclin D1, MUM-1, CD43, or CD3. A Ki-67 immunostain showed a proliferation rate of 80%. These findings confirm the diagnosis of diffuse large B-cell lymphoma, germinal center subtype, with a high proliferation index. A fine needle aspiration of the thyroid gland showed findings consistent with a follicular lesion. No evidence of lymphoma was present in the thyroid fine needle aspiration.

Discussion

Bone is the second most common site of metastasis from thyroid cancer. It is seen in up to 10% of patients with papillary thyroid carcinoma and approximately 30% of patients with follicular thyroid cancer [2]. Skull metastasis from thyroid cancer has been reported in only 1.8–5.8% of thyroid carcinoma patients [2–4]. Our patient has a clinical presentation similar to previously reported cases of thyroid carcinoma metastatic to the skull. Most occur in the sixth and seventh decades and there is a predilection for women [3]. Detection of metastatic disease can occur months to years after diagnosis of the primary [2–4], with a mean of 23.3 years in one study [3]. Cases of follicular thyroid carcinoma presenting as longstanding skull metastases have also been reported [6]. Our patient’s findings on imaging also resemble other cases of skull metastases from thyroid cancer. Like thyroid cancer metastases to other bony sites, almost all skull lesions are osteolytic, and periosteal reaction and osteoblastic activity are usually not present unless radiation or radioiodine treatment has occurred [2, 3].

Most cases of skull metastases were from follicular thyroid carcinoma, with papillary thyroid carcinoma being the next most common. Nagamine et al. found all 12 cases of skull metastases to be well-differentiated [3]. Tickoo et al. reported three cases of bone metastases from thyroid carcinoma where the histologic appearance in the metastatic tumor was so well differentiated that it may be considered benign if taken out of context [7]. Our case shows a similar well-differentiated morphology. The bland microscopic appearance of the tumor, along with slow growth, caused this tumor to be described in the past as benign metastasizing thyroid tumor, metastasizing adenoma, and malignant adenoma [7–9]. Despite the often bland microscopic appearance and long interval between primary tumor and diagnosis of metastatic disease, survival after diagnosis of skull metastases is poor, with mean of 4.5 years in one study [3].

The thyroid gland is rarely the recipient of metastatic disease, with published incidence of 0.07–3% in clinical series [10, 11]. Secondary involvement of the thyroid gland has been reported in 11–27% of adult lymphoma patients [12–14]. However, many of these were discovered on autopsy and clinically evident involvement appears to be quite rare [15]. The phenomenon of tumor-to-tumor metastasis is also rare, and one study found only two cases in 75,083
malignant tumors [5]. Campbell et al. defined tumor-to-tumor metastases with the following criteria: more than one primary tumor must be present, the recipient tumor must be a true neoplasm, the donor tumor must be a true metastasis and not due to contiguous growth or embolization, and metastases to lymphatics are excluded [16]. Donor tumors to thyroid neoplasms from the kidney, lung, colon, breast, prostate, malignant melanoma and pancreas have been reported, with renal cell carcinoma being the most common [5, 17, 18]. The most frequent type of recipient tumor in the thyroid gland is follicular adenoma [17].

The presence of thyroid carcinoma and lymphoma in the same patient has also been documented. The most well established link is in patients who developed thyroid cancer after treatment for childhood leukemias, lymphomas, and other cancers [19–21]. Only isolated cases of apparently simultaneous occurrences of thyroid carcinoma and lymphomas can be found in the literature [22–24]. Secondary lymphoma involvement of a renal cell carcinoma has also been reported [25]. However, to our knowledge, this is the first reported case of diffuse large B-cell lymphoma involving a metastatic thyroid tumor.

Conclusion

This case represents an unusual presentation of a patient with metastatic follicular thyroid carcinoma to the skull, who then developed a diffuse large B-cell lymphoma that secondarily infiltrated the skull metastasis. The primary thyroid carcinoma (diagnosed subsequently) and the thyroid gland did not appear involved by lymphoma. Thyroid metastases to the skull can be clinically indolent for long periods of time and appear morphologically bland. Although these features can mimic a benign process, a careful investigation will often reveal an undiagnosed primary thyroid malignancy. Once they become clinically apparent, these tumors generally behave like other bone metastases from the thyroid and carry a poor prognosis. To the best of our knowledge, this is the first reported case of tumor-to-tumor metastasis in which both malignant counterparts represent metastases.

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