

Case Reports

Papillary Carcinoma of the Thyroid with Distant Metastases to the Cerebrum: a Case Report

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Cerebral metastases from papillary carcinoma of the thyroid are a very uncommon condition, but such metastases behave more aggressively and show poor prognosis. These metastases almost always involve concomitant lung or bone metastases which may be the first metastatic sites. Here we report a 53-year-old man with diffuse goiter and cervical lymphadenopathy who developed symptoms of elevated intracranial pressure. Computed tomography demonstrated ring-enhanced lesions showing a severe mass effect in the right cerebrum and a nodule in the right thyroid gland accompanied by swollen lymph nodes. Biopsied specimens of the thyroid nodule demonstrated malignant cells of papillary carcinoma. Surgical excision of the metastatic brain lesions was followed by total thyroidectomy with regional lymphadenectomy. Histological examinations confirmed that the patient had cerebral metastases from papillary carcinoma of the thyroid without other distant metastasis. Neurological abnormality disappeared after surgery and treatment with radioactive iodine (¹³¹I) and oral thyroxine were initiated thereafter. This case suggests that the thyroid gland is potentially a primary source of metastatic brain carcinoma. Moreover, early detection of cerebral metastases is crucial because these metastatic lesions can be life threatening, in contrast to the relatively less severe clinical course of this malignancy unless it is associated with any distant metastasis.

Key words: thyroid papillary carcinoma – cerebral metastases – neurological deficit – craniotomy

INTRODUCTION

Papillary carcinoma of the thyroid, the most common form of thyroid malignancy, generally carries a good prognosis since it usually remains intrathyroidal and tends to metastasize locally to regional lymph nodes alone (1–4). However, distant metastases mainly including lung and bone lesions are very uncommon. Especially, cerebral metastases from this type of cancer, which suggest an aggressive disease and have an unfavorable prognosis (5–7), are very rare, with a frequency of 0.4–1.2% of the overall patient population, but cerebral metastases show almost the same potential as a first metastatic site as the lungs or bones (8–11). However, early detection and treatment of these metastatic lesions can lead to long-term survival (8,9,12,13).

We report a patient with papillary carcinoma of the thyroid associated with cerebral metastases in the absence of other sites of tumor dissemination. He first developed signs and symptoms of an intracranial space-occupying lesion, revealing severe brain damage that was considered irreversible and life threatening. We also observed the beneficial effects of early detection and surgical removal of this metastatic lesion.

CASE REPORT

A 53-year-old man without personal or family history of thyroid disease was referred to our hospital in June 1997 complaining of frontal headache and impaired vision that had persisted for 2 weeks. He had first developed some recent memory loss in November 1995 and subsequently made excessively vague mistakes in his daily life 1 year later. Physical examination revealed a diffuse thyroid swelling with enlarged left cervical lymph nodes ~2 cm in diameter. The nodes were not tender and showed an elastic, firm consistency with immo-

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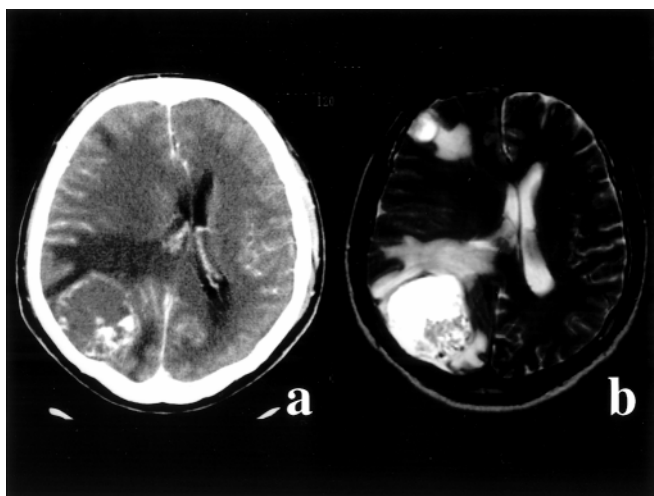


Figure 1. (a) Brain computed tomography (CT) revealing a ring-enhanced lesion with mass effect in the right parieto-occipital region. (b) T2-weighted magnetic resonance imaging (MRI) clearly demonstrates multiple cerebral metastases with hemorrhage.

bility. He also presented disorientation and left homonymous hemianopsia. Fundoscopic examination revealed papilledema in the eyes, but the pupils were equal in size, not dilated and reacted promptly to light and accommodation. Neurological examination showed normal symmetric reflexes, the cranial nerves were intact except for the optic nerve and there were no meningeal signs. He showed a steady gait and normal muscle strength. Hematological and biochemical examinations, including thyroid function test and chest X-ray, did not reveal any abnormal findings.

Since these neurological symptoms suggested the existence of intracranial space-occupying lesions, cranial computed tomography (CT) was immediately performed. These images disclosed a 4.5×4 cm ring-enhancing lesion in the right parieto-occipital portion accompanied by surrounding edema and definite midline shift to the opposite side (Fig. 1a). T2-weighted magnetic resonance imaging (MRI) disclosed another 1×1 cm high-intensity mass in the right frontal lobe within which a high-intensity area was present, possibly indicating intratumorous hemorrhage (Fig. 1b). A neck CT revealed a low-density mass accompanied by small foci of calcification in the right lobe of the thyroid gland and regional lymph node involvement, suggesting this lesion potentially to be a primary malignancy. Other examinations including thoracic and abdominal CT with contrast enhancement did not reveal other tumorous lesions elsewhere in the body. Fine-needle aspiration cytology of the thyroid revealed malignant cells of papillary carcinoma characterized by ground-glass nuclei with intranuclear pseudoinclusions and nuclear grooves.

Since the size of the brain tumors progressively increased with deterioration of neurological symptoms, they were removed surgically through a right parieto-occipital and frontal craniotomy on day 7 of the hospital stay. The hemorrhagic and well-circumscribed tumors surrounded by xanthochromic

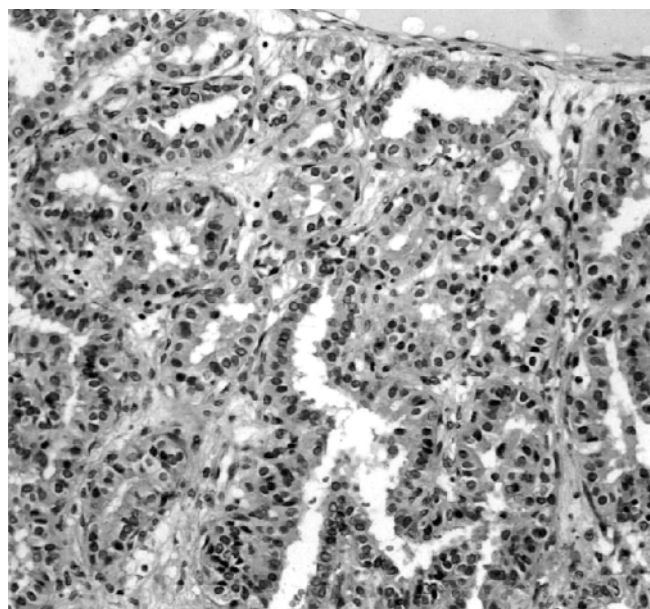


Figure 2. Well-differentiated metastatic carcinoma replacing cerebrum (hematoxylin-eosin, 400 \times).

fluid were readily separated from cerebral parenchyma and appeared non-invasive. Tissue histopathology revealed papillary carcinoma characterized by a follicular growth pattern containing colloid (Fig. 2).

Headache, disorientation and visual field defects disappeared immediately after surgery and other neurological examinations did not disclose any abnormal findings. Total thyroidectomy with regional cervical lymphadenectomy was performed 2 weeks after craniotomy. On gross examination, the tumor occupied the entire thyroid gland, showing a white appearance with nodular shape and stony consistency. Small foci of calcification (psammoma bodies) were also noted on a cross-section of the thyroid.

Histopathology confirmed the diagnosis of papillary carcinoma of the thyroid with regional lymph node invasion showing extracapsular extension accompanied by evident vascular invasions (Fig. 3), where the appearance was definitely identical with that of the cerebral papillary carcinoma. Moreover, all the resected brain metastases stained positively for thyroglobulin (Tg) with anti-Tg antibody (Fig. 4). Based on these findings, a definite diagnosis of multiple cerebral metastases from papillary carcinoma of the thyroid was made.

Six months after the thyroidectomy, the patient developed rapid swelling of the left cervical lymph nodes, suggesting local recurrence. Thyroid function tests showed definitely decreased free thyroxine (FT4) 0.20 ng/dl (normal range 0.85–1.72 ng/dl) and free triiodothyronine (FT3) 1.03 pg/ml (normal range 2.31–4.07 pg/ml) associated with a marked increase in thyrotropin (TSH) 156 μ U/ml (normal range 0.32–4.57 μ U/ml), while he was taking 50 μ g of triiodothyronine daily as postoperative replacement therapy. A total body radioiodine scan showed marked activity in the neck with no focal uptake

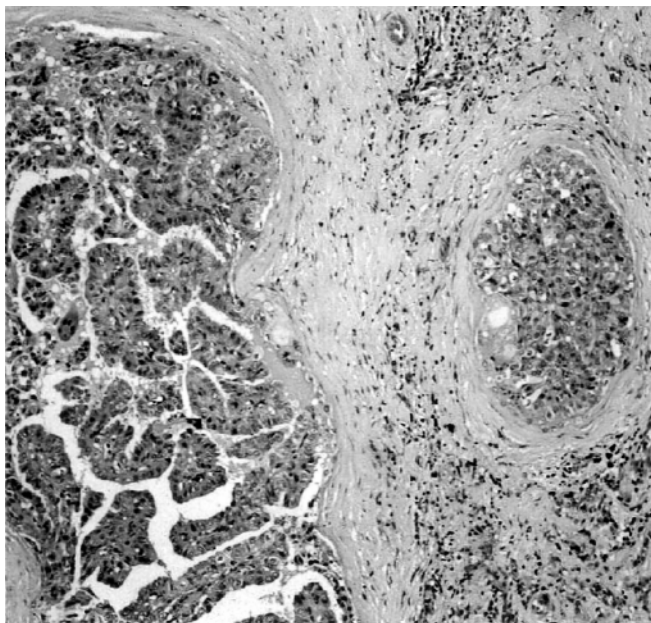


Figure 3. Well-differentiated papillary carcinoma of the thyroid with evident vascular invasions (hematoxylin–eosin, 200×).

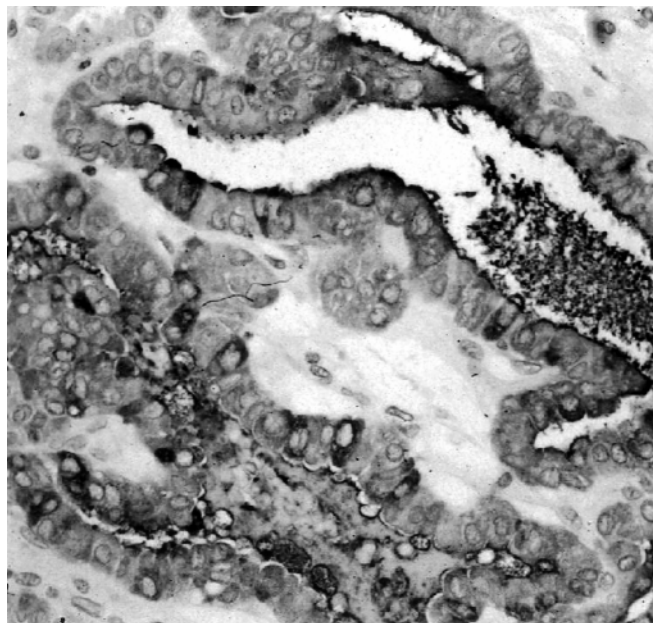


Figure 4. Cerebral metastases: immunostaining with anti-Tg antibody. Note the intense staining of most cells (400×).

in the cerebrum and lungs. He underwent left neck dissection and lymphadenectomy again and received 200 mCi of radioactive iodine (^{131}I) thereafter, followed by replacement therapy with 75 μg of triiodothyronine daily. Since his general condition remained well, he was discharged from our hospital 1 week after completing radiotherapy. A follow-up cranial and neck CT scan taken 1 year after completion of treatment showed no tumor recurrence. No other neurological deficits appeared, but he did not report for follow-up after January 1999.

DISCUSSION

Papillary carcinoma of the thyroid has commonly a relatively less severe clinical course and thus behaves unlike other thyroid cancers such as follicular or anaplastic carcinoma, which more readily metastasize or infiltrate locally (1–4). However, the subgroup of papillary carcinoma of the thyroid which develops distant metastases is known to have a worse prognosis (5–7). Distant metastases from papillary carcinoma of the thyroid are uncommon. Moreover, brain metastases are extremely rare and few reports have appeared in the literature. In a series reported by Hoie et al. (2), 91 of 731 patients with papillary carcinoma of the thyroid had distant metastases and only nine of these patients (1.2%) had brain metastases. According to a clinicopathological study of this malignancy by Carcangiu et al. (3), only one of 241 (0.4%) patients had brain metastases. Further, McConahey et al. (4) reviewed 859 patients with this malignancy and 11 (1.3%) were identified as having cerebral metastases.

Based on a summary of clinicopathological findings from previous case reports describing papillary carcinoma of the thyroid accompanied by brain metastasis (Table 1), the present case showed some interesting clinical characteristics. First, a focal neurological deficit due to cerebral metastases developed as the initial symptom while the primary and metastatic cancers were detected at the same time. All previous cases revealed neurological deficit as a result of brain metastasis after surgery for primary thyroid cancer (8–11), except for one case report with metastatic brain tumor from occult papillary carcinoma of the thyroid which presented with frontal headache and impaired vision as the initial symptoms (12). Second, no other sites of tumor dissemination were detected regardless of our vigorous systemic examinations. As shown in previous case reports (Table 1), patients with brain metastases almost always showed complications with other sites of metastasis such as the lungs, bones or liver (8–11), which may be primary metastatic sites potentially through hematogenic dissemination. Similarly, in the present case, cerebral metastases may develop through direct hematogenic routes based on histological findings of evident vascular invasions of malignant cells (Fig. 3). Third, metastatic brain lesions observed in our case behaved in an unusual progressive manner compared with previous case reports (Table 1), finally showing lethal signs of elevated intracranial pressure: papilledema, midline shift, surrounding edema and intratumorous hemorrhage. Probably the metastatic brain tumors gradually induce elevated intracranial pressure when they become large enough, because the two cerebral metastases incidentally developed at sites without showing any focal symptoms.

Table 1. Clinicopathological features of patients with papillary carcinoma of the thyroid associated with brain metastases

Ref.	Age/gender	Initial symptom	Metastases to regional nodes	Other metastatic sites	Therapy for brain metastasis	Evolution (time of reporting)
7	67/M	Neck mass	Yes	Skull	¹³¹ I	Dead of tumor
8 (2 cases)	67/M	Neck mass	Yes	Rib and lung	¹³¹ I	Alive with disease
	79/M	Neck mass	Yes	None	CR + ¹³¹ I	Alive with disease
12	47/M	Headache	No	None	CR + ¹³¹ I	Alive with disease
6	52/F	Hoarseness	No	None	Ext. X-rays	Dead of tumor
9	55/F	Neck mass	Yes	Vertebra	Ext. X-rays	Alive with disease
10 (2 cases)	51/M	Neck mass	No	Lung	CR + ¹³¹ I	Alive with disease
	59/M	Neck mass	Yes	None	CR + ¹³¹ I	Alive with disease
11	82/F	Neck mass	Yes	Lung and vertebra	CR + ¹³¹ I	Dead of pneumonia

CR, excision of brain metastases with craniotomy; Ext., external.

However, the patient was successfully treated by surgical removal followed by ¹³¹I radiotherapy leading to immediate disappearance of clinical symptoms and signs. According to the previous reports (8–11), successful removal of the brain metastatic lesion significantly improves neurological dysfunction and lowers the rate of cancer mortality. Supportive treatment with radioiodine may develop tumor regression resulting in improvement of disease-free intervals (5,13,14). Therefore, early detection of the metastases and surgical removal with subsequent adequate radiotherapy are essential for obtaining increased patient survival and improved long-term prognosis. (3–5,13–15).

In summary, we have reported a case of a papillary carcinoma of the thyroid with multiple cerebral metastases in the absence of other distant disseminations, which was well controlled by surgical removal of the tumors and postoperative ¹³¹I treatment. The present case suggested that the thyroid gland should not be excluded as the primary source of metastatic brain carcinoma and rapid detection and appropriate treatment including surgical removal of the metastatic lesions are critical for obtaining a good prognosis.

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