

CEREBELLOPONTINE ANGLE METASTASIS FROM PAPILLARY CARCINOMA OF THE THYROID: CASE REPORT AND LITERATURE REVIEW

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BACKGROUND

Papillary thyroid carcinoma is the most common type of well-differentiated thyroid malignancy and typically has an excellent prognosis and a low incidence of distant metastasis. However, once metastasis has developed in a distant site, prognosis is markedly diminished. Brain metastases from papillary thyroid carcinoma are extremely rare. Currently, there are no established therapeutic guidelines for treating brain metastases from thyroid carcinoma.

CASE DESCRIPTION

We report on the case of a patient who presented with worsening neurological symptoms 3 years after resection of a thyroid papillary carcinoma. Magnetic resonance imaging identified a lesion of the cerebellopontine angle that encased the lower cranial nerves. The patient underwent a left retrosigmoid craniotomy with a 98% resection of the mass and received postoperative adjuvant radioiodine therapy, external beam radiation, and Gamma Knife radiosurgery. The patient tolerated the procedure well and demonstrated significant progressive improvement in her neurological symptoms postoperatively. After the multimodal approach to therapy, she remains symptom-free at 3-year follow-up. Radiographic monitoring of the small tumor remnant reveals a decrease in size from the postoperative period.

CONCLUSION

This article is the first formal case report of cerebellopontine angle metastasis from papillary thyroid carcinoma. Therapeutic protocols for brain metastases of papillary thyroid carcinoma are not firmly established. This case illustrates the unique event of a cerebellopontine angle metastasis from papillary thyroid carcinoma, which was successfully treated with a combination of surgical, chemical, and radiological modalities. This aggressive

course of therapy has resulted in an excellent outcome in this instance. © 2000 by Elsevier Science Inc.

KEY WORDS

Distant metastases, papillary carcinoma, thyroid, cerebellopontine angle.

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. Metastasis is usually to regional lymph nodes, especially the cervical and mediastinal nodes. Regional lymph node metastases do not typically affect the overall prognosis of PTC [16,17], but distant metastases, most commonly to lung and bone and present in 1% to 7% of patients with PTC, alter survival dramatically [5,10,16,17].

Metastases to the brain are extremely rare, constituting 0.1–5% of distant metastases of papillary carcinoma [4,5,10,17,28]. Only 71 cases of brain metastases have been reported in the English literature. To date, however, there have been no formal case reports of CP angle metastasis from PTC. Our patient's lesion was located anterior to the cerebellum and extended medially into the brainstem, encasing the lower cranial nerves. An aggressive multimodal approach to treatment was undertaken with excellent results. We review the literature on this rare clinical entity and discuss therapeutic modalities available for distant metastases of PTC.

CASE REPORT

The patient is a 78-year-old woman who initially presented in January 1994 with complaints of a neck

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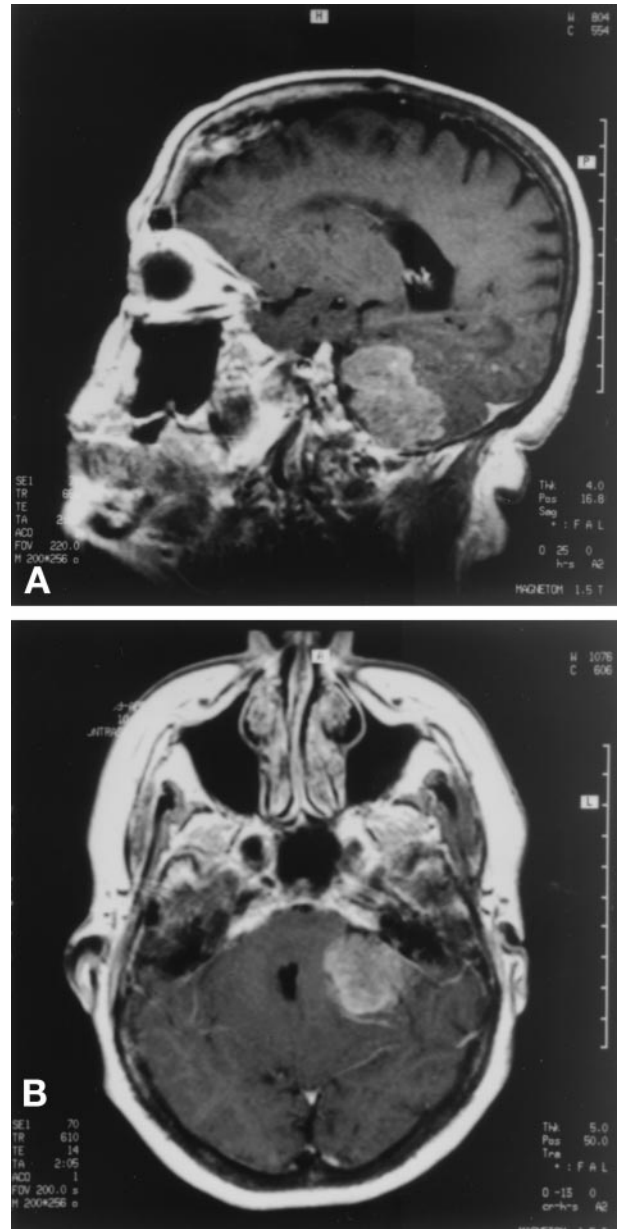
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mass. She was noted to have a palpable mass in the left lobe of the thyroid gland, and she eventually underwent a left thyroidectomy with an intraoperative fine needle aspiration from the right lobe. Histopathology confirmed papillary carcinoma in both specimens. This prompted a complete thyroidectomy and isthmusectomy, which was performed during the same hospitalization 2 days later. The patient was discharged home on postoperative day 5 after an uneventful recovery.

In March 1997, the patient returned with complaints of increasing dizziness, frequent falls, and persistent headaches. She was noted to have bilateral horizontal gaze nystagmus and an ataxic gait on examination; the remainder of her detailed physical examination was normal. A magnetic resonance imaging (MRI) scan was then performed, demonstrating a $4.2 \times 3.0 \times 2.5$ cm mass in the left CPA angle with associated mild hydrocephalus (Figure 1 A, B). The patient was seen in surgical consultation and was scheduled for elective resection of the mass.

Over the next week, she developed intractable vomiting and an inability to walk for which she was admitted to the hospital. She was placed on intravenous dexamethasone and underwent a cerebral angiogram and an attempt at preoperative embolization of the tumor. The angiogram revealed a left posterior fossa mass with its blood supply originating mainly from the left occipital artery. Additionally, arterial collaterals from the left cerebellar branches were present. Angiographic embolization was not technically possible.

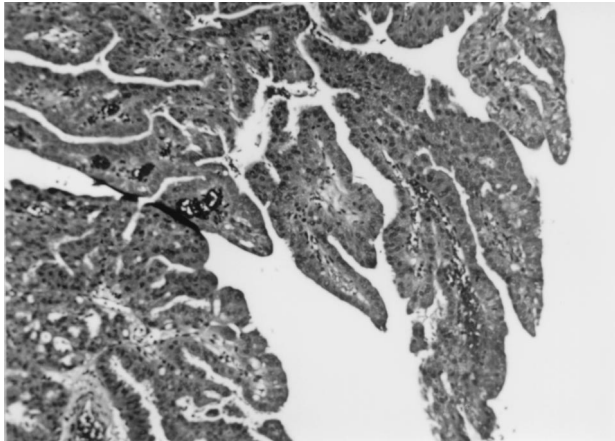
She was taken to the operating room 2 days later. A left retrosigmoid craniotomy and microsurgical resection of the tumor was performed. Intraoperatively, the tumor was found to be immediately anterior to the cerebellum, compressing it posteriorly. The tumor extended medially to the brainstem, encased the lower cranial nerves, and displaced the acousticofacial bundle superiorly. The anterior inferior cerebellar and vertebral arteries were identified and dissected free from the tumor. Microdissection of the tumor from the skull base confirmed that the mass was adherent superiorly to the acousticofacial bundle. Facial nerve monitoring was performed during the entire dissection, and the tumor was dissected free without injury to the VIIth or VIIIth cranial nerves. The anterior and inferior borders of the mass also completely encased the ninth cranial nerve and partially involved the tenth and eleventh cranial nerves. The glossopharyngeal nerve was sacrificed, but both the vagus and spinal accessory nerves were preserved. A 98% resection of the tumor was



1 Sagittal (A) and axial (B) T1-weighted magnetic resonance imaging following intravenous gadolinium contrast demonstrate an irregular enhancing mass in the left cerebellopontine angle compressing the cerebellum posteriorly.

performed with a minute amount left at the junction of the cranial nerves and the brainstem, because the tumor infiltrated the latter. Frozen section was diagnostic for metastatic tumor with epithelial cells, but a more specific etiology could not be identified at that time.

Postoperatively, the patient was extubated in the operating room and was observed for 24 hours in the Surgical Intensive Care Unit. She remained free from neurologic deficits but complained of throat



2 Cerebellopontine angle metastasis from papillary thyroid carcinoma. Histopathology shows papillae with fibrovascular core lined by tall cells with an abundant cytoplasm (Hematoxylin and eosin \times 200).

soreness that was partially attributed to the loss of the IXth cranial nerve. Her postoperative course was otherwise uncomplicated, and she received 2 weeks of inpatient rehabilitation before being discharged home.

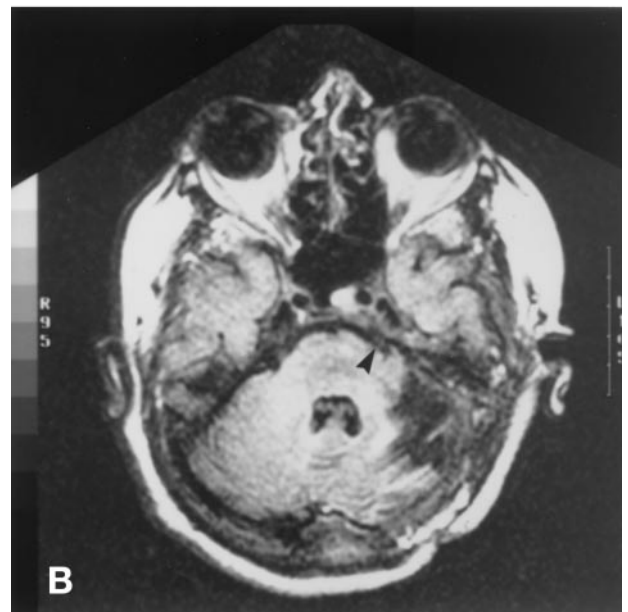
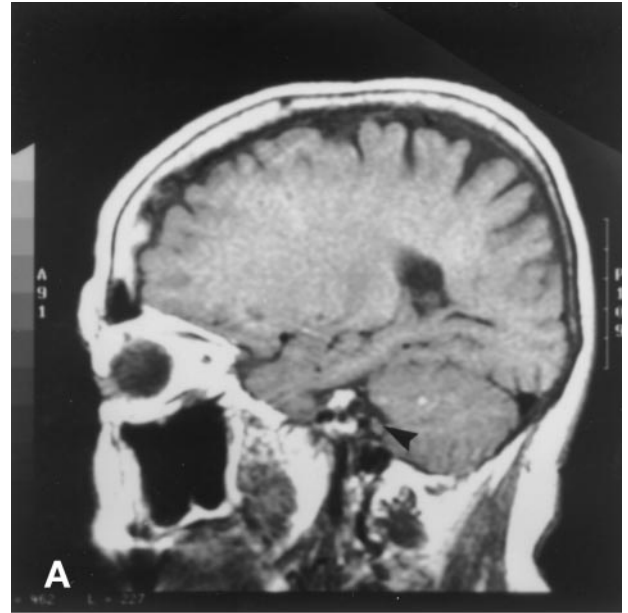
Histopathology was diagnostic for metastatic carcinoma from a primary papillary carcinoma of the thyroid gland. Hematoxylin and eosin stained sections showed papillae with a fibrovascular core lined by tall cells with an abundant cytoplasm (Figure 2). The neoplastic cells showed positive immunohistochemistry staining for thyroglobulin and low molecular weight keratin. Psammoma bodies were rare.

One month later, the patient was evaluated for systemic metastasis with a thyroid I^{131} scan, which showed a small amount of residual thyroid tissue in the thyroid bed without evidence of intracranial residual tissue or systemic metastases. Serum thyroglobulin was elevated at $27 \mu\text{g/l}$ (normal = $<0.1 \mu\text{g/l}$), and the patient then underwent I^{131} radioiodine therapy with 147.1 mCi of I^{131} given orally.

A postoperative MRI was taken one month later (Figure 3A, B) and revealed a small residual tumor in the CP angle measuring 0.7 cm in maximal diameter. The patient then underwent adjuvant whole brain radiation therapy (WBRT) with parallel opposed 6 megavolt photon beams to a dose of 44 Gy in 22 fractions over 31 calendar days at 2 Gy per fraction.

The patient was then referred for Gamma Knife radiosurgery in an effort to further reduce any residual tumor. She underwent this procedure in February 1998.

Subsequent serial MRI scans performed at



3 Sagittal (A) and axial (B) T1-weighted MRI taken one month postoperatively. A 0.7 cm focus of residual tumor (arrow) and postoperative changes are seen.

6-month intervals revealed progressive resolution of the mass. At 3-year follow-up, the patient is symptom free, her ataxia, headaches, and throat discomfort have resolved entirely, she is independent in her daily activities, and she exhibits no signs of dementia.

DISCUSSION

The incidence of thyroid carcinoma is estimated to be 1 in 25,000 people [28]. Papillary carcinoma is

the most common type of well-differentiated carcinoma of the thyroid, constituting 81.2% of all thyroid malignancies [16]. The typical clinical course of papillary carcinoma is indolent, and overall prognosis is usually excellent. Reported survival rates for nonmetastatic lesions are 97.8% at 5 years and 94.9% at 10 years [16]. The peak prevalence is the third decade of life for both men and women, and the tumors behave differently in patients of different ages. In younger patients, the tumor is usually confined to the neck with or without spread to regional lymph nodes, but in older patients papillary carcinoma tends to be more aggressive and may give rise to distant metastases [6].

PTC usually metastasizes to local regional lymph nodes and extrathyroidal tissue. Spread to lymph nodes has been reported to range from 37% to 43% of patients with metastatic disease with cervical and upper mediastinal lymph nodes being the most common sites of regional lymph node invasion [16, 17]. Long-term prognosis, however, is not influenced by regional invasion [16,17].

The incidence of distant metastasis from PTC ranges from 1 to 7% [4,16,17]. McConahey et al [17] and Hoie et al [10] describe risk factors for distant metastasis of PTC. These include male gender, advanced age, histologic grade, and extrathyroidal invasion at initial examination. Other risk factors reported by Dinneen et al [6] are completeness of surgical resection of the primary tumor and nuclear DNA content. Lung is the most common site of distant metastasis, comprising 77% of all metastases, followed by bone with a rate of 20% [6,17]. Distant metastasis seriously affects survival rates. Dinneen et al [6] report 5 and 10-year survival rates of 37% and 24%, respectively, for patients with metastatic PTC.

Metastases to the brain from PTC are extremely rare. Large retrospective series of papillary carcinoma report an intracranial metastasis frequency of 0.1–5% [4,10,17,28]. Only 71 references to brain metastases from PTC have been made in the medical literature [1,2,4,5,7,9–13,15,17,18,20,21,24,28]; of these only 13 have been presented as isolated case reports [1,2,9,11,12,13,15,18,20,21]. (Table 1) The intracranial distribution of lesions in these case reports is varied. Nine of these cases were supratentorial cerebral masses [2,9,12,13,18,21,28], 2 were cerebellar [12,20], and 2 involved the pituitary gland [15]. In a retrospective review of 241 cases of PTC, Carcangiu [4] briefly noted one case of an intracranial metastasis specifically affecting the CP angle without elaborating upon the details of the case. This represents the only other direct refer-

ence to PTC CP angle metastasis aside from this case report.

There is no clearly defined treatment protocol for patients with intracranial metastatic lesions from 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.

Other than the information obtained from the patient's history, physical exam, and diagnostic studies, there are no definitive methods for diagnosing metastases of PTC to the brain. Only histologic examination provides confirmation of the diagnosis. As demonstrated in our patient, a high serum thyroglobulin level may be helpful for detecting distant metastases or residual tumor in cases of well-differentiated thyroid carcinoma [7]. I^{131} may or may not accumulate metastatic tumor tissue in cases of PTC [9,23]; therefore, using I^{131} to detect metastatic brain lesions from thyroid carcinoma may not be reliable. There are several theories as to why I^{131} accumulates poorly in metastatic thyroidal cancerous tissues [27]. It has been reported that metastatic PTC that does accumulate I^{131} carries a better prognosis, as these tumors tend to be more well-differentiated, less aggressive, and more susceptible to radioiodine therapy [6].

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 (Table 1). Although the presence of a brain metastasis is an overall negative prognostic indicator, Chiu [5] has found that surgical resection of brain metastases may help to significantly prolong survival in patients with differentiated thyroid carcinoma.

Due to our patient's otherwise excellent physical and mental health, collaboration between the patient and a multidisciplinary team of surgeons, neurologists, oncologists, and radiation oncologists resulted in the decision to pursue an aggressive course of therapy. Surgery was scheduled on a semi-urgent basis due to the patient's deteriorating neurological status. The resection was incomplete due to the involvement of critical neurovascular structures in the posterior fossa, but did achieve the primary goal of halting the progressive decline in neurological function. The decision regarding subsequent adjuvant therapy was based upon several factors. Discovery of residual thyroid tissue in

1 Distant Metastases of Papillary Thyroid Carcinoma to the Brain

| INITIAL Dx OF PTC (AGE/SEX) | INITIAL THERAPY | INTERVAL FROM INITIAL DX | | LOCATION | TREATMENT | OTHER DM | BRAIN REACTIVITY TO SCAN | EVOLUTION AFTER SURGERY |
|--|---|-----------------------------------|-----------------------------------|--|--|-------------------|--|----------------------------|
| | | | | | | | | |
| Ibanez [11] (1966) Parker [21] (1986) | None | 12 Years | Rt parietal | Surgery | Lung, bone | N/A | Immediate postop death | |
| | Rt radical neck dissection & XRT | 35 Years | Rt frontoparietal | Surgery + I ¹²⁵ seeding | Lung, bone | Negative | Alive and well | |
| Michie* [18] (1986) | TT | 4 Years | Rt temporo- parietal | Surgery | None | Negative | Recurrence in the brain after 4 months | |
| | None | None | Lt occipital | Surgery + XRT | None | N/A | Recurrence in the brain after 6 months | |
| Goolden [9] (1990) | Radio-iodine ablation | 4 Years | Rt frontal | XRT | None | Negative | Death after 6 months | |
| Aihara [1] (1991) | SubTT & XRT | 15 Years | Rt parietal | Surgery | Bone | N/A | No recurrence for 1 year | |
| Biswal [2] (1994) | Near TT & radio-iodine therapy | 8 Weeks | Rt frontal | XRT | Lung | Negative | Death after 4 months | |
| Jyothirmayi [12] (1995) | TT | 19 Years | Rt cerebellum | Surgery | Lung | N/A | Recurrence in the ileum & bone after 14 months | |
| Pacak [20] (1998) | TT | 2 Years | Rt frontal | Surgery | None | N/A | N/A | |
| | TT | 8 Years | Lt cerebellum | Surgery | Lung, bone | Negative | No recurrence for 1 year | |
| Kapusta [13]** (1999) | TT & radioiodine therapy | 30 Years | Rt inf-frontal, Lt parietal | XRT | Lung | N/A | N/A | |
| Masiukiewicz [15] (1999) | TT & node dissection & radioiodine therapy | 5 Years | Pituitary | Radioiodine therapy | Lung | Focal positive | Recurrence in bone and lung after 1 year | |
| This case | SubTT | 20 Years | Rt cavernous sinus & pituitary | Stereotactic radiosurgery | Lung, retroorbital & lower neck | Positive | Recurrence in submandibular & parapharyngeal space after 5 months | |
| | TT | 3 Years | Lt CP angle | Surgery + radioiodine therapy+ XRT + radiosurgery | None | Negative | Alive and well for 3 years | |

Dx: Diagnosis, DM: Distant metastasis, PTC: papillary thyroid carcinoma, XRT: Radiotherapy, TT: Total thyroidectomy, CP: Cerebellopontine angle
*Cerebral metastases from occult papillary carcinoma. Brain surgery was performed before thyroidectomy.
**Two foci of metastasis in the brain developed in chronological order.

the neck prompted radioiodine therapy targeted toward that remnant. As uptake by the remaining intracranial disease was unlikely [6,9,23,27], radiation therapy was implemented to address the possible presence of other intracranial metastases that might have been undetectable as well as the potential for the development of subsequent secondary sites of intracranial metastasis. Occurrence of both of these phenomena has been documented [5,26]. WBRT has been commonly used in the management of patients with incomplete resection of brain tumors [5,22]. Furthermore, several reports have documented improved tumor control with combined WBRT and radiosurgery in comparison to the use of either modality alone [8,14,19,25].

In the absence of established treatment protocols to follow in patients with intracranial metastasis from PTC, the practitioner is especially challenged when faced with this disease. Our experience has demonstrated the importance of specifically tailoring the treatment to the individual case. This patient underwent an aggressive multimodal approach to therapy and has had an excellent result. Although guidelines for clinical practice cannot be derived from a solitary report, this case exemplifies how surgery, radioiodine therapy, and radiation may be combined to yield prolonged and asymptomatic survival.

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COMMENTARY

The authors present an unusual case of an elderly woman who presented 3 years after a diagnosis of papillary thyroid carcinoma with a metastasis to the cerebellopontine angle. The CP angle tumor was resected, and subsequently she was treated with radioactive iodine, whole-brain radiation, and gamma knife radiotherapy. The authors review the literature and, noting the few reported cases, correctly conclude that there are few treatment guidelines for this disease. The patient was treated aggressively with surgery, iodine, radiotherapy, and gamma knife. She remains well 3 years later, and the authors assert that she exhibits no signs of dementia.

At the risk of second-guessing the patient's physicians, I would not have favored whole-brain radiation therapy. The literature does not include examples of multiple brain metastases from this tumor. The patient's tumor was in the posterior

fossa and was mostly resected; I would have limited the radiation to the posterior fossa, perhaps even to gamma knife radiation alone. At 78 years of age, whole-brain radiotherapy is likely to be damaging and could produce dementia.

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Papillary carcinoma of the thyroid is not an uncommon type of cancer. It has a generally good prognosis. Metastases to the brain are uncommon, and one to the CP angle has apparently not been formally described previously.

The question of how to manage a lesion when there is no specific precedent is clearly a difficult one. The authors assumed that it would be best to use a multimodality approach, and in fact it was successful for this patient. It is, of course, difficult to determine the exact role that radiosurgery played in the favorable outcome. Given the lack of precedent, using this additional modality was quite reasonable.

As the review of the literature indicates, PTC has an excellent prognosis, but in those cases that do metastasize, the lesions are quite difficult to treat.

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Thinking well is wise; planning well, wiser; doing well, wisest and best of all.

—PERSIAN PROVERB

Change is one thing, progress is another. "Change" is scientific, "progress" is ethical; change is indubitable, whereas progress is a matter of controversy.

—BERTRAND RUSSELL

If you wish to be brothers, drop your weapons.

—POPE JOHN PAUL II