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CASE REPORT

Intrathyroideal Papillary Thyroid Carcinoma Presenting with a Solitary Brain Metastasis

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Papillary thyroid carcinoma (PTC) is the most common type of well-differentiated thyroid carcinoma and typically has an excellent prognosis. The incidence of distant metastasis from PTC is low. However, once metastasis has developed in a distant site, prognosis is markedly diminished. Brain metastases from PTC are extremely rare. No consensus regarding management has yet been reached. We report on the case of a patient who presented with signs of intracranial hypertension. Cranial magnetic resonance imaging (MRI) identified a lesion of the right temporofrontoparietal lobe. The patient underwent a craniotomy with a total removal of the tumor. Histologic examination of the lesion showed a metastasis of papillary adenocarcinoma. We observed a cold nodule in the right lobe of the thyroid on physical examination and imaging techniques (e.g., CT and scintigraphy). Fine-needle-aspiration cytology of the nodule was reported as PTC. A total thyroidectomy was performed and histopathological examination showed intrathyroidal variant of PTC. Postoperatively adjuvant whole brain radiation therapy with 44 Gy to multiple brain metastases of PTC was applied. One month later, the patient then underwent ^{131}I radioiodine therapy with 150 mCi of ^{131}I given orally. In conclusion, the present case underwent an aggressive multimodal approach to therapy. This report indicates that the early detection and control of brain metastases may contribute to a better quality of life for patients affected by brain metastases.

Key Words: Papillary thyroid carcinoma; brain metastasis; management.

Introduction

Papillary thyroid carcinoma (PTC) is the most common type of well-differentiated thyroid carcinoma. It is classically described as having an indolent nature and, consequently, a favorable prognosis. Metastases usually occur in the regional lymph nodes, including the cervical and upper mediastinal nodes at the time of initial diagnosis *(1)*. Regional lymph node metastases do not typically affect the overall prognosis of PTC *(2,3)*, but distant metastases, most commonly to lung and bone and present in 1–7% of patients wih PTC, alter survival dramatically *(2,4,5)*.

Brain metastases are extremely rare, constituting 0.1–5% of distant metastases of PTC *(4–9)*. However, this type of metastasis also presents potentially serious complications such as cerebral edema, tonsillar herniation, or intracranial hemorrhage *(10,11)*. Therefore, an early and accurate diagnosis followed by the proper management of brain metastases may prevent irreversible brain damage and thus prolong the patient's survival *(12)*. In addition, only 76 cases of brain metastases have been reported in the English literature. To date, however, there have been a few case reports of multiple brain metastases (parenchymal and leptomeningeal) from intrathyroideal PTC.

We report a patient with PTC metastatic to the supratentorial space and to the posterior to the medulla oblongata. The clinical diagnosis, pathological features, and management of these neoplasms are discussed.

Case Report

A 45-yr-old-woman presented to Neurosurgery Clinic with a 3-mo history of nausea, vomiting, and headache. The patient was hospitalized to Neurosurgery Clinic. A cranial magnetic resonance (MR) scan revealed a heterogeneous enhanced mass, 4 cm in diameter, in the right temporofrontoparietal lobe, associated with a mass effect (Fig. 1). The patient whose neurological status was deteriorated underwent a craniotomy with a total removal of the tumor. A microscopic examination of the lesion showed a metastasis

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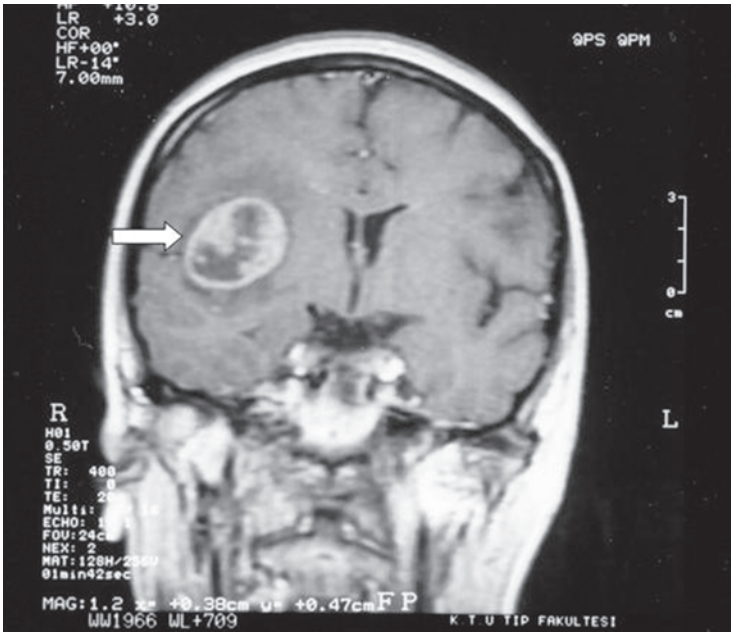

Fig. 1. Contrast-enhanced T1-weighted coronal cranial MR imaging shows peripheral nodular enhancing mass in the right temporofrontoparietal lobe, associated with a mass effect (arrow).

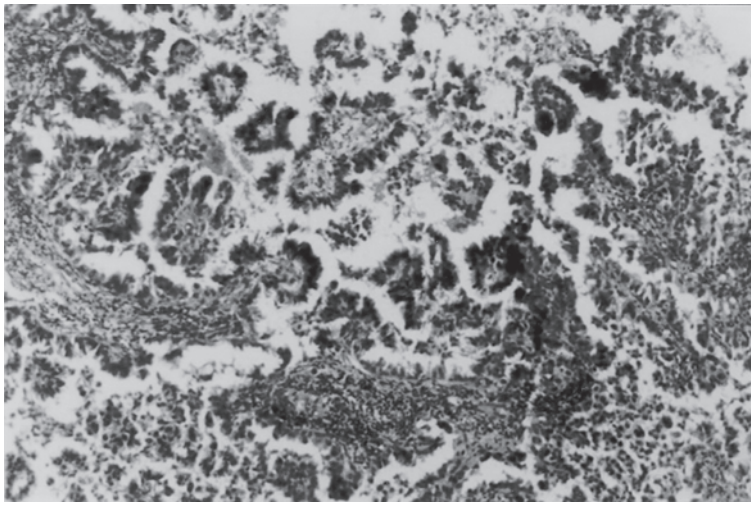

Fig. 2. Light microscopic examinations of a surgical resection specimen from a brain PTC metastasis. The papillary architecture can be observed (hematoxylin and eosin; original magnification, ×100).

of papillary adenocarcinoma (Fig. 2). Thyroglobulin staining was negative. The patient was transferred to Internal Medicine Clinic. On physical examination, she was noted to have a palpable hard mass, 3 cm in diameter, in the right lobe of the thyroid gland. Serum total triodothyronine (TT_3) was 1.10 ng/mL (normal range 0.8–2.0), serum total thyroxine was (TT_4) 8.7 μg/dL (normal range 5.1–14.1), serum thyrotropin (TSH) was 0.08 mIU/L (normal range 0.27–4.2), serum free-triodothyronine (FT_3) was 2.47 pg/mL (normal range 1.8–4.6), and free thyroxine (FT_4) was 1.56 ng/dL (normal range 0.9–1.7).

Postoperatively, 1-mo later, a cranial MR scan demonstrated metastatic multiple hyperintense nodular lesions in the brain parenchyma associated with leptomeningeal involvement (Fig. 3). Cervical spiral CT scan revealed a hypodense nodule, 3 cm in diameter in the right thyroid lobe (Fig. 4). Thyroid scintigraphy showed a cold nodule in the right thyroid lobe (Fig. 5). Chest CT scans revealed a mass, 3 cm in diameter, in the superior segment of the lower lobe of right lung and metastatic mediastinal lympadenopathy (Fig. 6). Bone scintigraphy was normal.

Fine-needle-aspiration cytology of the cold nodule in the right thyroid lobe was reported as PTC (Fig. 7). A total thyroidectomy was performed and histopathological examination showed intrathyroidal PTC (Fig. 8). The cells showed negative immunohistochemistry staining for thyroglobu-

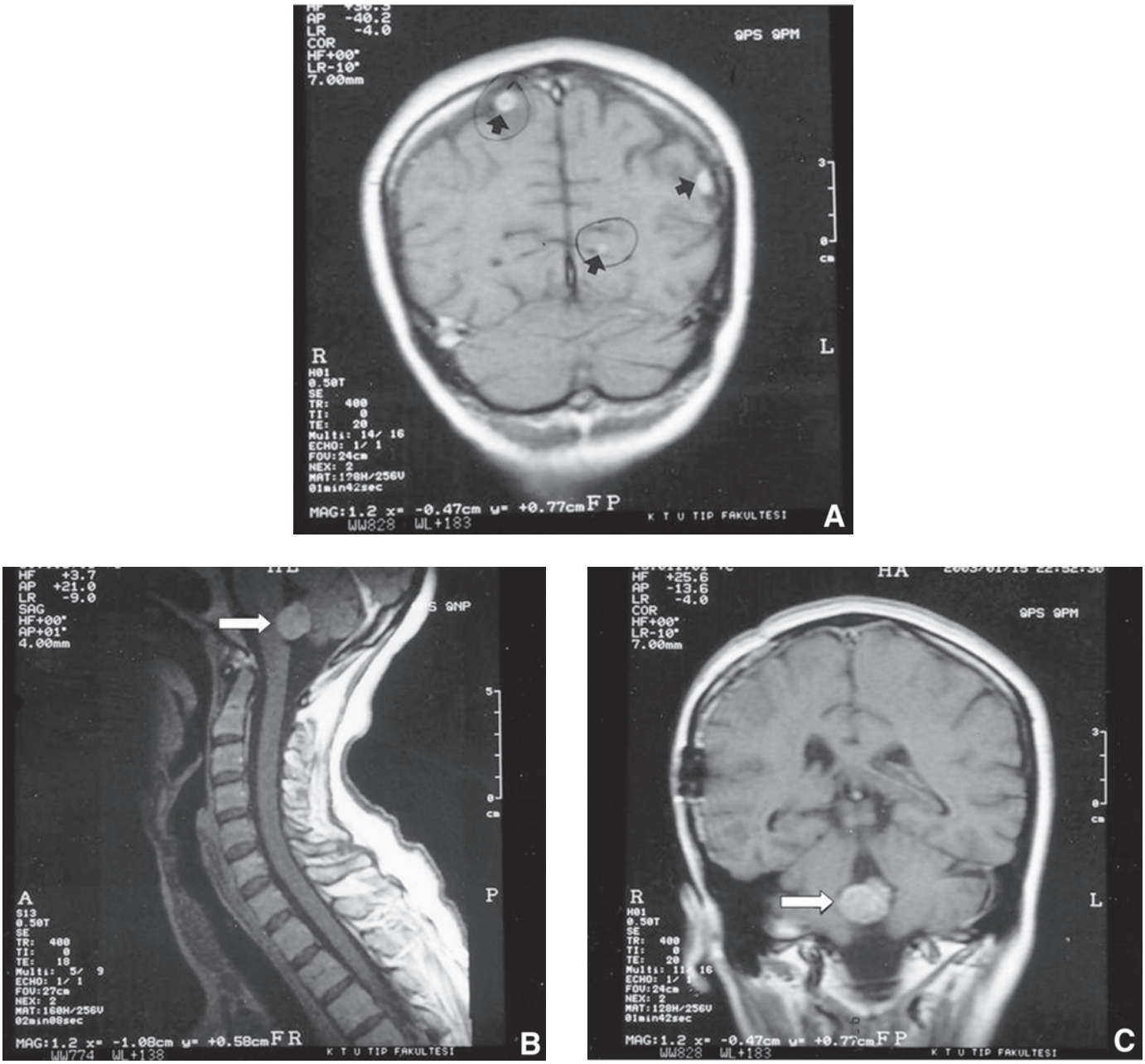

Fig. 3. Contrast-enhanced T1-weighted coronal cranial MR images. (**A**) Multiple enhancing nodular masses in the bilateral parietal and left ocipital lobes (arrows). (**B**) Contrast-enhanced T1-weighted sagittal cranial MR imaging shows enhancing solid mass at the base of the fourth ventricle (arrow). (**C**) Appearance of same mass in **B** on coronal T1-weighted MR imaging (arrow).

lin and showed positive immunohistochemistry staining for low-molecular-weight keratin. Psammoma bodies were rare. Postoperatively, the serum thyroglobulin levels was 6.7 ng/mL.

The patient then underwent adjuvant whole brain radiation therapy (WBRT) with parallel opposed 6 mv photon beams to a dose of 44 Gy in 22 fractions over 31 calender days at 2 Gy per fraction.

One month later, the patient then underwent ^{131}I radioiodine therapy with 150 mCi of ^{131}I given orally. At 7-mo follow-up, the patient is symptom free.

Discussion

The incidence of thyroid carcinoma is estimated to be 1 in 25,000 to 1 in 27,000 people *(13)*. PTC is the most comon type of well-differentiated carcinoma of the thyroid, constituting 81.2% of thyroid malignancies *(2)*. This tumor is two to three times more common among female subjects than among male subjects. The typical clinical course of PTC is indolent, and overall prognosis is usually excellent. Reported survival rates for nonmetastatic lesions are 97.8% at 5 yr and 94.9% at 10 yr *(2)*. The peak prevalence is the third decade of life for both men and women. In younger

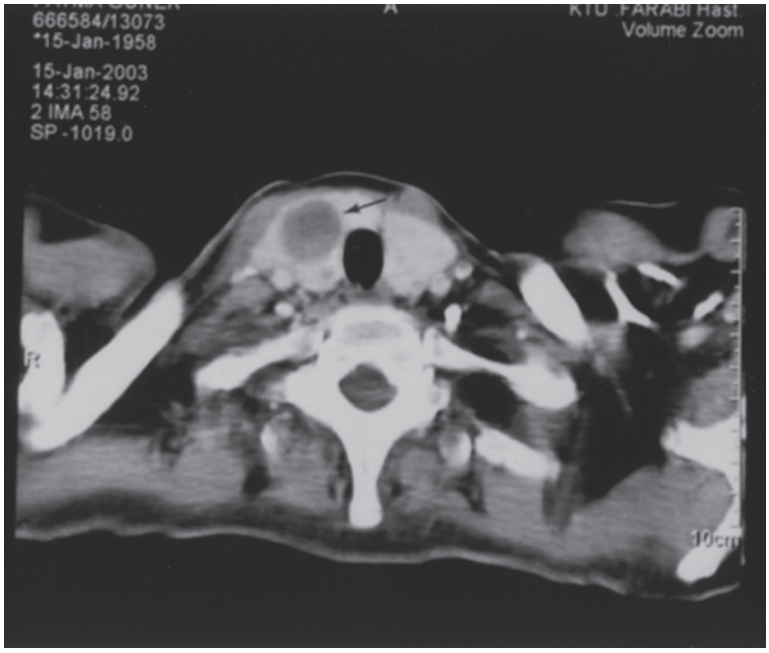

Fig. 4. Contrast-enhanced cervical CT scan shows a hypodense nodule in the right lobe at the thyroid (arrow).

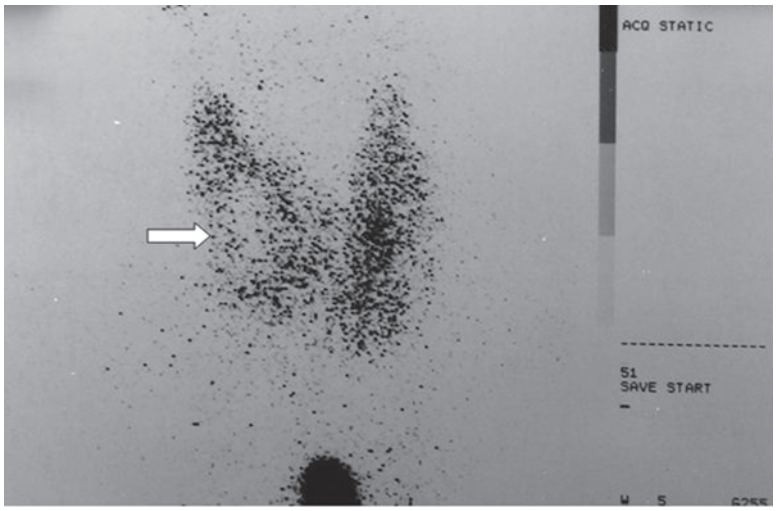

Fig. 5. Thyroid scintigraphy shows a cold nodule in the right thyroid lobe (arrow).

patients, the tumor is usually confined to the neck with or without spread to regional lymph nodes, but in older patients PTC tends to be more agressive and may give rise to distant metastases *(14)*.

The incidence of distant metastases from PTC ranges from 5% to 14% at the time diagnosis *(7)*. McConahey et al. *(3)* and Hoie et al. *(5)* describe risk factors for distant metastases of PTC. These include male gender, advanced age, histologic grade, and extrathyroidal invasion on initial examination. The most frequent sites for distant metastases are the lung (72–76% of cases), the mediastinum (24%), and the bone (19–23%) *(1,3,15)*.

Metastases to the brain from PTC are extremely rare. To our knowledge, the incidence of intracranial metastases of PTC is approx 0.1–to 5% in all reported series *(3,5,15,16)*. Only 78 references to brain metastases from PTC have been made in the medical literature *(4,6,7,12,17–20)*. Cerebral metastases usually present in association with other previously treated thyroid tumors or with disseminated metastases *(15,21,22)*. There were only 17 reported cases of solitary brain metastases *(7,19)*.

The anotomic sites of the central nervous system (CNS) PTC metastases were reported in 36 of the 80 cases, and included the cerebrum (69%), the cerebellum (13%), and the spinal cord (18%).

Biopsy and fine needle aspiration of the primary thyroid lesions are generally the diagnostic methods of choice for PTC *(23,24)*. These neoplasms generally exhibit a small

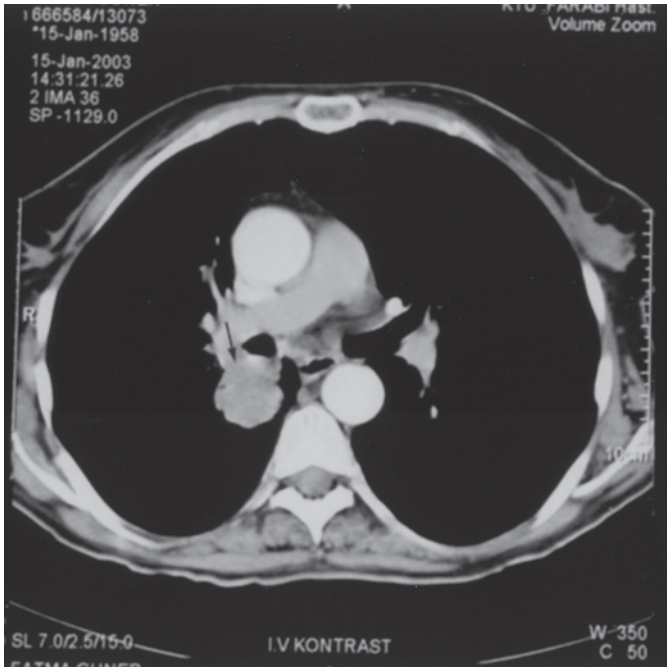

Fig. 6. Contrast-enhanced thoracal CT scan shows in the superior segment of lower lobe of right lung (arrow).

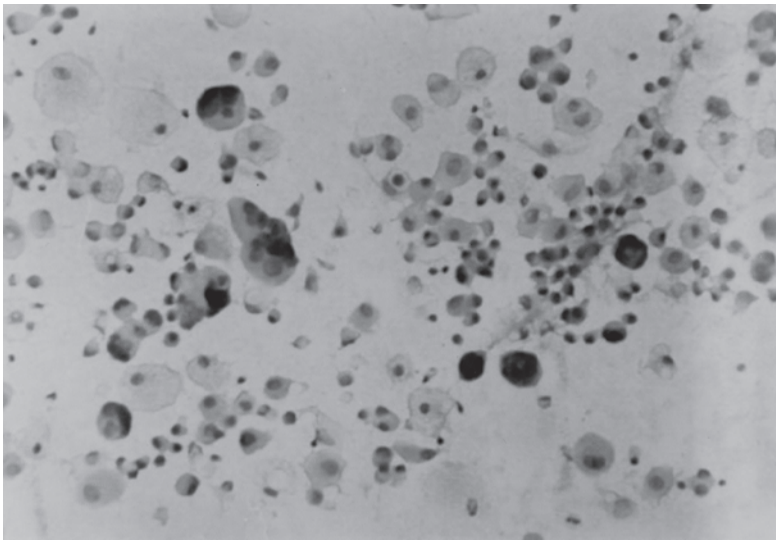

Fig. 7. Fine-needle aspiration biopsy demonsrating papillary clusters with inflammatory cells (Hematoxylin and eosin, original magnification ×100).

amount of smearing colloid, described as "bubble colloid." They can exhibit papillary architecture, form flat sheets, or exhibit follicle formation. The nuclei are usually large and overlapping, with a vesicular or optically clear chromatin pattern ("Orphan Annie nuclei"). Other important nuclear features are nuclear groves, nuclear pseudoinclusions, dense cytoplasm with a squamoid appearance, and psammoma bodies *(15)*. The typical findings described above were observed in the case reported here (Figs. 2 and 8).

Mizukami et al. reported that, in 24 PTC associated with distant metastases, nine were follicular variant type, seven were trabecular type, and eight were well-differentiated type *(25)*. In well-differentiated PTC, most of the tumors have exhibited an extrathyroidal extension, and only one case was intrathyroidal carcinoma. Distant metastases from intrathyroidal carcinoma are extremely rare.

There is no clearly defined treatment protocol for patients with intracranial metastatic lesions of PTC. Therapy must therefore be tailored to each individual patient. Such lesions could induce life-threatening complications such as increased intracranial pressure, cerebral edema, tonsillar herniation, or intracranial hemorrhage. Early recognition of the presence of an intracranial mass should prompt immediate attention and the institution of a treatment plan *(4,6–9,25)*.

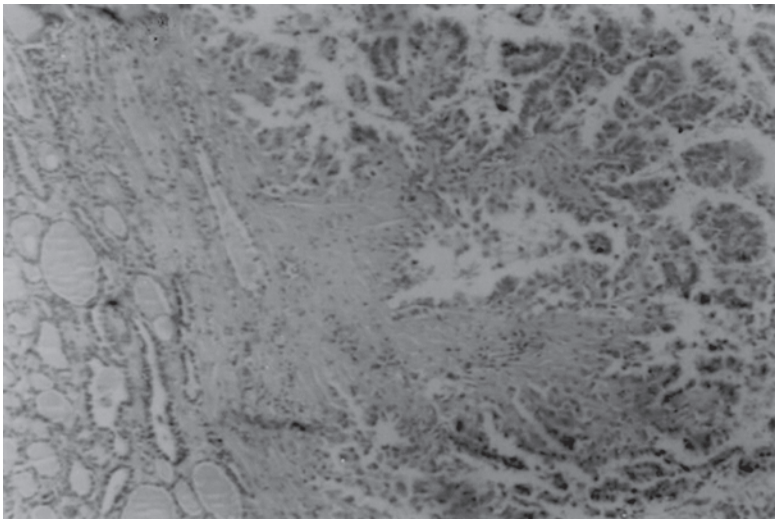

Fig. 8. Papillary carcinoma, well-differentiated type. Well-developed papillary proliferation of follicular cells is visible. Distinct "ground-glass" nuclei are characteristic. Neoplasm is seen beside the normal thyroid tissue (hematoxylin and eosin, original magnification ×100).

Several treatment modalities have been used in the limited number of cases of intracranial metastatic PTC, including surgical resection, external beam radiation, and radioiodine therapy. Results have been equivocal *(4,6,7,19,20)*. Although the presence of a brain metastasis is an overall negative prognostic indicator, Chiu et al. *(4)* have found surgical resection of the brain metastases may help to significantly prolong survival in patients with differentiated thyroid carcinoma.

In our case, surgery was scheduled on a semi-urgent basis due to the patient's deteriorating neurological status. The resection was incomplete due to involvement of critical structures in the posterior fossa, but did achieve the primary goal of halting the progressive decline in the neurological function.

In general, PTC has a good prognosis, with an overall mortality rate of less than 6.5%. However, a considerable number of patients with PTC die as a result of distant metastases or local tumor infiltration *(7,25)*. According to McConahey et al. *(3)*, CNS metastases from PTC are associated with high mortality rates. Surgery to treat the primary neoplasms, as well as resection of single metastases to the CNS or irradiation of multiple lesions, yielded improved patient survival rates. WBRT has been commonly used in the management of patients with incomplete resection of brain tumors *(4,26)*. Furthermore, several reports have documented improved tumor control with combined WBRT and surgery in comparison to the use of either modality alone *(27,28)*.

In conclusion, the present case underwent an aggressive multimodal approach to therapy. This report indicates that the early detection and control of brain metastases may contribute to a better quality of life for patients affected by brain metastases.

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