Craniun Metastasis: An Unusual Presentation of Differentiated Thyroid Carcinoma

Kranyum Metastazı: Diferansiye Tiroid Karsinomunun Nadir Görülen Bir Prezentasyonu

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Introduction

Differentiated thyroid carcinoma (DTC) usually have good prognosis, shows slow progression. It has been reported that the prevalence of DTC presenting with distant metastatic disease ranges from 1% to 9% (1). Long-term survival in patients with metastatic DTC has been reported to be 31-43% (2).

The most frequent organs that DTC shows distant metastasis are the lung and bone; rarely, the brain, breast, liver, kidney, muscle and skin (3). Rarely, distant metastasis may be the initial sign of thyroid carcinoma. In this case, the treatment approach for DTC is usually individualized. Unlike other cancers, local treatment of the primary tumor (total thyroidectomy) is preferred as ablative surgery; so that radioactive iodine (RAI) therapy may be more effective. After ablative treatments, L-thyroxine treatment to suppress thyroid-stimulating hormone (TSH) is given (4). Herein, we report a female who presented with bone metastasis with rapid progression.

Case

A 61-year-old woman presented with a palpable mass on calvarium. Magnetic resonance imaging (MRI) of cranium showed a 4x5 cm. mass on the parietal region which was originated from the calvarium with diffuse contrast enhancement. The dura and sagittal sinus were displaced because of mass effect and sagittal sinus thrombosis was evident (Figure 1A, 1B). The 18-fluorodeoxyglucose-positron emission tomography (18-FDG-PET) scan performed to identify the origin of the tumor showed increased FDG uptake on
the left parietal bone, cervical vertebrae, left scapula, left costa VII, left iliac crest, right acetabulum and bilateral ramus pubis. Also the nodule in left lobe of the thyroid gland showed increased uptake for FDG (SUD max:7.4). Fine needle aspiration biopsy revealed follicular tumor; adenomatous nodule, well differentiated follicular carcinoma and follicular type papillary carcinoma were meaningful in the differential diagnosis. Because dorsal MRI showed cervical vertebrae fractures (Figure 2) and the cranial mass had mass effect on the brain parenchyma and also it grew up externally, we consulted neurosurgeons for debulking surgery which would increase the efficacy of RAI therapy. Complex morphology of this region was important in neurosurgical procedures because drilling through bone has a potential risk of damaging the tumor or the adjacent anatomical structures, such as superior sagittal sinus, and might cause massive hemorrhage. Large veins from the surface of the brain empty into this sinus and a great amount of blood drains from the brain ultimately through it into the internal jugular veins. Therefore, they did not prefer surgical approach and indicated that the operation might be mortal because of close proximity to the superior sagittal sinus (5).

Laboratory results at initial evaluation were as follows: TSH: 0.34 mIU/mL, thyroglobulin (Tg): >5000 ng/mL and, antithyroglobulin (AntiTg): negative. Serum calcitonin level was normal. She underwent total thyroidectomy. Pathological examination of the thyroid tissue showed 2.7 cm. of poorly differentiated diffuse invasive follicular carcinoma. Tumor showed necrosis, calcification, vascular invasion, and capsule invasion for tumor and thyroid and, intrathyroidal dissemination was evident. Two months after the ablative surgery, 200 mCi I-131 RAI therapy was given under dexametasone treatment to prevent edema. Post-therapeutic whole body scan (WBS) showed diffuse I-131 uptake on the parietal region of the skull, thyroid bed at three different focus, left anterior cervical region, left hemipelvis (iliac bone), and the right femur neck (Figure 3). Subsequently, 30 Gy conventional radiotherapy (250 cGy per 12 fractions) was performed to C2-C4 vertabrae to prevent pathological fractures. We performed radiotherapy for cervical vertabrae at first because of paraplegia risk associated with possible pathological fractures. Subsequently, the mass of calvarium was irradiated. Six months after the first high-dose RAI treatment, a slight decrease in tumor size on calvarium was noted, and also she subjectively reported decrease in pain severity. A second RAI treatment with a dose of 200 mCi was given eight months after the first dose when the following values were obtained: TSH: 32; Tg >5000 ng/mL, and antiTg: negative. Intravenous zoledronic acid 4 mg was initiated to inhibit the osteoclastic activity and stabilize the bone metastasis. Zoledronic acid was given every month for the first three months and then it was repeated every three months. However, the clinical and radiological findings showed a rapid progression despite radiotherapy and a cumulative dose of 800 mCi RAI in 46 months of follow-up period.
She was brought to our emergency room because of a new onset of left hemiparesis. We hospitalized her to complete consultations and to evaluate for further treatment modalities. A 20x28 mm mass lesion located on C3 vertebrae, hypointense in T1A and hyperintense in T2A images with contrast enhancement caused expansion on bone tissue, completely surrounding left vertebral artery (in 360°) and caused a decrease in caliber resulted in occlusion. Radiation oncologists did not give an indication for a second radiotherapy for C3 vertebrae because the tumor showed progression after the radiation therapy. Neurosurgeons indicated that the tumor on the parietal region of calvarium was expansive, showed invasion into the brain parenchyma and caused brain edema. During her follow-up in the hospital, left hemiplegia developed and she was unable to walk and to maintain her daily activities. We could not plan a new high-dose RAI treatment because the metastatic tumor was unresponsive to radioiodine and her health condition was not suitable for this treatment. Although we decided to start sunitinib, a tyrosine kinase inhibitor, we were unable to obtain this agent.

Discussion

Several tumor-related and patient-related factors are commonly found in multivariate analysis to be predictors of disease-specific death in thyroid cancer [6]. Old age, less-well differentiated histological variant, large size of the primary tumor, and locally invasive thyroid cancer (incompleteness of resection) were the factors associated with poor prognosis in our patient. Distant metastases at the time of diagnosis cause the poorest prognosis in patients with thyroid carcinoma. Five-year and 15-year tumor-specific mortality rates in patients with distant metastases are 36%-47% and 70%, respectively. In addition, localization of metastases in the bone rather than in the lung is associated with poor prognosis. However, it is shown that the extent of metastatic involvement rather than the site (lung or bone) has prognostic value (in our patient the metastatic mass on calvarium was in large size). The only factor for good prognosis in our patient was the presence of I-131 uptake (6,7). However, she did not respond to radioiodine therapy.

In patients with DTC complicated with bone metastases, treatment modalities should include total thyroidectomy, metastasectomy -if possible-, RAI therapy, and external radiation therapy [8]. The treatment approach for DTC presenting with distant metastatic disease is usually individualized. Previous studies have reported that 10-year survival is 0-34% [9]. The mean survival for patients with skeletal metastases is estimated at only 4 yr. In these studies, nearly all patients received radioiodine, and many also underwent adjuvant therapy including surgical excision of metastatic bone lesions, external radiotherapy, arterial embolization or chemotherapy [10,11].

Bone surgery may be needed as palliative treatment to prevent pathologic fractures or to ameliorate neurologic symptoms and pain severity resulting from spinal cord compression by vertebral metastases. After surgical treatment, reduced quality of life may be improved. Curative surgery is possible in single, localized resectable metastases. Radical resection is unlikely for large metastases; but surgery may be of help in reducing tumor mass to allow more effective action of radioiodine therapy [8]. Unfortunately, neurosurgeons concluded that all metastatic bone lesions in our patient were unresectable.

The effectiveness of RAI treatment is associated with increased I-131 uptake of tumor cells and size of the metastatic bone mass. Larger lesions show poorer prognosis as in the present case. In adult patients, 100-200 mCi I-131 was the dose repeated in every 6-8 months. Also, we repeated the radioiodine treatment with 200 mCi I-131 in every 6 months for four times; the cumulative dose was 800 mCi. No major complication (i.e. bone marrow suppression, pulmonary fibrosis) was noted [12].

Studies evaluating the effects of pamidronate and zoledronate on skeletal metastases of thyroid cancer have been reported. Rosen et al. [13] used IV pamidronate (30 mg every three months for two years) for patients on suppressive doses of LT4 for thyroid cancer. After this treatment, suppression of bone resorption and increase in bone mineral density were achieved. In another study, IV pamidronate 90 mg every month for one year was given to 10 patients with bone metastases originating from thyroid cancer. Although only two of 10 patients demonstrated a partial radiographic response to pamidronate, and patients showed a non-significant decline in the amount of narcotic pain medication over time, bone pain decreased and quality of life was improved in patients on pamidronate treatment [14].

In a study of Orita et al. [15], treatment with Zoledronic acid was found to be more effective than pamidronic acid in reducing skeletal related events (i.e. bone fracture, spinal compression) or in delaying their appearance in patients with bone metastases from DTC. However, for how long bisphosphonate therapy for DTC patients with bone metastasis will be used is not well known. Wexler JA preferred to use bisphosphonates lifelong period (author’s personal opinion) [14]. For our patient, we used zoledronic acid 4 mg every month in the first three months, and thereafter, it was used every three months for 17 months. Before and after zoledronic acid, we controlled serum calcium levels and, calcium 600 mg with 400 mg calecalciferol twice daily was given routinely. No adverse effect of bisphosphonate other than fever, arthralgia and myalgia was noted. Left hemiplegia associated with cervical vertebral involvement was developed at the 46th month of follow-up (after she received 32 mg zoledronic acid-total dose).

Tyrosine kinase inhibitors may be promising agents in patients with advanced metastatic papillary thyroid carcinomas, particularly in those with no/low iodine uptake. Since the use of sunitinib for papillary thyroid carcinoma is limited with iodine-negative cases in our country, we could not use a tyrosine kinase inhibitor in the present case.

Conclusion

Bone metastasis of DTC is rare. Treatment modalities, survival, and quality of life vary according to the localization of the metastatic lesion.
References