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Case Report

Skull metastasis from follicular thyroid carcinoma: report of three cases and review of literature

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Abstract: Three patients' medical history, clinical manifestation, imaging characteristic, therapy and prognosis of calvaria metastasis from follicular thyroid carcinoma (FTC) in our hospital were retrospectively analyzed by reviewing medical literature. In case one, the tumor in frontal bone and fossa orbital was total resected, no further treatment was performed, the patient gave up on therapy and died of extensive metastasis at 22 months after the initial operation. In case two, the tumor in parietal and occipital bone was total resected, the subtotal resection of bilateral thyroid gland and isthmus was performed and combined with therapy of Levothyroxine and ^{131}I radio-iodine therapy, no evidence of tumor recurrence at 30 months after the primary operation. In case three, the tumor in occipital bone was gross total resected, total resection of bilateral thyroid gland and clearance of lymph node was performed after two months, adjunctive therapy with Levothyroxine, ^{131}I radio-iodine and skull radiotherapy, no evidence of tumor recurrence at 21 months after the primary operation. Correct diagnosis of calvaria metastasis from FTC preoperative is difficult because it's rarity, patients can survive for years after synthetic therapy including total resection of metastatic tumor, radical operation of thyroid carcinoma, adjunctive therapy of Levothyroxine, ^{131}I radio-iodine and skull radiotherapy.

Keywords: Thyroid carcinoma, papillary thyroid carcinoma, follicular thyroid carcinoma, calvaria, skull base

Introduction

The calvarium is a common site for metastasis, accounting for 15%-25% of all cancer patients [1]. The most common primary malignancy is breast cancer, followed by lung cancer, prostate cancer, and malignant lymphoma, but from thyroid cancers is extremely rare [1, 2], only a small number of reports are found in the literature. The largest series of skull metastasis from thyroid carcinoma described a frequency of only 2.5% among 473 patients. The majority of skull metastasis from thyroid cancers is of the follicular subtype [3]. Both skull base and calvaria can be invaded by thyroid carcinoma, it is hard to be diagnosed correctly preoperative for its atypical clinical manifestation and imaging findings. Primarily because of the rarity of skull metastasis with thyroid carcinoma, the role of standard postoperative therapy for this situation has not been definitively established. In this article, we report on three cases of skull metastatic lesions form follicular thyroid carcinoma (FTC) and reviewed the pertinent literature.

Cases report

Case 1

A 67-year-old man without remarkable medical history was found to have a painless mass in the right frontal region since 3 months and gradual blurred vision in the right eye since 7 months. Physical examination showed a palpable, immobile and hard tumor in right frontal region measured 2 cm in sagital and 2 cm in coronal directions and 0.6 cm in vertical dimension. Visual acuity test showed that the left eye vision was 1.3 and 0.8 vision in his right eye. Orbital computed tomography (CT) revealed an isodense tumor with osteolytic characteristic in the right orbit and frontal sinus (**Figure 1A**, **1B**), the magnetic resonance imaging (MRI) of the brain disclosed a 2.8×3.4×3.5-cm homogeneously enhanced, well-demarcated extradural mass (**Figure 1C**). A diagnosis of extroverted meningioma or metastatic carcinoma was taken in our consideration preoperative. The patient underwent a right frontal craniotomy, after skin incision, a redness, hyper vascular,

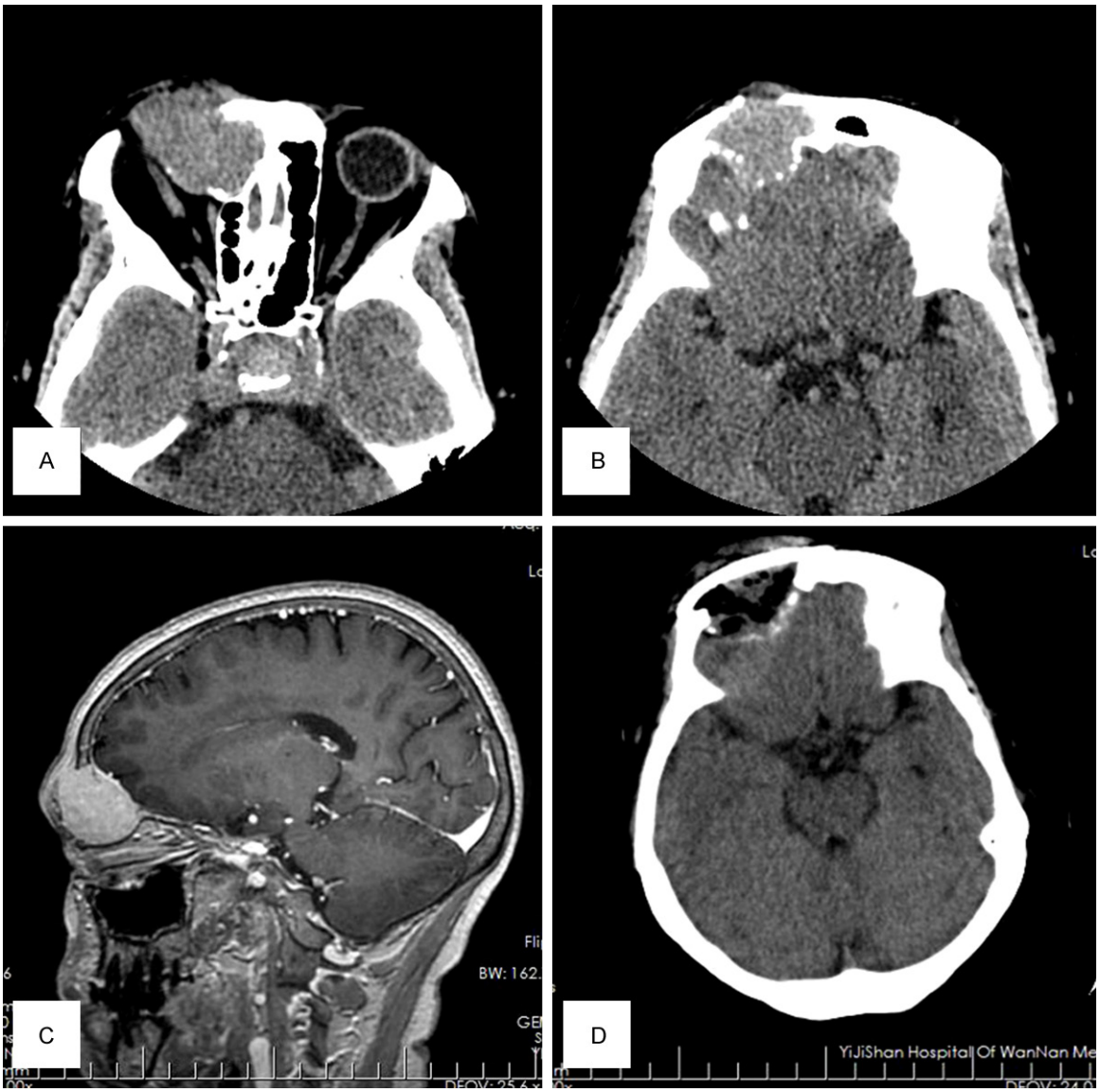

Figure 1. A, B. Orbital CT revealed an isodense tumor with osteolytic characteristic in the right orbit and frontal sinus. C. MRI of the brain disclosed a 2.8×3.4×3.5-cm homogeneously enhanced, well-demarcated extradural mass. D. Postoperative CT of brain revealed both the tumor and invaded bone were total resected and cranioplasty was performed with digital shaping titanium mesh.

soft mass was exposed, the tumor was invaded the sclerotin of right roof of orbit and frontal sinus and was strongly adherent to the dura mater, both the tumor and invaded bone were total resected and cranioplasty was performed with digital shaping titanium mesh which prepared preoperative (**Figure 1D**). Histopathological examination showed the diagnosis of metastatic FTC (**Figure 2A**, **2B**). Immunochemical studies demonstrated that immunonegative for glial fibrillary acidic protein (GFAP) but some of the cells were immunopositive for thyroglobulin (TG) (**Figure 2C**, **2D**). Postoperative course was uneventful, the patient manifested normal physical and mental development and no neurological deficits. The patient was discharged for refusing further treatment. The patient was admitted to another hospital again with thoracodynia 20 months later, CT of the chest in the hospital revealed extensive disease including neck, stethidium and mediastina; she gave up on therapy and died 22 months after the initial surgery.

Case 2

A 61-year-old female presented to our hospital with a complaint of gradual exaggerated mass

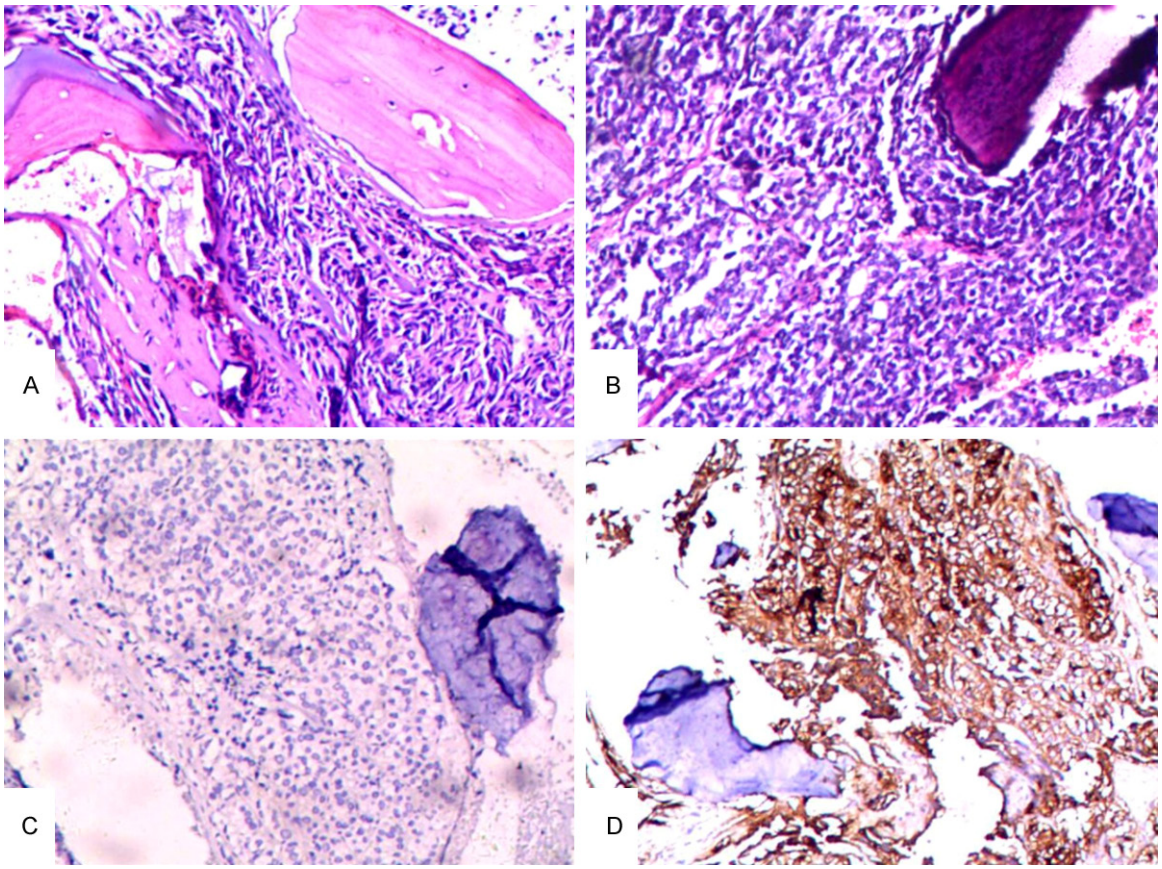

Figure 2. (A, B) Histopathological examination showed the diagnosis of metastatic FTC (HE×100). Immunochemical studies demonstrated that immunonegative for glial fibrillary acidic protein (GFAP) (×100) (C), but some of the cells were immunopositive for thyroglobulin (TG) (×100) (D).

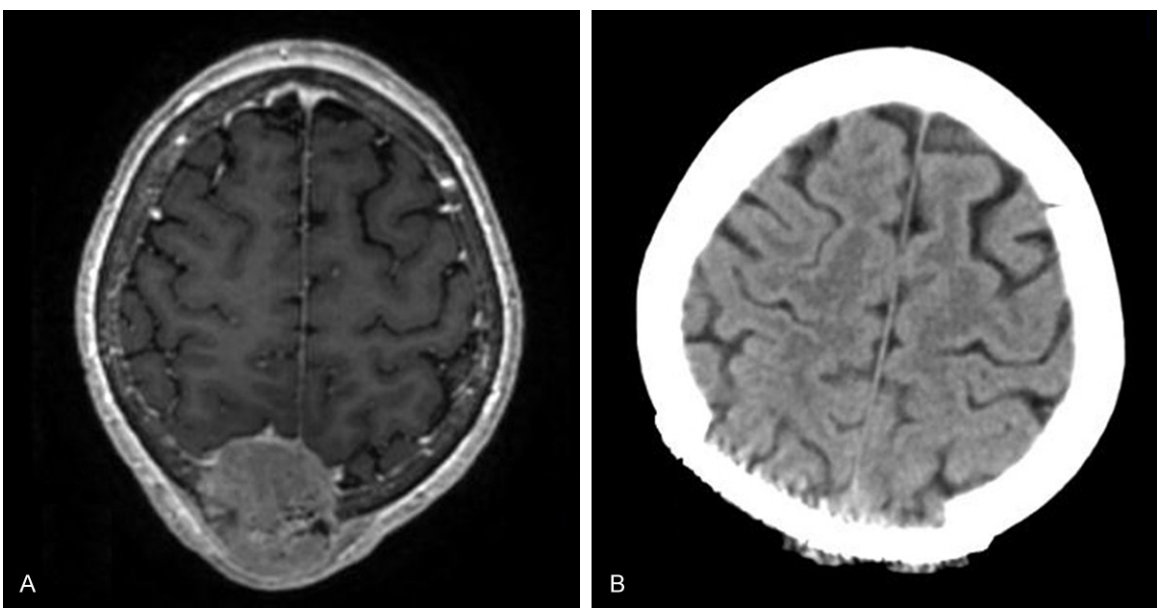

Figure 3. A. MRI demonstrated an extradural tumor with bone destruction and enhanced homogeneously by gadolinium. B. Postoperative CT of brain revealed the tumor was total resected and cranioplasty by digital shaping titanium mesh was performed.

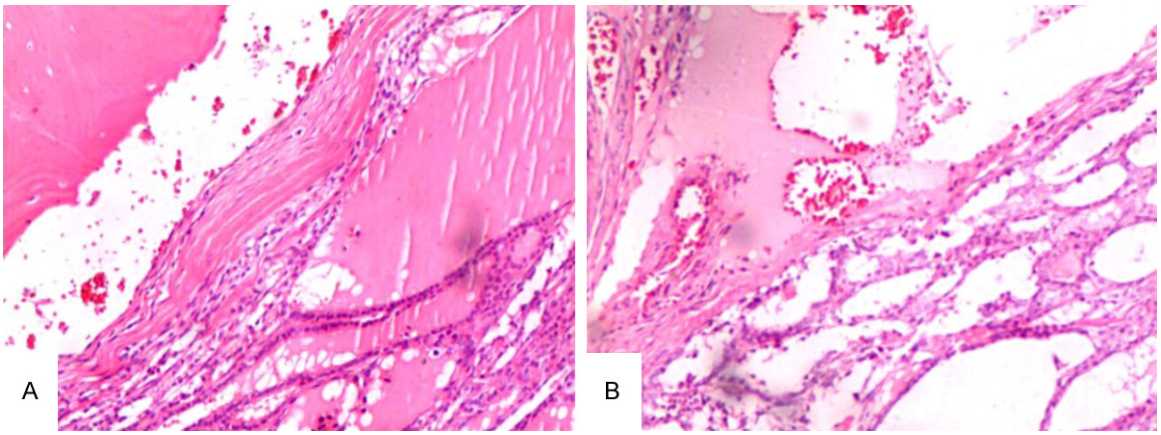

Figure 4. A, B. Histopathological examination showed the diagnosis of metastatic FTC (HE×100).

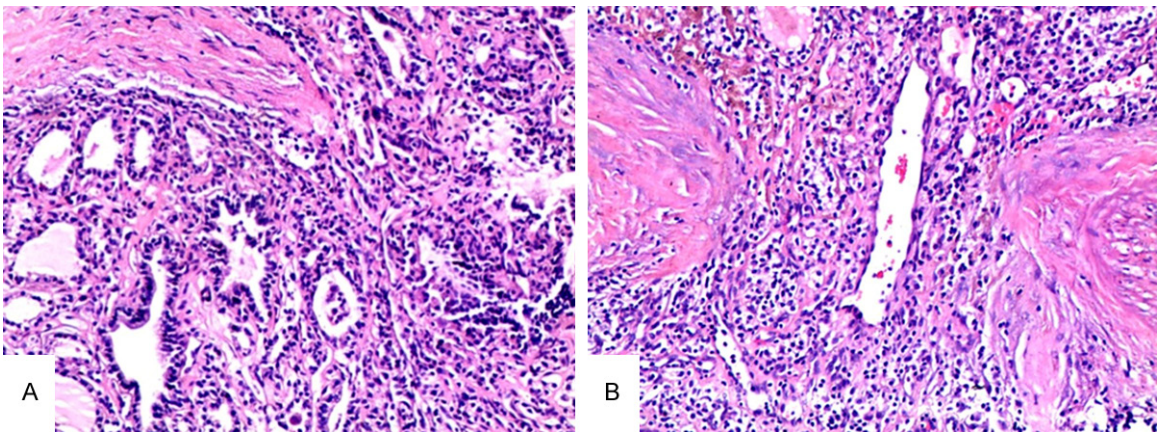

Figure 5. A, B. The histopathological examination of the thyroid cancer confirmed the diagnosis of FTC and demonstrated that some of the cells were penetrated the thyroid capsule (HE×100).

in her right parietooccipital region in the last year. She had a history of thyroid adenoma and total excised at another hospital 3 years ago. Physical examination showed an 8.0 cm×8.0 cm, firm, painless, and immobile mass of the parietal and occipital area. MRI demonstrated an extradural tumor with bone destruction and enhanced homogeneously by gadolinium (**Figure 3A**). A tumor completely resection and cranioplasty by digital shaping titanium mesh was performed (**Figure 3B**). Intraoperative observation, a beige, abundant vascular, soft mass was found, the tumor adjacent to the superior sagittal sinus (SSS) and strongly adherent to the dura mater but not invaded it. Histopathological examination showed the diagnosis of metastatic FTC (**Figure 4A**, **4B**). Thyroid ultrasonography was performed and revealed multiple nodules in the right thyroid lobe. The patient underwent a right total thyroidectomy and left near total thyroidectomy two weeks later. The histopathological examination confirmed the diagnosis of FTC and demonstrated that some of the cells were penetrated the thyroid capsule (**Figure 5A**, **5B**). Postoperatively levels of thyroid hormones were normal. The patient received thyroid replacement therapy with 125 μg L-thyroxine daily and underwent adjuvant radioiodine treatment using ^{131}I. The patient was discharged without discomfort or clinical symptoms. To date, she is alive without evidence of tumor recurrence or metastasis at 30 months after surgery.

Case 3

This healthy 67-year-old male was admitted to our emergency room with ulcerated and durative bleeding in his occipital mass which gradu-

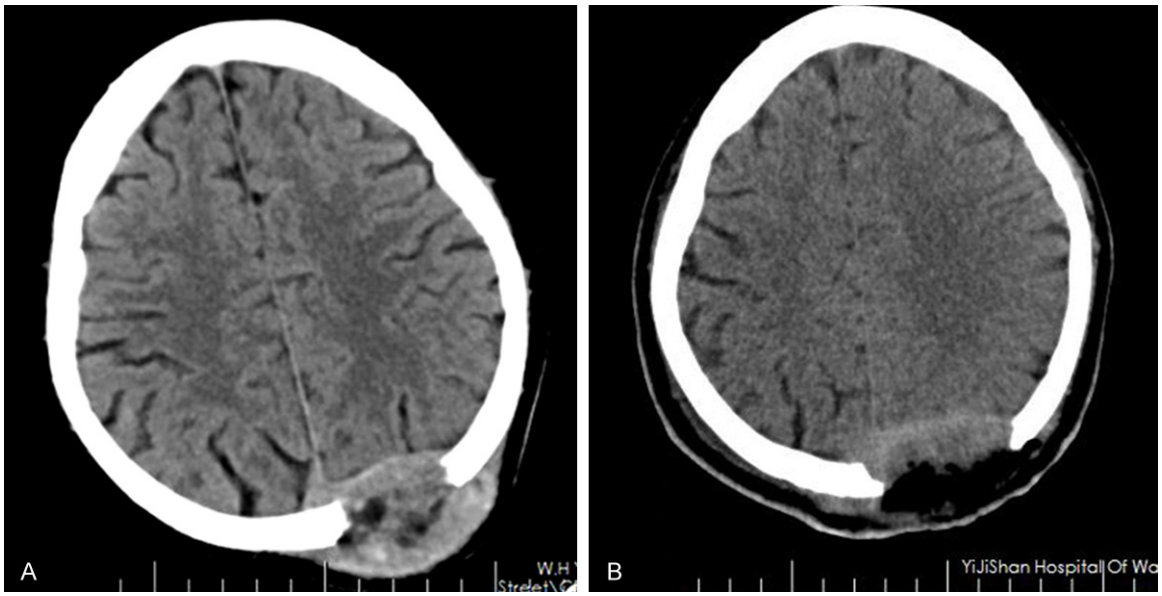

Figure 6. A. Head CT scan exhibited an occipital mass, 6.0 cm×8.0 cm in size, isodense with central necrosis, and with osteolytic destructive features. B. The tumor was gross total resected.

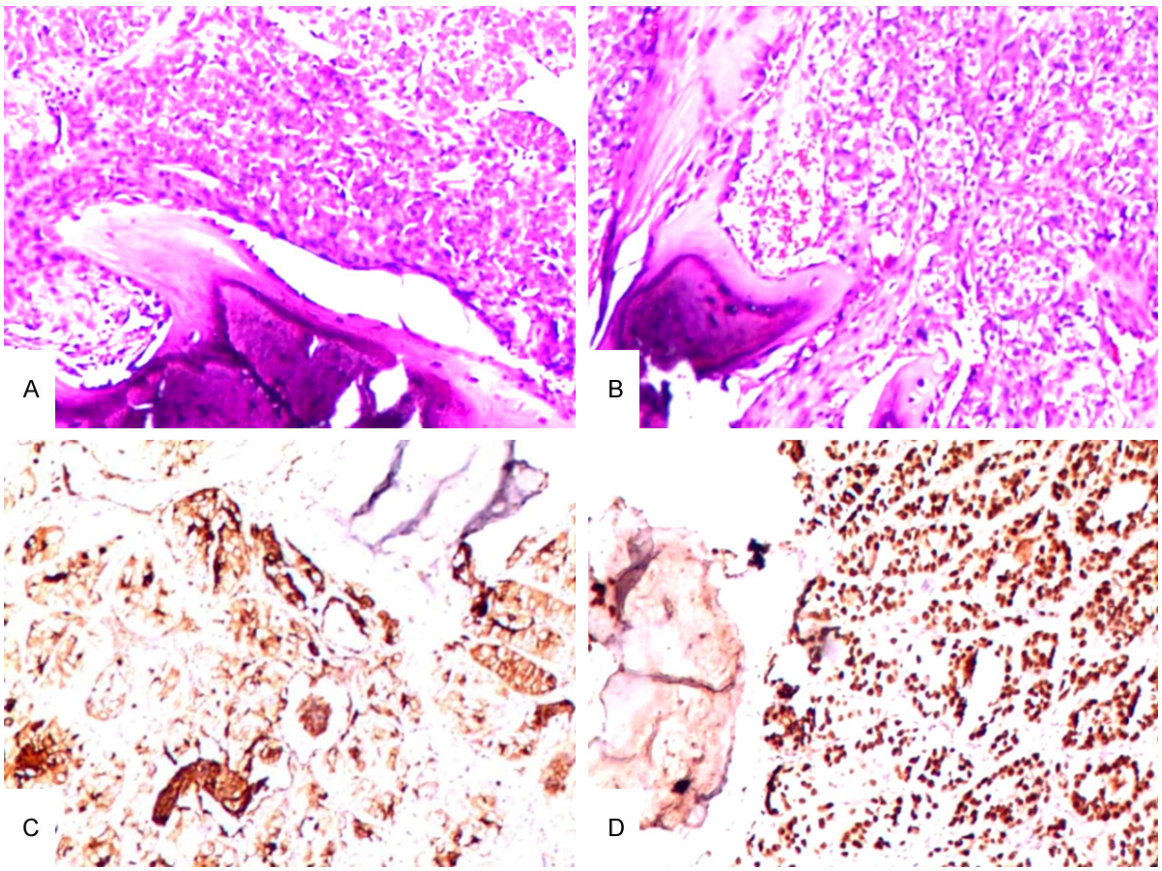

Figure 7. (A, B) Histological examination revealed the diagnosis of FTC and osseous tissue can be found encircled by some of the tumor cells (HE×100). The tumor cells were positive staining for thyroid transcription factor-1 (TTF-1) (×100) (C), and thyroglobulin (TG) (×100) (D).

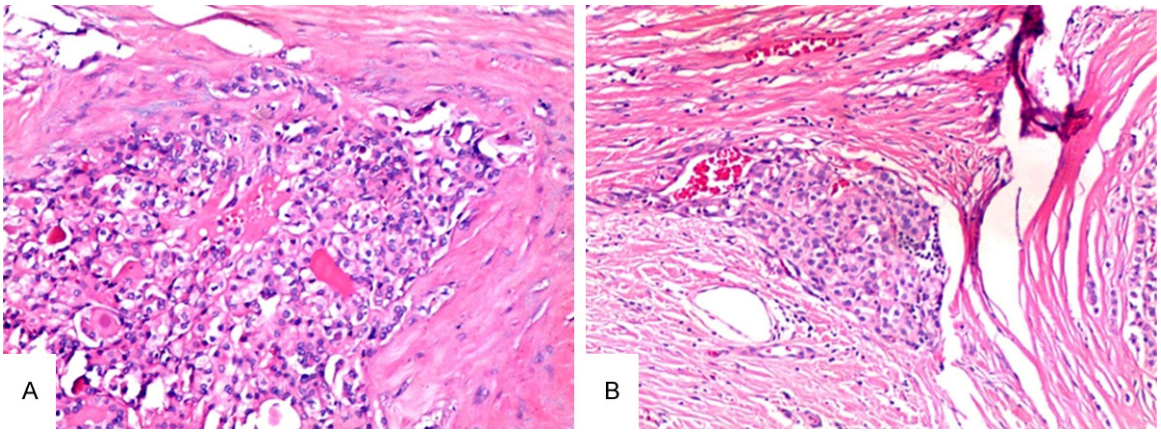

Figure 8. A, B. Histopathological examination of the thyroid cancer showed the diagnosis FTC and the tumor cells penetrated the thyroid capsule and vessels (HE×100).

al exaggerated in the last 4 months. A head CT scan exhibited an occipital mass, 6.0 cm×8.0 cm in size, isodense with central necrosis, and with osteolytic destructive features (**Figure 6A**). Intraoperative observation found a hypervascular, beige-colored mass, a large amount of blood was gushed out when we resect the tumor, about 2000 ml in a short time, the tumor was gross total resected (**Figure 6B**). Histological examination revealed the diagnosis of FTC with positive staining for thyroid transcription factor -1 (TTF-1) and thyroglobulin (TG), and osseous tissue can be found encircled by some of the tumor cells (**Figure 7A-D**). Thyroid ultrasonography revealed thyromegaly accompanied of multiple cystic-parenchyma lesions. Total resected of bilateral thyroid gland and clearance of lymph node was performed after two months, Histopathological examination showed the diagnosis FTC and the tumor cells penetrated the thyroid capsule and vessels (**Figure 8A**, **8B**). The patient received thyroid replacement therapy with 125 μg L-thyroxine daily, underwent adjuvant radioiodine treatment using ^{131}I, and skull radiotherapy to residual tumor. At present, the patient is alive symptom-free and without evidence of tumor recurrence or metastasis 21 months after the primary operation.

Discussion

Thyroid cancer is the most common endocrine malignancy and its incidence has been increasing dramatically throughout the world in the past few decades. Thyroid cancers are divided into four major histological subtypes, papillary, follicular, medullary, and anaplastic. The most common subtype of thyroid cancer is papillary thyroid cancer (PTC). The second most common subtype is follicular thyroid cancer (FTC). Together, papillary and follicular cancers are termed differentiated thyroid cancer (DTC) which accounts for 90% of all thyroid cancers [4, 5]. Despite an overall excellent prognosis and survival in patients of DTC, 5-23% of patients have distant metastasis, which confers on them a relative poor prognosis despite of adequate treatment [4, 6]. Bone was the most common single site for FTC and the second most common single site for PTC [6]. Bone metastases from FTC are more often to the long bones, such as the femur and flat bones, particularly the pelvis and sternum, the bones most often involved in metastasis of PTC are ribs, vertebrae and sternum, while skull metastasis form both FTC and PTC are extremely rare, accounting for 2.5% of all bone metastasis, the majority of skull metastasis from thyroid cancers is of the FTC, followed by PTC [3, 7, 8].

Calvaria metastases from DTC can occur at any age, the youngest patient was just 18 years old [9], but most patients are between 60 and 70 years old [3]. The age of patients with skull base metastasis from FTC ranges from 23 to 74 years (mean, 54.6 years), and that of those from PTC ranges from 35 to 73 years (mean, 53.5 years) [10]. Both calvaria and skull base metastases from DTC revealed a female predominance [3, 10]. Mean period from initial diagnosis of thyroid carcinoma to calvaria

metastasis was 23.3 years, ranging from 4 to 52 years [3]. Mean period from initial diagnosis of FTC to skull base metastasis was 3.9 years, ranging from 0 to 18 years, mean period from initial diagnosis of PTC to skull base metastasis was 6.8 years, ranging from 0 to 18 years [10].

Anatomically, calvaria metastatic lesions are most frequently located at the midline of the frontal and parietooccipital region [9, 11-19], skull base metastatic lesions are most frequently located over the clivus [10, 20, 21], petrous ridge, sella turcica, sphenoid sinus, cavernous sinus and infratemporal fossa can also be found in the literature [10, 20-24]. To our best knowledge, metastatic DTC arising from the orbit communicate to frontal sinus (case 1) has not previously been reported, just two cases of DTC metastasis to the orbital have been described [25, 26].

The diagnosis of metastatic DTC of the skull base is a challenge prior to surgical intervention, to date, only 28 cases of skull base metastasis from DTC have been reported. The most common symptom of skull base metastasis from DTC is cranial nerve dysfunction. The metastatic lesion is usually revealed bone destruction and local invasion to the surrounding soft tissues on radiological examination, so that skull base metastasis from DTC is often mistaken as chordoma, chondrosarcoma, melanoma and other metastatic cancers [10, 27-29].

The calvarium is more favorite than skull base by DTC invasion, which usually presents as a soft painless slow growing scalp mass, growth of the disease causes the brain compression can result in increased intracranial pressure and neurological symptoms including headaches, neurological deficits, meningeal irritation, and seizures [3, 9, 11, 16, 30], it occasionally causes scalp ulceration and bleeding (case 3). Combined with our three cases, we reviewed the pertinent literature and summarized the radiological characteristics of calvarium metastasis from DTC. (i) most of the lesions were single, (ii) the tumors were total extradural and not invaded dura mater, but can invade the subcutaneous tissue, (iii) the lesions were oval or round-shaped with clear boundaries and revealed osteolytic feature, (iv) the tumors usually disrupt both the inner and outer tables of calvarium and the length-diameter of the tumor is longer than the bone defect, (v) the lesions mimicked a meningioma in both CT and MRI, and enhanced homogeneously, central necrosis can be found if the tumor growth voluminous [3, 9, 11-19, 31]. However, those features can also be found in other calvarium metastatic carcinoma such as hepatocellular carcinoma [32]. If a gradual exaggerated scalp mass with the radiological characteristics aforementioned, a diagnosis of calvarium metastasis should be taken in our consideration and the SPECT and biopsy should be performed [9, 12, 19].

Total or nearly total thyroidectomy and removal of as much of the metastatic lesions remain the first choice whenever possible, however, total excision in most cases of skull base metastasis is hazardous because of the presence of vital structures and profuse bleeding [3, 10, 16]. Bleeding is often profuse during surgical resection of calvarium metastasis which still interfered the tumor total resection [9, 16], in our case three, the tumor was just gross total resected for about 2000 ml of blood was gushed out in a short time when we resect the tumor. Adjunctive radiation with ^{131}I and replacement therapy with L - thyroxine should be performed postoperative [3, 9, 11]. External radiotherapy should be administered for unresectable or residual tumors [3, 20]. Kotecha et al reported that Gamma Knife surgery (GKS) is an effective treatment modality for patients with metastases to the calvarial bones or skull base [1]. Patients with larger lesions near vital structures or in a previously irradiated field might benefit from the fractionated stereotactic radiation technique [2]. Measurement of circulating TG to predict the recurrence of the DTC during follow up may be useful [20]. Despite a synthetical therapy, the outcomes for patients with skull metastasis form DTC are relatively poor, Nagamine et al reported that the mean survival time was 4.5 years, ranging from 5 months to 17 years in a series of 12 patients [3]. Li X et al reviewed the previous reports and calculated that overall survival among patients undergoing definitive treatment ranged from 14 months to 3.5 years from the discovery of the skull metastasis, the survival of untreated patients was even shorter [12].

In conclusion, we further contribute to the literature on the rare occurrence of skull metastasis from DTC, discussed the clinical manifes-

tation, imaging characteristics, differential diagnosis and postoperative management, and highlight that a systematical and multidisciplinary therapy of this rare entity should be performed.

Disclosure of conflict of interest

None.

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References

[1] Kotecha R, Angelov L, Barnett GH, Reddy CA, Suh JH, Murphy ES, Neyman G, Chao ST. Calvarial and skull base metastases: expanding the clinical utility of Gamma Knife surgery. J Neurosurg 2014; 121 Suppl: 91-101.

[2] Mitsuya K, Nakasu Y, Horiguchi S, Harada H, Nishimura T, Yuen S, Asakura K, Endo M. Metastatic skull tumors: MRI features and a new conventional classification. J Neurooncol 2011; 104: 239-245.

[3] Nagamine Y, Suzuki J, Katakura R, Yoshimoto T, Matoba N, Takaya K. Skull metastasis of thyroid carcinoma. Study of 12 cases. J Neurosurg 1985; 63: 526-531.

[4] Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, Mazzaferri EL, McIver B, Pacini F, Schlumberger M, Sherman SI, Steward DL, Tuttle RM. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2009; 19: 1167-1214.

[5] Jasim S, Ozsari L, Habra MA. Multikinase inhibitors use in differentiated thyroid carcinoma. Biologics 2014; 8: 281-291.

[6] Khan SH, Hassan MU, Bhau RS. Iodine-131 avid distant metastasis in differentiated thyroid cancer: An initial institutional experience from the northern part of India. Indian J Nucl Med 2015; 30: 227-232.

[7] Zettinig G, Fueger BJ, Passler C, Kaserer K, Pirich C, Dudczak R, Niederle B. Long-term follow-up of patients with bone metastases from differentiated thyroid carcinoma - surgery or conventional therapy? Clin Endocrinol (Oxf) 2002; 56: 377-382.

[8] Atkinson AL, Rosenthal A, Nardiello D. Follicular Thyroid Carcinoma Presenting as a Palpable Head Mass: A Case Report. Case Rep Oncol 2010; 3: 106-109.

[9] Wong GK, Boet R, Poon WS, Ng HK. Lytic skull metastasis secondary to thyroid carcinoma in an adolescent. Hong Kong Med J 2002; 8: 149-151.

[10] Matsuno A, Murakami M, Hoya K, Yamada SM, Miyamoto S, Yamada S, Son JH, Nishido H, Ide F, Nagashima H, Sugaya M, Hirohata T, Mizutani A, Okinaga H, Ishii Y, Tahara S, Teramoto A, Osamura RY, Yamazaki K, Ishida Y. Clinicopathological and molecular histochemical review of skull base metastasis from differentiated thyroid carcinoma. Acta Histochem Cytochem 2013; 46: 129-136.

[11] Feng D, Rhatigan R, Shuja S, Wolfson D, Makary R, Koch K, Masood S. Papillary thyroid carcinoma with metastasis to the frontal skull. Diagn Cytopathol 2009; 37: 522-526.

[12] Li X, Zhao G, Zhang Y, Ding K, Cao H, Yang D, Zhang J, Duan Z, Xin S. Skull metastasis revealing a papillary thyroid carcinoma. Chin J Cancer Res 2013; 25: 603-607.

[13] Ozdemir N, Senoğlu M, Acar UD, Canda MS. Skull metastasis of follicular thyroid carcinoma. Acta Neurochir (Wien) 2004; 146: 1155-1158; discussion 1158.

[14] Hashiba T, Maruno M, Fujimoto Y, Suzuki T, Wada K, Isaka T, Izumoto S, Yoshimine T. Skull metastasis from papillary thyroid carcinoma accompanied by neurofibromatosis type 1 and pheochromocytoma: report of a case. Brain Tumor Pathol 2006; 23: 97-100.

[15] Lu J, Frater JL, Kreisel FH, Marcus JN, Hassan A. Secondary lymphoma involving metastatic follicular thyroid carcinoma to the skull: a unique example of tumor-to-tumor metastasis. Head Neck Pathol 2008; 2: 209-212.

[16] Miyawaki S, Yamazaki R, Harada T, Takanashi S, Nagashima T, Nakaguchi H, Okazaki R, Yamazaki K, Ishida Y, Matsuno A. Skull metastasis of thyroid papillary carcinoma. J Clin Neurosci 2007; 14: 481-484.

[17] Kelessis NG, Prassas EP, Dascalopoulou DV, Apostolikas NA, Tavernaraki AP, Vassilopoulos P PP. Unusual metastatic spread of follicular thyroid carcinoma: report of a case. Surg Today 2005; 35: 300-303.

[18] Lin JD, Chan EC, Chao TC, Chen KT, Hsueh C, Ho YS, Weng HF. Expression of sodium iodide symporter in metastatic and follicular human thyroid tissues. Ann Oncol 2000; 11: 625-629.

[19] Sioka C, Skarulis MC, Tulloch-Reid MK, Heiss JD, Reynolds JC. "Hidden" bone metastasis from thyroid carcinoma: a clinical note. Rev Esp Med Nucl Imagen Mol 2014; 33: 36-38.

[20] Matsuno A, Katakami H, Okazaki R, Yamada S, Sasaki M, Nakaguchi H, Yamada SM, Hoya K, Murakami M, Yamazaki K, Ishida Y, Iwasaki H, Kuyama J, Kakudo K. Skull base metastasis from follicular thyroid carcinoma -two case re-

ports-. Neurol Med Chir (Tokyo) 2010; 50: 421-425.
[21] Tunio MA, Al Asiri M, Al-Qahtani KH, Aldandan S, Riaz K, Bayoumi Y. Skull base metastasis from papillary thyroid carcinoma: a report of three cases. Int Med Case Rep J 2015; 8: 127-131.
[22] Hugh SC, Enepekides D, Wong J, Yeung R, Lin VY. Metastasis of follicular variant of papillary thyroid carcinoma masquerading as primary temporal bone tumour. J Laryngol Otol 2011; 125: 528-532.
[23] Mydlarz WK, Wu J, Aygun N, Olivi A, Carey JP, Westra WH, Tufano RP. Management considerations for differentiated thyroid carcinoma presenting as a metastasis to the skull base. Laryngoscope 2007; 117: 1146-1152.
[24] Chrisoulidou A, Pazaitou-Panayiotou K, Flaris N, Drimonitis A, Giavroglou I, Ginikopoulou E, Vainas I. Pituitary metastasis of follicular thyroid carcinoma. Horm Res 2004; 61: 190-192.
[25] Pagsisihan DA, Aguilar AH, Maningat MP. Orbital metastasis as initial manifestation of a widespread papillary thyroid microcarcinoma. BMJ Case Rep 2015; 2015.
[26] Altinay S, Taşkin Ü, Aydin S, Oktay MF, Özen A, Ergül N. Metastatic follicular thyroid carcinoma masquerading as olfactory neuroblastoma: with skull-base, cranium, paranasal sinus, lung, and diffuse bone metastases. J Craniofac Surg 2015; 26: e3-6.
[27] Pallini R, Sabatino G, Doglietto F, Lauretti L, Fernandez E, Maira G. Clivus metastases: report of seven patients and literature review. Acta Neurochir (Wien) 2009; 151: 291-296.
[28] Rosahl SK, Erpenbeck V, Vorkapic P, Samii M. Solitary follicular thyroid carcinoma of the skull base and its differentiation from ectopic adenoma--review, use of galectin-3 and report of a new case. Clin Neurol Neurosurg 2000; 102: 149-155.
[29] Deconde AS, Sanaiha Y, Suh JD, Bhuta S, Bergsneider M, Wang MB. Metastatic disease to the clivus mimicking clival chordomas. J Neurol Surg B Skull Base 2013; 74: 292-299.
[30] Miyawaki S, Yamazaki R, Harada T, Takanashi S, Nagashima T, Nakaguchi H, Okazaki R, Yamazaki K, Ishida Y, Matsuno A. Skull metastasis of thyroid papillary carcinoma. J Clin Neurosci 2007; 14: 481-484.
[31] Nigam A, Singh AK, Singh SK, Singh N. Skull metastasis in papillary carcinoma of thyroid: A case report. World J Radiol 2012; 4: 286-290.
[32] Guo X, Yin J, Jiang Y. Solitary skull metastasis as the first symptom of hepatocellular carcinoma: case report and literature review. Neuropsychiatr Dis Treat 2014; 10: 681-686.