

CASE REPORT

Thyroid follicular carcinoma presenting as metastatic skin nodules

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Background: Follicular thyroid cancer (FTC) metastasizes most commonly to the lungs and non-cranial bones. Skull and skin are uncommon sites and usually manifest well after the diagnosis of primary malignancy. Metastasis to skull and skin as the presenting feature of FTC is infrequently reported in the literature.

Case presentation: A 65-year-old Caucasian woman with a history of thyroid nodule presented with the complaint of rapidly growing skull nodules which had been present for 3 years but were stable previously. She denied any fevers, chills, history of trauma, or weight loss. She denied any history of smoking or head and neck irradiation. On physical examination, she had two non-tender gray cystic lesions – one on her left temporal region and the other on the right parietal region. Biopsy was consistent with metastatic FTC. Magnetic resonance imaging of the brain demonstrated 7.1 × 3.8 cm and 3.7 × 4.5 cm fairly homogeneous, enhancing, relatively well-defined masses centered in the posterior and left anterior lateral calvarium with intracranial and extracranial extensions but without any vasogenic edema or mass effect on the brain. Thyroid ultrasound showed numerous nodules in both lobes. The patient underwent a total thyroidectomy. Histopathological studies of the thyroid gland revealed a well-differentiated FTC in the left lobe. Then she underwent resection of the tumor in multiple stages. She did not have any recurrence of the FTC or metastases during the follow-up period and will be receiving radioactive iodine treatment.

Conclusion: Bone and lung are the common sites of metastasis from FTC, but involvement of skull or skin is unusual, particularly as the presenting feature. Metastases from FTC should be in the differential of patients with new osteolytic hypervascular skull lesions or cutaneous lesions in head and neck area.

Keywords: thyroid nodule; adenocarcinoma; follicular; neoplasm metastasis; skull nodules; thyroidectomy; radioactive iodine

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Follicular thyroid cancer (FTC) generally spreads via hematogenous dissemination, most commonly to the lungs and non-cranial bones. The skull and skin are uncommon sites of metastases (1). Although distant metastases at the time of diagnosis are reported in 11–20% of patients, metastasis to skull as the presenting feature of FTC is exceedingly uncommon with only a handful of cases reported (2–4). Cutaneous metastases are also rare from differentiated thyroid cancers (DTC) (4). In this case report, we describe a case of FTC which presented as skull and cutaneous metastases.

Case presentation

A 65-year-old Caucasian woman with a history of thyroid nodule presented to dermatology clinic with the complaint

of rapidly growing skull nodules. She reported that the nodules had been present for 3 years but had been stable, so she had not sought medical attention. She denied any fevers, chills, pain, or redness over the nodules, fatigue, weight loss, recent infections, or history of trauma. She admitted to drinking alcohol on social occasions but denied any history of smoking or head and neck irradiation. Her family history was positive for leukemia in her father and melanoma in her mother. She indicated a remote history of thyroid nodule which she reported was benign on biopsy. On physical examination, she had two non-tender gray cystic lesions – one on her left temporal region measuring about 5 cm in diameter and the other on the right parietal region measuring about 7 cm in diameter. Exam was negative for signs of inflammation or regional

lymphadenopathy. The rest of the exam, including a thorough neurological exam, was benign. Laboratory tests revealed a normal TSH of 0.52 μ IU/ml (reference range 0.3–5.0 μ IU/ml) and T4 of 0.68 ng/dL (reference range 0.58–1.64 ng/dL). A complete metabolic panel including serum creatinine, BUN, and hepatic panel was normal. Complete blood count did not reveal any leukocytosis or anemia.

Biopsy was attempted under local anesthesia which revealed possible extension to the bone with vascular origin and hence the patient was referred to surgery for debulking. During surgery, total excision of the nodules could not be performed as there appeared to be skull erosion underneath. An immunohistochemical panel showed positive staining for CK7, thyroglobulin, and HBME-1 while it was weakly positive for pankeratin, suggesting a thyroid origin of these lesions, that is, metastatic FTC (Fig. 1). On computed tomography (CT) of the head, two large extra-axial enhancing masses with both intra- and extracranial components were seen (Figs. 2, 3). Magnetic resonance imaging (MRI) of the brain demonstrated 7.1 \times 3.8 cm and 3.7 \times 4.5 cm fairly homogeneous, enhancing, relatively well-defined masses centered in the posterior and left anterior lateral calvarium with intracranial and extracranial extensions but without any vasogenic edema or mass effect on the brain (Fig. 4). Positron emission tomography (PET) or CT of the skull demonstrated the two skull lesions to be lytic. Two foci of hypermetabolic activity were also seen in the thyroid gland in the left lobe and thyroid isthmus. Thyroid ultrasound showed numerous nodules in both lobes, the largest measuring up to 2.5 cm in greatest dimension.

The patient underwent a total thyroidectomy (Fig. 5). Histopathological studies of the thyroid gland revealed a well-differentiated FTC in the left lobe, pathological stage pT₂N_xM₁, a 1-cm focus of classic papillary thyroid cancer in the right lobe of thyroid, with a background of multinodular goiter (Fig. 6). She underwent intravascular

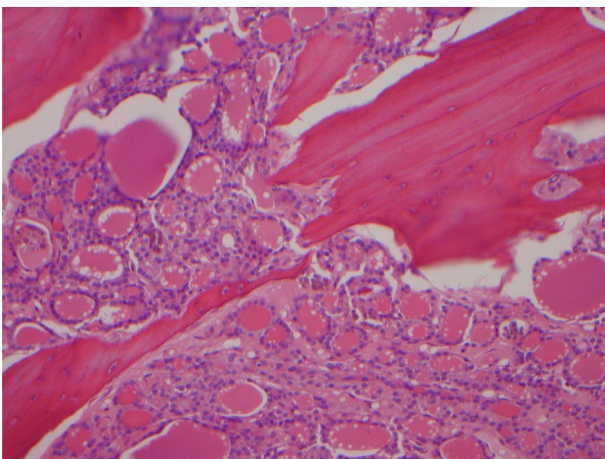


Fig. 1. Metastatic follicular carcinoma to cranial bone.

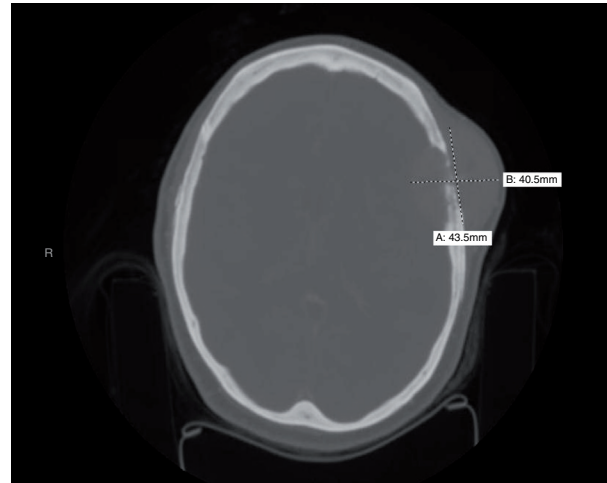


Fig. 2. CT head with and without contrast showing a large, round, relatively smoothly margined enhancing extra-axial left frontal mass (4.4 cm in anteroposterior diameter and 4.1 cm in transverse diameter) that has eroded and partially destroyed the calvarium and extends into the subcutaneous scalp.

embolization of the feeding blood vessels of her metastatic skull lesions from the external carotid system. Then she underwent resection of the tumor in multiple stages with resection of the posterior and left frontal tumor, and calvaria, followed by cranioplasty. Although she had other unrelated postoperative complications, she did not have

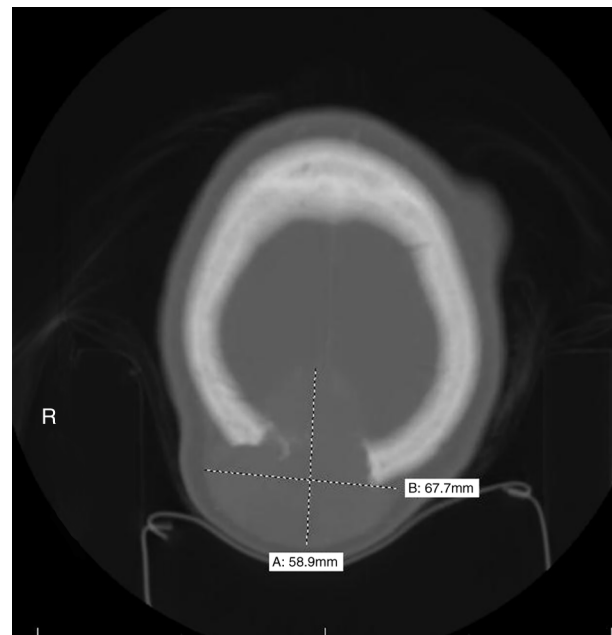


Fig. 3. CT head with and without contrast demonstrating a large, round, relatively smoothly margined enhancing extra-axial mass (measuring 6.8 cm in transverse diameter, 5.9 cm in AP diameter) involving the right and left parietal region, straddling the posterior falx cerebri and superior sagittal sinus.

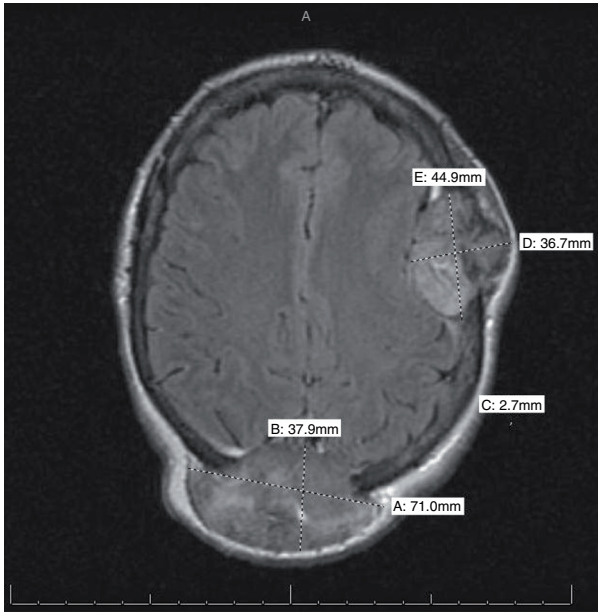


Fig. 4. MRI brain revealing a large 7.1×3.8 cm fairly homogeneous enhancing relatively well-defined mass centered in the posterior calvarium with intracranial extension into the extra-axial space as well as extracranial extension. The mass abuts the superior sagittal sinus. There is a similar appearing 3.7×4.5 cm fairly homogeneous relatively well-defined enhancing mass centered in the left anterior lateral calvarium also extending into the extra-axial space as well as extracranially.

any recurrence of the FTC or metastases during the follow-up period, had a normal thyroglobulin of 4.9 ng/mL (reference range 2.8–40.9 ng/mL), and will be receiving radioactive iodine treatment.

Discussion

FTC has a peak incidence in the sixth decade of life. It typically presents as a thyroid nodule, either noted by the



Fig. 5. Total thyroidectomy specimen with follicular carcinoma.

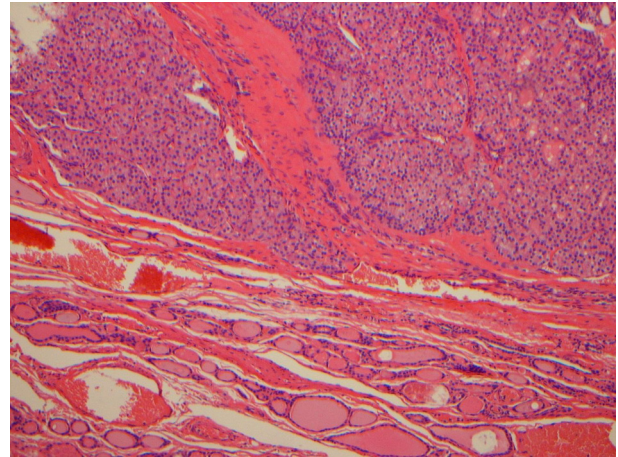


Fig. 6. Follicular carcinoma of thyroid invading adjacent thyroid parenchyma.

patient or the physician on routine physical examination or incidentally on routine imaging (1). Vascular invasion is characteristic for follicular carcinoma accounting for more common distant metastasis (5). These metastases occur in 10–15% of patients with FTC, with lung and bone being the commonest sites of involvement. Bone metastases from FTC tend to be multiple and often involve sternum, ribs, and vertebrae (3). Skull metastases are uncommon with recent decline in incidence because of early detection and treatment of thyroid cancer; among thyroid carcinomas, these metastases tend to occur more commonly in FTC and have a female preponderance (6–8). There were only 12 reported cases of skull metastases out of 473 patients of thyroid cancer in one study, accounting for 2.5% of cases (8). Likewise cutaneous metastases from DTC are uncommon with less than 30 reported cases of cutaneous metastases in the English literature until 2010 (9). These cutaneous metastases are more common in head and neck region and can manifest in a variety of histological appearances (10–12). However, in most of these cases metastases occurred long after the diagnosis and institution of treatment for FTC and it is extremely unusual to encounter skull and cutaneous metastases as the presenting feature of FTC (3). The exact incidence of such cases therefore is unknown.

Skull metastases from FTC most commonly present as a slow-growing soft, painless usually hemispheric and singular lump in the occipital region (6, 7, 12). Unusual presentations include headaches, hemiparesis, exophthalmos, cranial nerve dysfunction, and altered consciousness (13). These skull lesions are osteolytic on skull X-ray, and CT scans generally show homogeneous lesions with density slightly greater than the brain and a highly vascular appearance on angiographic assessment with blood supply most commonly from external carotid system (7, 14). In patients with scalp lesions, PET/CT can be used to determine the biopsy site (5). In patients with established

diagnosis of FTC with no documented metastases, evaluation of possible metastatic lesions can be done with (131)I single photon emission CT/CT [(131)I-SPECT/CT] (15). (99m)Tc-MIBI scan has been reported to be a highly sensitive technique for the detection of DTC metastases that have lost the capability to uptake (131)I; the combined (99m)Tc-MIBI scintigraphy and serum thyroglobulin (Tg) estimation appear to be an alternative method of radioiodine imaging in cases with DTC and elevated Tg (16).

Bone metastases uncommonly respond to radioactive iodine therapy and are associated with poor prognosis (7). Surgical approach should be considered as one of the treatments of choice for bone metastasis, if possible, and curative resection of solitary bone metastasis is associated with improved survival (7). Bone defects often require extensive bone resection, bleeding is often profuse during surgical resection, and deaths have been reported from extreme hemorrhage (1, 4, 13, 14). Because of the life-threatening nature of such hemorrhages, preoperative angiographic assessment of these lesions with prophylactic ligation or embolization of feeding vessels is recommended (14). When surgical excision is not possible, internal radiation with I-131 is recommended; external radiation is generally reserved for cases where uptake of I-131 by metastatic foci is poor (8). Thyroid hormone should be administered after complete excision of thyroid gland to suppress endogenous TSH from promoting tumor growth (17). Frequent follow-up examination is recommended and monitoring thyroglobulin measurement can be useful during follow-up (13).

FTC is thought to have the most optimistic prognosis even with metastases to the lymph nodes and lung. However, when combined with distant, especially widespread, metastases, the quality of life is compromised and the overall survival rate significantly decreases (2). In one case series, the mean time from the diagnosis of thyroid tumor until discovery of skull metastasis was 23.3 years (8). Prognosis in case of metastasis is generally poor and the 10-year survival with bone metastases from DTC is reported to be 27% (7). However, mean survival time of 4.5 years was reported with skull metastases in one case series, suggesting even worse prognosis and warranting an aggressive and multidisciplinary approach in this subset of patients (5). A regular follow-up is crucial in these patients for early detection and management of any residual or recurrent metastatic FTC (6).

Conclusion

Bone and lung are the common sites of metastasis from FTC but involvement of skull is unusual, especially as the presenting feature. Metastases from FTC should be included in the differential of patients with new osteolytic hypervascular skull lesions or cutaneous lesions in head and neck area (7, 14).

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