Brain metastases with exceptional features from papillary thyroid carcinoma: report of three cases

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Abstract

We present three papillary thyroid carcinoma PTC patients with brain metastases who are unusual in many aspects. The first case is a unique 3mm papillary thyroid microcarcinoma (PTMC) patient with metastases to the cerebrum and lung. The solitary cerebral lesion was identified by iodine-131 whole-body scan (^{131}I-WBS) and ^{131}I single photon emission tomography/computed tomography (SPET/CT). Almost complete response achieved after radiosurgery. The second case is a unique PTC patient with coexistent ^{131}I-negative cerebrum, adrenal gland and ilium metastases, which were identified by ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) and magnetic resonance imaging (MRI). Partial response achieved after radiosurgery. The third case is a patient with an incident solitary cystic cerebellar mass as a primary presentation of follicular variant of PTC and absent other distant metastases. *In conclusion,* widespread metastases from small PTMC may occur. Concomitant brain and adrenal metastases may occur in a same PTC patient. Brain metastasis may present as a cystic lesion.

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Introduction

The incidence of metastatic spread of thyroid carcinoma to the brain is unusual, with a frequency of about 0.15%-1.3% [1-4]. Only a few cases had been reported in the literature. Such metastases usually behave more aggressively and show poor prognosis. Because of its rarity, diagnosis and treatment of brain metastasis from differentiated thyroid carcinoma (DTC) are often problematic. Early detection of brain metastasis is crucial because the intracranial metastatic lesion can be life threatening. The reported survival time after diagnosis of brain metastases from thyroid cancer is less than 1 year [3, 5]. Appropriate treatment can lead to long-term survival and obtain a good prognosis because DTC is a relatively less severe clinical course unless associated with distant metastases.

Unusual clinical features contribute to the early detection of brain metastases. In this article, three papillary thyroid carcinoma (PTC) cases with brain metastases, which presented with exceptional features, were reported.

Cases description

Case 1

A 46 years old woman presented with a cervical mass and ultrasound examination detected thyroid nodes and calcifications. The patient underwent total thyroidectomy and lymph nodes dissection subsequently. Postoperative pathology confirmed papillary thyroid microcarcinoma (PTMC) 3mm in diameter and three cervical lymph nodes metastases. She was treated with 3.7GBq ^{131}I for ablation of the post-surgical thyroid remnant a month after thyroidectomy. The post-therapy ^{131}I whole-body scan (^{131}I-WBS) revealed diffuse pulmonary and a solitary cephalic uptake of ^{131}I in addition to the cervical uptake (Fig. 1A). The cervical ^{131}I uptake was due to residual thyroid tissue after surgery. The pulmonary uptake was due to lung metastases confirmed by the chest CT scans. To differentiate the cephalic uptake of ^{131}I, the patient was scheduled to the low-dose integrated ^{131}I single photon emission tomography/computed tomography (SPET/CT) scan. The ^{131}I SPET/CT fusion images showed that the cephalic lesion was located in the right side of the cerebrum (Fig. 1B, C). Further examination with magnetic resonance imaging (MRI) revealed a solitary metastatic lesion in the area of the right internal capsule of the cerebrum with marked peritumoral edema extending from the tumor margin (Fig. 1D). Because this metastatic lesion can be life threatening and surgical excision may lead to more compli-

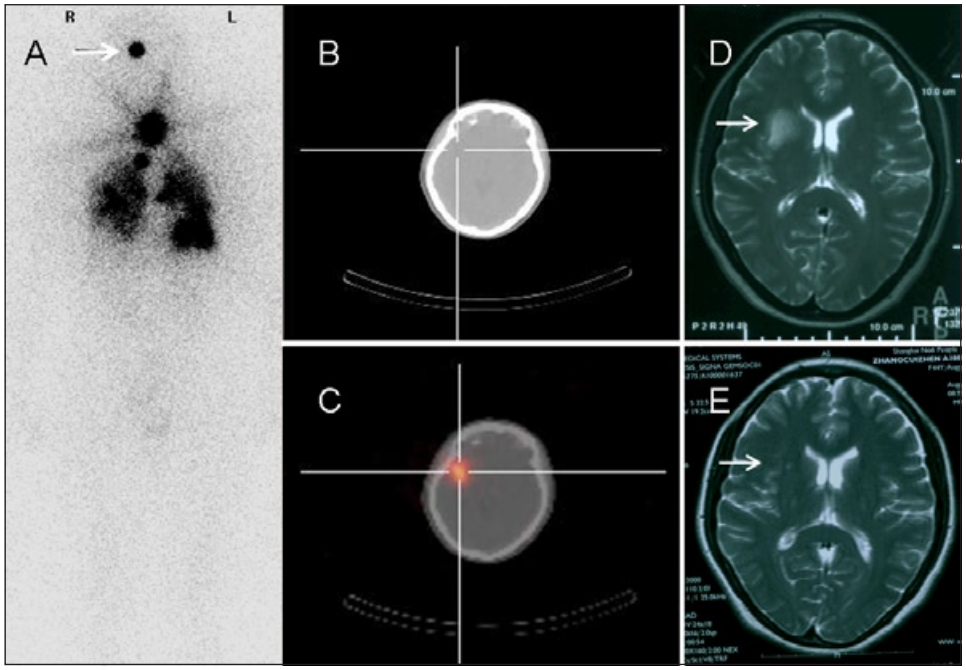

Figure 1. Brain metastasis of case 1. (**A**) ^{131}I-WBS revealed pulmonary and a single cephalic uptake (white arrow) of ^{131}I in addition to the cervical uptake. (**B**, **C**) ^{131}I SPET/CT fusion images showed the cephalic foci located in the right side of the cerebrum. (**D**) Brain MRI before radiosurgery. (**E**) Brain MRI after radiosurgery.

cations which may affect quality of life of the patient, the brain metastasis was subsequently treated by gamma knife radiosurgery with a total dose of 25Gy. Scan MRI images obtained 3 months after the radiosurgery showed that peritumoral edema was nearly totally disappeared and almost complete response of the lesion was achieved (Fig. 1E). The patient survived with no complication and has a normal performance.

Case 2

A 58 years old man had developed a left neck mass with biopsy positive for PTC. Total thyroidectomy and pathological examination revealed a 1.6cm well-differentiated PTC in the upper left lobe. He was treated with oral administration of 3.7GBq of ^{131}I for the ablation of remnant thyroid tissue one month after surgery and 5.55GBq of ^{131}I for detection and treatment of potential metastatic disease five months later. ^{131}I-WBS demonstrated no evidence for residual active thyroid tissue or metastatic disease after two courses of radioiodine treatment. However, serum thyroglobulin (Tg) was 2569ng/mL. The patient was suspected for high risk of metastatic disease and then ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) was performed to confirm whether or not the metastatic disease existed. A solitary metastatic lesion in the area of the right cerebrum (Fig. 2B), a left adrenal metastasis (Fig. 2D) and left iliac bone metastasis (Fig. 2E) were unexpectedly found by the ^{18}F-FDG-PET/CT scan (Fig. 2A). A head MRI revealed several brain metastatic lesions (Fig. 2C), of which only one lesion was ^{18}F-FDG-positive. Because the patient had multiple metastatic lesions, surgical excision could lead to more complications which could affect the quality of life. Thus brain, adrenal and iliac metastases were subsequently treated by gamma knife radiosurgery. Serum Tg obtained 3 months after radiosurgery dropped to 368ng/mL. Partial response was obtained.

Case 3

A 48 years old woman was presented at the emergency room with dizziness after a traffic *accident*. She was referred to have a MRI scan of the brain. A cystic tumor with a small nodule in the left cerebellum was found incidentally in T1 and T2 weighted MRI (Fig. 3A-C). The patient then under-

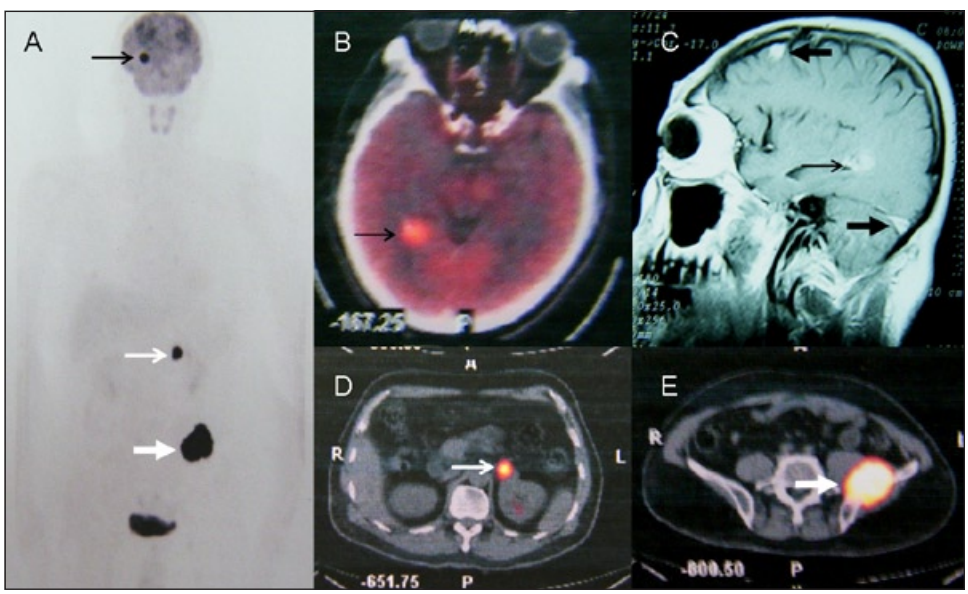

Figure 2. Brain metastases of case 2. (**A**, **B**, **D**, **E**) ^{18}F-FDG-PET/CT revealed a cerebrum metastasis (black arrow), a left adrenal metastasis (white thin arrow) and left iliac bone metastasis (white thick arrow). (**C**) Head MRI revealed two ^{18}FDG-negative brain metastatic lesions (black thick arrows).

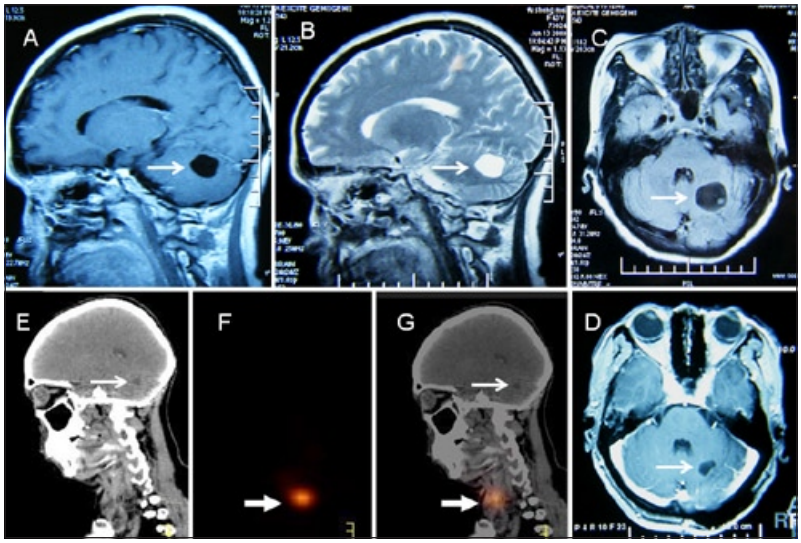

Figure 3. Brain metastasis of case 3. (**A**, **B**) Brain MRI showed a cystic tumor (white thin arrow). (**C**) Brain MRI with i.v. contrast revealed a cyst with a small mural nodule. (**D**) Brain MRI after surgery. (**E**, **F**, **G**) ^{131}I SPET/CT fusion images showed only radioiodine retention in the cervical residual thyroid and no uptake of ^{131}I in the remnant cerebellar metastatic lesion (white thin arrow).

went a left occipital craniotomy and excision of the cerebellar tumor. Histopathology showed that the tumor originated from the thyroid gland. A neck ultrasound found the presence of an ill-defined nodule with multiple calcifications located in the left thyroid lobe and several calcified cervical lymph nodes. The patient then underwent total thyroidectomy and left neck lymph nodes dissection. A 2.0X1.5X1.5cm follicular variant of PTC and 12 cervical lymph nodes with metastases were histopathologically confirmed. Post-surgery, MRI showed a sub-total excision of the metastatic cerebellum lesion (Fig. 3D). Six weeks postoperatively, the patient was treated with 5550MBq ^{131}I after a low-iodine diet and became hypothyroid by thyroid hormone withdrawal. ^{131}I-WBS and ^{131}I SPET/CT after ^{131}I treatment showed only ^{131}I uptake in the cervical residual thyroid tissue. However, no uptake of ^{131}I was found in the remnant cerebellar metastatic lesion (Fig. 3E, F, G).

Discussion

Differentiated thyroid carcinoma is a relatively uncommon malignancy that may metastasize in the body. Metastatic lesions from DTC are usually seen in the cervical lymph nodes, lungs or bones [6]. Brain metastases from DTC are extremely rare with a frequency of approximately 0.15-1.3% in the documented data. Most patients are asymptomatic, only a few have suggestive symptoms, including headache, nausea, focal motor weakness, and etc. It was reported that patients who developed brain metastases tended to have characteristics of aggressive DTC: older age, larger primary tumor, frequent evidence of extrathyroidal invasion and locoregional and distant metastases [4, 5, 7, 8].

A subset of PTC, PTMC is defined as measuring less than or equal to 1.0cm. It has been reported that PTMC>7mm has aggressive tumor features and disease recurrence similar to conventional PTC [9]. However, distant metastasis, especially brain metastasis from PMTC<5mm is very uncommon. Small PTMC usually remains clinically silent until its incidental histologic diagnosis in surgery. The present case 1 is the first patient with brain and lung metastases due to an occult 3mm PTMC. Thus the widely perceived notion that small PTMC are clinically insignificant and do not require active treatment will be questioned. Brain metastases were not all accompanied with a large primary thyroid malignancy in DTC patients. Widespread metastases from small PTMC may occur. Computed tomography and MRI provide excellent morphologic information on the extent of disease but have limited ability to differentiate or identify lesions. Recently developed SPET/CT can provide both the metabolic and anatomic information of a lesion [8, 10-12]. Case 1 demonstrated that ^{131}I SPET/CT fusion images can differentiate the brain metastasis from the cranium metastasis in DTC (Fig. 1).

Adrenal metastasis from PTC is an extremely rare event, only four cases reported in the past [13-16]. According to the literature, a unique PTC patient (case 2) with brain metastases involving concomitant adrenal metastasis was herein presented for the first time. This is a typical ^{131}I-negative and ^{18}F-FDG-positive metastatic case. ^{131}I-WBS is not reliable to detect brain metastasis which has no ability to accumulate ^{131}I. Metastatic lesions from DTC are usually less differentiated than the primary tumor. Some metastatic lesions, especially brain metastases are absence of differentiation, leading to no accumulation of ^{131}I in the metastatic site [17]. Others have reported 12 patients with single brain metastases and no metastasis was ^{131}I-positive [18]. Fluorine-18-FDG-PET/CT is a sensitive method to detect metastases which were negative for ^{131}I-WBS in patients with elevated serum Tg levels. However, compared to MRI, ^{18}F-FDG-PET/CT can not reveal all brain metastatic lesions in this case. Therefore, MRI is the most sensitive method for the detection of brain metastases.

Brain metastasis, especially solitary cerebellar metastasis, may rarely be the initial presentation of DTC. To our knowledge, only six cases with cerebellar metastases from PTC were reported in the literature [2, 19-23]. Moreover, most brain metastases from all cancers are solid masses with necrosis and surrounding edema, whereas purely cystic lesions are very uncommon and malignant cells creating the wall of these cysts are usually resistant to radiotherapy, requiring neurosurgical strategies. Cystic brain metastases from DTC are extremely rare and were not reported previously in the literature. Case 3 in this study is an interesting patient presented with PTC that metastasized to the cerebellum as a solitary cyst, which was the initial presentation of PTC in the absence of other distant disseminations. In addition, brain T1-weighted MRI with i.v. contrast in case 3 revealed a cyst with a small mural nodule (Fig. 3C), which can be easily confused with intracranial hemangioblastomas, therefore, differential diagnosis should be carefully taken into account in the clinical setting. In this case, no radioiodine uptake in the post-surgery remnant cerebellar metastasis may be probably related to the dedifferentiation and cystic change of the lesion.

Brain metastases due to *DTC* occur rarely and represent a diagnostic challenge. Exceptional cases are dedicated to the

rationale method for screening brain metastases in DTC patients. Primarily, the usual syndrome of a brain metastasis is a neurologic problem such as headache, nausea, focal motor weakness, sensory loss, or cognitive impairment. A DTC patient with a neurologic symptom should be suspected of brain metastasis. However, others have reported 47 cases with brain metastases from thyroid cancer, of which, 23% were asymptomatic and discovered at postmortem examination [3]. An unexplained elevation of serum Tg is helpful to indicate metastasis from DTC. Therefore, it is important to consider the possibility of a brain metastasis when the serum Tg level is unexpectedly elevated. Moreover, given the frequent association of brain metastases coexistent with other sites of distant metastases, it would seem reasonable to consider routine MRI examination of the brain in an old patient with DTC who develops any evidence of distant metastatic disease [3].

The presence of brain metastasis is a negative prognostic factor; therefore, treatment must be tailored to the individual patient [24]. Surgery, radiotherapy, and radioiodine treatment have been used with varying results for treatment of brain metastases from DTC. A solitary lesion with complete surgical resection was found to be associated with a better prognosis [3]. However, if patients are at high risk for surgery or if surgery is impossible, radiosurgery may be considered as the best therapeutic choice. Radiosurgery is an effective and minimally invasive strategy for management of brain metastases, especially solitary metastasis [25]. Whole brain irradiation is usually used to treat multiple lesions [26]. Radioiodine treatment is a reasonable treatment option if the ^{131}I-WBS is positive. Chemotherapy has only a limited role in the management of DTC with extracranial metastases, and this appears to hold true for intracranial metastases as well [25].

In conclusion, we present three DTC patients with brain metastasis who are unusual in many aspects. We learned from this experience that widespread metastases from small PTMC may occur. The aggressiveness was not related to tumor size. Furthermore, this report firstly presented a DTC patient with concomitant brain and adrenal metastases and a patient with a solitary cystic cerebellar metastasis as initial presentation in the absence of other distant metastasis. Radiosurgery is an effective and minimally invasive strategy for management of brain metastases in DTC.

All authors have no conflicts of interest

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