Skull Base Metastasis From Follicular Thyroid Carcinoma
—Two Case Reports—

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Abstract

A 58-year-old woman and a 71-year-old woman presented with extremely rare skull base metastases from follicular thyroid carcinoma (FTC). Surgical removal and external radiotherapy were performed followed by iodine-131 (131I) brachytherapy and thyroid hormone administration. The metastatic tumors in the skull base were well controlled. Treatment for skull base metastasis from FTC includes surgical debulking of the metastatic lesion, as well as complete resection of the thyroid gland, followed by internal irradiation with 131I, external irradiation, and administration of thyroid hormone to prevent tumor growth by suppression of endogenous thyroid-stimulating hormone. Skull base metastases may be the initial clinical presentation of FTC, with silent primary sites. The possibility of skull base metastasis from FTC should be considered in patients with clinical symptoms of cranial nerve dysfunction and radiological findings of bone destruction.

Key words: skull base metastasis, follicular thyroid carcinoma, iodine-131 brachytherapy, thyroid-stimulating hormone suppression, bisphosphonate

Introduction

Thyroid carcinoma includes 5 histological subtypes: papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC), medullary carcinoma, undifferentiated carcinoma, and poorly differentiated carcinoma. PTC is a major differentiated subtype that has slow growing characteristics and a good prognosis. FTC is another differentiated subtype that compared to PTC has a greater tendency to distant metastasis to such organs as lung and bone. Medullary carcinoma is included in a dissimilar category originating from different thyroid cells. In contrast to these subtypes, undifferentiated carcinoma and poorly differentiated carcinoma have a very poor prognosis. About 10% of patients with PTC and 20–40% of patients with FTC die of the disease, despite the slowly progressive, low grade malignancy of these subtypes. Most deaths result from poor control of local disease and distant metastases. The lung is the most common metastatic site for thyroid carcinoma followed by the bone, but skull metastasis of thyroid carcinoma is rare, with few reported cases. The largest series of skull metastasis from thyroid carcinoma reported a frequency of only 2.5% among 473 patients. Moreover, skull base metastasis from differentiated thyroid carcinoma is even rarer, with only 23 reported cases, including 17 cases of skull base metastasis from FTC that involved the clivus, cavernous sinus, sella turcica, petrous apex, and petrous ridge.

We treated two patients with skull base metastasis from FTC, and discuss the treatment modalities.

Case Reports

Case 1: A 58-year-old woman underwent surgery for a left thyroid tumor under a diagnosis of FTC in 1996. The patient developed hearing disturbance on the right and swelling of the right maxilla in 2003. Magnetic resonance (MR) imaging disclosed a tumor with bone destruction in the right temporal base extending to the infratemporal fossa and the cavernous sinus (Fig. 1A), as well as another tumor in the left occipital bone (Fig. 1B). Needle biopsy of the tumor in the right temporal bone suggested FTC metastasis, but a final diagnosis was not made. External
radiotherapy of 60 Gy was delivered to the tumor in the right temporal base, which effectively reduced the tumor size. The patient was referred to the Neurosurgical Department of Teikyo University Chiba Medical Center with complaints of motor weakness of bilateral lower extremities and lumbago in 2006.

Physical and neurological examination revealed swelling of the right maxilla, decreased right facial sensation, disturbed right hearing acuity, and paraparesis in the lower extremities. Serum free thyroxine (T4), free triiodothyronine (T3), thyroid-stimulating hormone (TSH), and thyroglobulin (TG) levels were 0.50 ng/dl (normal value: 0.95–1.74), 3.95 pg/ml (2.13–4.07), 0.339 μIU/ml (0.34–3.5), and 280 ng/ml (0–30), respectively. Spinal MR imaging disclosed mass lesions at the L5 level and the sacrum, which compressed the spinal roots. External radiotherapy of 30 Gy was delivered to the lumbar-sacral mass for pain relief, under a diagnosis of metastatic FTC based on the biopsy carried out prior to the radiotherapy. The pain in the lower extremities and the lumbago improved after the radiotherapy.

Both computed tomography (CT) and MR imaging revealed the tumor with bone destruction in the right temporal base extending to the infratemporal fossa and the cavernous sinus, as well as another tumor in the left occipital bone. Thoraco-abdominal CT revealed no mass lesions. Bone scintigraphy detected uptake lesions in the right temporal bone, the left occipital bone, and the lumbar-sacral spine. The bone destructive lesions in the right temporal base were partially removed under guidance with a neuronavigation system without impairment of the right internal carotid artery or the right 5th and 7th cranial nerves in October 2006. The tumor located in the left occipital bone was partially removed under electrophysiological monitoring of the lower cranial nerves in November 2006. The histological diagnosis of both lesions was metastatic FTC (Fig. 2).

Postoperative serum free T4, free T3, TSH, and TG levels were 0.79 ng/dl, 3.16 pg/ml, 0.225 μIU/ml, and 86 ng/ml, respectively. The patient received thyroid replacement therapy with 100 μg L-thyroxine daily. The residual thyroid gland was removed at Atami Hospital of the International University of Health and Welfare in January 2007. Oral administration of iodine-131 (131I), carried out in May 2007 at Chiba Cancer Center, revealed prominent accumulation of 131I in the metastatic lesions in the skull and lumbar spine. Serum TG level was reduced to 55 ng/ml after 131I brachytherapy. The second and third 131I brachytherapy sessions were performed in August 2007 and in July 2008, respectively. Currently, the metastatic lesions are well controlled, and MR imaging has shown no tumor growth (Fig. 1C, D). No adverse effects of external and internal radiotherapy have been observed.

Case 2: A 71-year-old woman underwent right hemithyroidectomy for a right thyroid carcinoma in 1993, under a diagnosis of FTC at another hospital (Fig. 3A). After surgery, the patient had paresis of the right recurrent nerve. In recent years, the patient developed hoarseness. During a medical check-up in July 2007, MR imaging revealed a tumor with bone destruction in the left petrous bone (Fig. 4A), and the patient was admitted to the Neurosurgical Department of Teikyo University Chiba Medical Center.

Physical and neurological examination revealed paresis of the bilateral recurrent nerves, without dysfunction of the facial and acoustic nerves. Serum free T4, free T3, TSH, and TG levels were 1.12 ng/dl, 2.92 pg/ml, 0.926
tumor. Urinary type I collagen N-telopeptide (uNTX) was decreased from 71.4 to 9.0 nmol bone collagen equivalents (BCE)/mmol creatinine (CRE) (normal value: < 55 nmol BCE/mmol CRE). The residual left thyroid gland was removed at Atami Hospital of the International University of Health and Welfare in December 2007. Oral administration of $^{131}$I, carried out in May 2008 and in February 2009 at Chiba Cancer Center, revealed prominent accumulation of $^{131}$I in the metastatic lesions in the left petrous bone. Currently, the metastatic lesion is well controlled. MR imaging has shown no tumor growth (Fig. 4B). No adverse effects of external and internal radiotherapy have been observed. Serum TG level was not elevated throughout the clinical course of this patient, which can be caused by endogenous autoantibody against TG.

**Discussion**

Nineteen cases of skull base metastasis from FTC, including the present two cases, have been reported.\(^{4,5,12,17,25,26,29,32–34,41,42,45}\) Mean age was 55.6 years, ranging from 23 to 74 years. Bone metastasis from thyroid carcinoma is often observed in the sixth and seventh decades of life.\(^{22}\) Skull base metastasis of differentiated thyroid carcinoma shows female predominance (14 females and 5 males), and this female predominance is generally observed in thyroid carcinoma. Although PTC is more common than FTC, FTC is more prone to spread hematogenously, especially to the lungs and bone.\(^{24}\) The metastatic lesion is usually hypervascular and osteolytic on radiological examination.\(^{14}\) Bleeding is often profuse during surgical resection.\(^{26}\) The most common symptom of skull base metastasis from FTC is cranial nerve dysfunction, which was observed in 17 of the 19 cases. Bone destruction and local invasion to the surrounding soft tissues are common on radiological imaging, so that skull base metastasis from FTC is often mistaken as chordoma or chondrosarcoma.\(^{4,33}\) The period between initial diagnosis and skull base metastasis from FTC ranged from 0 to 18 years, with a mean of 4 years. The possibility of skull base metastasis should be considered in the clinical course of FTC, and the patient should be meticulously followed up. Moreover, skull base metastases can be the initial clinical presentation of FTC in the presence of silent primary sites, which emphasizes the unpredictable nature of FTC. The possibility of skull base metastasis from FTC should be considered in patients with clinical symptoms of cranial nerve dysfunction and radiological findings of bone destruction.

The treatment algorithm for primary thyroid carcinomas includes nearly total or total thyroidectomy, followed by oral administration of $^{131}$I and TSH suppression.\(^{80}\) However, there is no clear consensus concerning the treatment of skull base metastasis from FTC because of the rarity of these lesions. Several thyroidologists have recommended, as the first-line therapy, complete excision of the thyroid gland with as many of the metastatic lesions as possible.\(^{11,20}\) Surgical debulking is hazardous in most cases of skull base metastasis because of the presence of vital structures and profuse bleeding. Therefore, the sec-
Bisphosphonates have been used widely to control bone metastasis of solid tumors such as breast and prostate cancers. Only one case of the use of bisphosphonates for bone metastasis of solid tumors such as breast and prostate can-


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