

Pituitary Metastases from Thyroid Carcinoma: Case Series and Literature Review

Brett A. Fadrique¹, Levi Sanchez Ramirez², Trevor Abts³, Salmaan Ahmed⁴, J. Matthew Debnam^{4*},


¹Texas Tech University, Lubbock, USA

²Baylor College of Medicine, Houston, USA

³Creighton University School of Medicine, Omaha, USA

⁴Department of Neuroradiology, The University of Texas MD Anderson Cancer Center, Houston, USA

*Correspondence: J. Matthew Debnam, MD, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030, IUSA,

 matthew.debnam@mdanderson.org

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AUTHOR'S CONTRIBUTIONS

All authors contributed equally to this work and were responsible for the study concept and design. All authors drafted the manuscript, contributed to the article, and approved the final manuscript.

DISCLOSURES

The authors have no disclosures to report.

CONSENT

No.

HUMAN AND ANIMAL RIGHTS

Ethical standards followed the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5).

CONFLICT OF INTEREST

None

ABSTRACT

Metastases to the pituitary gland are extremely rare. Most of the reported cases arise from breast and lung cancer, with metastases from thyroid cancer seldom reported. Thyroid cancer metastases to the pituitary gland may occur as the initial presentation of metastatic disease or part of widespread disease and may occur years after the primary thyroid cancer diagnosis. Herein, we present three cases of thyroid cancer that metastasized to the pituitary gland and review the literature to address its clinical and radiologic features, prognosis, treatment, and differential diagnosis.

CASE REPORT

BACKGROUND

Metastasis to the pituitary gland is extremely rare, with most of the cases arising from breast and lung cancer. Thyroid cancer metastases to the pituitary gland may occur as the initial presentation of metastatic disease or part of widespread disease and may occur years after the primary thyroid cancer diagnosis. It is important for radiologists to be aware that thyroid cancer can metastasize to the pituitary gland and, in the appropriate clinical setting, provide the correct differential diagnosis.

CASE DESCRIPTIONS

Case 1

A 61-year-old male originally presented to an outside institution with hoarseness, dysphagia, and right vocal cord

paralysis. He was diagnosed with papillary thyroid carcinoma, underwent a thyroidectomy, and was treated with radioactive iodine therapy. He had several recurrences in the neck that were treated with surgery and radiation.

Several years later, he presented with polydipsia, polyuria, severe headaches, and hot flashes. He was referred to an endocrinologist and diagnosed with new-onset diabetes insipidus. Magnetic Resonance Imaging (MRI) of the brain and sella turcica revealed a pituitary and infundibular mass (Figure 1A,1B) and multiple brain parenchymal lesions (Figure 1C). Imaging obtained for staging also demonstrated lesions in the bones and chest with an incidental pulmonary embolism. The pituitary mass was suspected to be a metastasis and was biopsied via an endonasal transsphenoidal approach confirming

metastatic papillary thyroid carcinoma. The patient received whole brain radiation for the brain metastases with a boost to the sella turcica. Following discussions for treatment of the pulmonary embolism and disseminated metastatic disease, the patient was lost to follow-up.

Case 2

A 20-year-old male presented to an outside institution with diarrhea and weight loss and was diagnosed with panhypopituitarism. An MRI revealed a 2.6 cm suprasellar mass (Figure 2). Further imaging identified thyroid and pulmonary nodules, neck and mediastinal nodes, renal and adrenal lesions, and bone lesions, including involvement of the mandible, thoracic spine, and ribs. Biopsy of the mediastinal mass revealed neuroendocrine carcinoma. Subsequently, the patient underwent transsphenoidal resection of what was believed to be a pituitary adenoma.

The patient was then referred to our institution, where a review of the pathology slides from the resected pituitary mass was interpreted as metastatic medullary thyroid carcinoma. The patient was enrolled in a clinical trial and started on chemotherapy with a favorable response. To manage the primary disease, a total thyroidectomy, central compartment and bilateral neck dissections, and sternotomy for resection of the mediastinal mass were performed. Follow-up imaging demonstrated stable treated metastasis at the various sites of disease involvement.

Case 3

A 67-year-old male underwent a biopsy of a right thyroid nodule at an outside institution that was interpreted as a follicular lesion. Subsequent right hemithyroidectomy revealed papillary thyroid carcinoma-follicular variant (PTC-FV). The patient was then referred to our institution, where a neck US revealed a suspicious right neck node. An ultrasound-guided fine needle aspiration (US-guided FNA) was performed and showed metastatic PTC-FV. The patient underwent a completion left thyroidectomy and right neck dissection, followed by radioiodine therapy and I-131 therapy.

Several years later, spinal metastases were detected and treated with stereotactic radiosurgery. Following treatment, progressive disease in the chest was noted, and the patient was enrolled in a clinical trial with immunotherapy and radiation therapy. The patient reported blurred vision in the right eye and progression was noted on subsequent imaging with new metastases to the pituitary gland (Figure 3), right eye (choroidal mass- Figure 4), brain, lung, and spine. Given the progressive disease, the patient declined further systemic therapy and was referred to hospice care for supportive management.

DISCUSSION

Introduction

Greater than 90% of all thyroid carcinomas are differentiated thyroid cancer (DTC), with the most common type being

papillary thyroid carcinoma, followed by follicular thyroid carcinoma and Hürthle cell carcinoma [1,2]. Typically treated with surgery, DTC has the best prognosis, with a 10-year survival rate of > 90% [1,2]. However, pituitary metastasis from DTC can complicate treatment and negatively affect the prognosis.

Over the last 2 decades, there has been an increased incidence of pituitary metastases. Lung cancer and breast cancer are the most common primary tumors to metastasize to the pituitary gland [3,4]. To the best of our knowledge, there are less than 30 cases in the literature describing the imaging appearances of thyroid carcinoma metastasizing to the pituitary gland. While metastases from the thyroid to the pituitary gland remain rare, appropriate treatment is required to maximize patient survival and avoid treatment-related complications [5].

Symptoms

Pituitary metastases have been reported to be diagnosed most often in the late stage of metastatic disease and cause symptoms in about 7% of patients [6,7]. The infundibulum and posterior pituitary gland are the main sites of metastases due to the arterial blood supply to these sites. A metastasis to these sites may cause diabetes insipidus and symptoms related to the pituitary mass [8]. Some patients experience pressure-related symptoms from mass effect caused by the tumor, including headache, nausea, vomiting, cranial nerve deficits, and symptoms from optic nerve compression [9,10]. Non-specific symptoms included fatigue, loss of appetite, and dizziness [10]. Pituitary metastases may be the first manifestations of cancer and can closely mimic symptoms related to pituitary adenoma, and should be considered in the differential diagnosis of patients with primary cancer and pituitary dysfunction [11,12]. Pituitary metastases have been reported to be an incidental finding in 7% of cases [10].

In our series, one patient presented with diabetes insipidus and one with non-specific symptoms of diarrhea and weight loss. The pituitary metastasis in the final patient was detected on the surveillance imaging. In two of the three patients, the pituitary metastasis was detected several years after the primary diagnosis of thyroid carcinoma. In the other patient (case 2), a pituitary mass was diagnosed as a pituitary adenoma that was resected and subsequently determined to be a metastasis, despite the presence of diffuse metastatic disease at presentation. Conceivably, surgery may have been performed on this patient to relieve symptoms related to the mass effect on the optic chiasm and edema in the optic tracts.

Imaging

Variable imaging appearances of thyroid cancer metastasizing to the pituitary have been reported. These include as a homogeneous [13-15] or a heterogeneous pituitary mass [16-18]. The metastases may also present with a thickened pituitary infundibulum. Expansion of the sella turcica and extension to involve the clivus have also been described [16-18]. In up to 15% of symptomatic patients with pituitary metastases,

cavernous sinus invasion may be present [13-15,19]. Imaging features with mass effect upon the optic apparatus have also been reported [8].

In our series, two of the three pituitary metastases were heterogeneous in appearance, and the other was homogeneous mass. All three lesions involved the pituitary gland and infundibulum, and one lesion had a mass effect upon the optic chiasm with edema in the optic tracts. Despite the fact that a pituitary adenoma would be in the differential diagnosis of the imaging appearance in cases 1 and 2, all three patients had other metastases on imaging at the time that the pituitary lesion was first visualized.

Prognosis

DTC has an excellent prognosis [1,2]; however, a pituitary metastasis in DTC can negatively affect survival, as shown in our review. Hong et al. [5] found that the overall survival rate of patients with pituitary metastases was 50-73% after 1 year, but that number dropped significantly to 26-52% for year 2. In cases #1 and #3 in our study, the patients were lost to follow-up and placed in hospice care due to rapid disease progression, respectively. However, the patient in case #2 responded well to chemotherapy following resection of the pituitary metastasis and has stable treated disease as of this writing. The younger age of the patient in case #2 may have played a role in his treatment response and recovery when compared to patients #1 and #3, as Ilerhunmwuwa et al. [15] found an inverse correlation between the survival rate and the age of patients at diagnosis.

Treatment

Effective management of metastatic thyroid carcinoma with pituitary metastases necessitates a multidisciplinary approach, involving endocrinologists, oncologists, neurosurgeons, radiologists, and palliative care specialists. Due to the aggressive nature of pituitary metastases arising from thyroid carcinoma, an accurate and rapid diagnosis is necessary to avoid delays in treatment [5]. For pituitary metastases, both surgical intervention and radiation therapy have proven effective in reducing tumor size, alleviating symptoms, and confirming the diagnosis. Even if local tumor control fails, some patients may still experience benefits from a continued treatment regime constituting radiation and/or systemic therapy [5].

The treatment received by the patients in our series demonstrates that varying treatments may benefit patients depending on their circumstances. In our series, one patient was treated with whole-brain radiation for intracranial metastasis and a boost to the pituitary metastasis. The second patient underwent resection of a pituitary mass that was later determined to be a metastasis, followed by chemotherapy for diffuse metastases. The final patient declined treatment due to the continued progression of metastatic disease and was referred to hospice.

Differential diagnosis

The imaging differential diagnoses of pituitary metastases include pituitary adenoma, craniopharyngioma, pituitary carcinoma, and pituitary apoplexy.

Pituitary adenoma

Pituitary adenomas represent the most common intracranial tumor, with an incidence of 10–17% [20,21]. Approximately 2.7% of pituitary adenomas occur in patients with Multiple Endocrine Neoplasia Type 1 (MEN-1), while 40% of patients with MEN-1 have a pituitary adenoma [22]. Most pituitary adenomas are asymptomatic and incidentally detected on imaging for other reasons [21]. However, a functional adenoma may secrete hormones, including prolactin, adrenocorticotrophic hormone, growth hormone, thyroid stimulating hormone, and gonadotropins [23,24]. Pituitary adenomas are classified depending on their size as follows: microadenomas (<1 cm), macroadenomas (≥1 cm), and giant pituitary adenomas (>4 cm) [20].

On imaging, the pituitary adenomas may be indented upon by the diaphragma sellae, giving it a “snowman” or “figure-eight” appearance [25]. Cystic and necrotic areas and intratumoral hemorrhage may be present in the adenoma, but calcification is rare. On CT, pituitary adenomas are isointense to the brain parenchyma and demonstrate moderate enhancement with contrast. On MRI, they are T1 hypo- to isointense and T2 iso- to hyperintense [26]. On PET/CT, pituitary macroadenomas are ¹⁸FDG-avid relative to the uptake in the normal gland [27].

Craniopharyngioma

There are two types of craniopharyngiomas: adamantinomatous and papillary. The adamantinomatous type can occur at any age, but it is most common in children, where it represents the most common suprasellar tumor. A second peak can occur between 40 and 70 years of age [28,29]. The papillary type is more common in adults, and both types occur equally in men and women [29].

On imaging, the adamantinomatous type appears as a mixed cystic and solid mass. With intravenous contrast, the solid components enhance, whereas the cystic components demonstrate peripheral enhancement. In addition, the cysts may contain blood products, cholesterol, and/or proteinaceous material, causing variable MR signal intensities [29,30]. Calcification has been reported in 90% of the pediatric cases [29]. On the other hand, the papillary type is predominately solid, but a cystic component has been reported to occur in over 85% of patients and is usually smaller in size as compared to the adamantinomatous type [28,29]. Calcifications are reported to be rare in the papillary type [28,29].

Pituitary carcinoma

Pituitary carcinoma is rare. It accounts for between 0.1% and 0.2% of pituitary malignancies and can be difficult to

diagnose. Pituitary carcinomas have aggressive behavior with a poor prognosis. They may not respond to conventional therapy and are reported to recur after resection [31,32]. These tumors present in the 3rd to 5th decade of life from a preexisting pituitary adenoma [31]. Pituitary carcinomas may present as an incidental finding in an asymptomatic patient, as a functional tumor with the symptoms attributed to the type of hormones that are secreted, or with symptoms related to mass effect including headache, double vision, and cranial nerve palsies [32,33]. On imaging, pituitary carcinoma can be difficult to distinguish from a macroadenoma [31]. Often, there is cavernous sinus involvement or invasion of adjacent structures [33].

Pituitary Apoplexy

Pituitary apoplexy represents an infarction and/or hemorrhage occurring in the pituitary gland and is usually related to the presence of an adenoma [34]. Patients may present with sudden enlargement of the gland and symptoms such as headaches, pituitary insufficiency related to compression on the pituitary gland or infundibulum, or visual complaints related to compression upon the optic chiasm or cavernous sinus [35].

On MRI, blood products are detected within an enlarging pituitary gland. T1 hyperintense subacute blood products can be difficult to distinguish from proteinaceous products if present in a Rathke's cleft cyst. Over time, serial MRIs demonstrate the evolution of the hemorrhagic products, whereas a Rathke's cleft cyst maintains the T1 hyperintense signal [36].

CONCLUSION

The three cases of metastatic thyroid cancer to the pituitary gland in our series underscore the complexities associated with diagnosing and treating metastatic thyroid carcinoma to the pituitary gland as well as the necessity for ongoing research to develop more effective treatment strategies. Multidisciplinary care and personalized treatment plans remain essential in managing these challenging cases. Additionally, patient-centered approaches that consider quality of life and patient preferences are vital, particularly in the context of advanced disease and end-of-life care.

TEACHING POINT

Metastases to the pituitary gland from a thyroid carcinoma are extremely rare, with symptoms including diabetes insipidus and headache. Knowledge of the clinical symptoms and imaging appearances, including cavernous sinus involvement and mass effect upon the optic apparatus and the presence of other metastases at remote locations, is imperative to ensure appropriate patient management.

QUESTIONS

Question 1: Imaging findings of thyroid cancer metastasizing to the pituitary gland include which of the following?

- Homogeneous appearance
- Heterogeneous appearance

- Involvement of the pituitary infundibulum
- Mass effect on optic chiasm
- All of the above.

Answer: e.

Explanation: All of the above are imaging findings of pituitary metastases.

Question 2: Associated imaging findings of pituitary metastases may include which of the following?

- Cavernous sinus invasion
- Expansion of the sella turcica
- Invasion the clivus
- Edema in the optic tracts
- All of the above.

Answer: e.

Explanation: All of the above are associated imaging findings of pituitary metastases.

Applies to article: Hong S, Atkinson JL, Erickson D, Kizilbash SH, Little JT, Routman DM, Van Gompel JJ. Treatment outcome of metastasis to the pituitary gland: a case series of 21 patients with pathological diagnosis. *Neurosurg Focus*. 2023 Aug;55(2):E13. doi: 10.3171/2023.5.FOCUS23185. PMID: 37527679.

Question 3: Which of the following statements is false?

- Metastases from thyroid cancer to the pituitary are common
- Breast and lung cancer are the most common pituitary metastases
- There is an increasing incidence of pituitary metastases
- Pituitary metastases can be visualized using MRI
- A pituitary metastasis can be the initial presentation of metastatic disease

Answer: a

Explanation: Metastasis to the pituitary gland from thyroid cancer is very rare. Pituitary metastases are more commonly seen in cases of lung and breast cancer.

Applies to article: Ilerhunmwuwa NP, Wasifuddin M, Perry J, Hakobyan N, Inyang L, Zavgorodneva Z, Gasparyan L, Tahir M. Pituitary Metastases From Differentiated Thyroid Cancers: A Systematic Review. *World J Oncol*. 2023 Jun;14(3):165-173.

Question 4: Presenting symptoms of pituitary metastases included all of the following except

- Diabetes insipidus
- Headache
- Abdominal pain
- Cranial neuropathies
- Visual problems

Answer: c

Explanation: Common symptoms of pituitary metastases include diabetes insipidus (due to involvement of the infundibulum and posterior pituitary), headaches, cranial neuropathies, and visual problems. These symptoms are related to mass effect, hormonal disruption, or direct invasion of nearby neural structures like the optic chiasm and cavernous sinuses. Abdominal pain is not typically associated with pituitary metastases.

Question 5: The differential diagnosis of a pituitary metastasis includes which of the following:

- Pituitary adenoma
- Craniopharyngioma
- Pituitary carcinoma
- Pituitary apoplexy
- All of the above

Answer: e.

Explanation: All of the above are in the differential diagnosis of pituitary metastasis.

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FIGURES

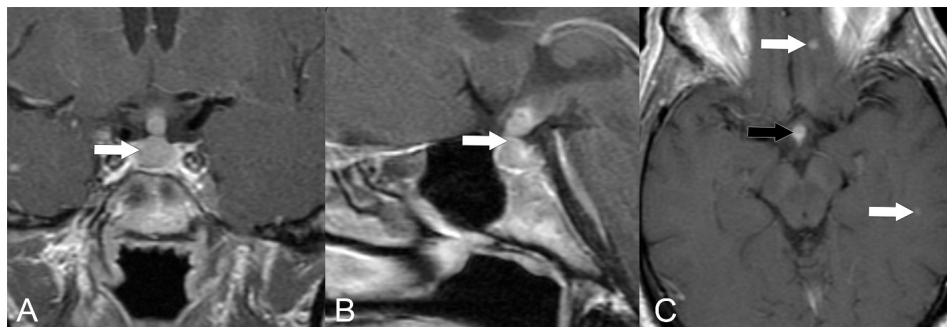


Figure 1: A 61-year-old male with a pituitary metastasis from papillary thyroid carcinoma. (A,B) Coronal and sagittal T1 post-contrast MRIs show a homogeneously enhancing metastasis involving the pituitary gland with narrowing of the mass at the diaphragma sella and thickening of the infundibulum (arrows). (C) Axial T1 post-contrast MRI shows metastases in the brain parenchyma (white arrows) and the pituitary infundibulum (black arrow).



Figure 2: A 20-year-old male with a pituitary metastasis from medullary thyroid carcinoma. (A,B) Coronal and sagittal T1 post-contrast MRIs show a heterogeneously enhancing metastasis involving the pituitary gland and infundibulum (arrows) with mass effect upon the optic chiasm. (C) Axial T2 FLAIR MRI shows an isointense appearance of the pituitary metastasis and hyperintense signal from edema in the optic tracts (circle).

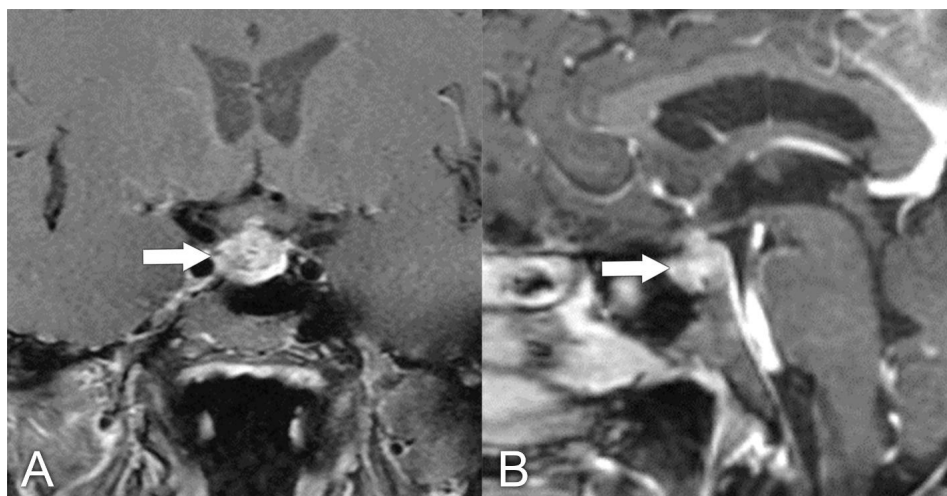


Figure 3: A 67-year-old male with a pituitary metastasis from papillary thyroid carcinoma-follicular variant (PTC-FV). (A,B) Coronal and sagittal T1 post-contrast MRIs show a heterogeneously enhancing metastasis involving the pituitary gland and infundibulum (arrows).

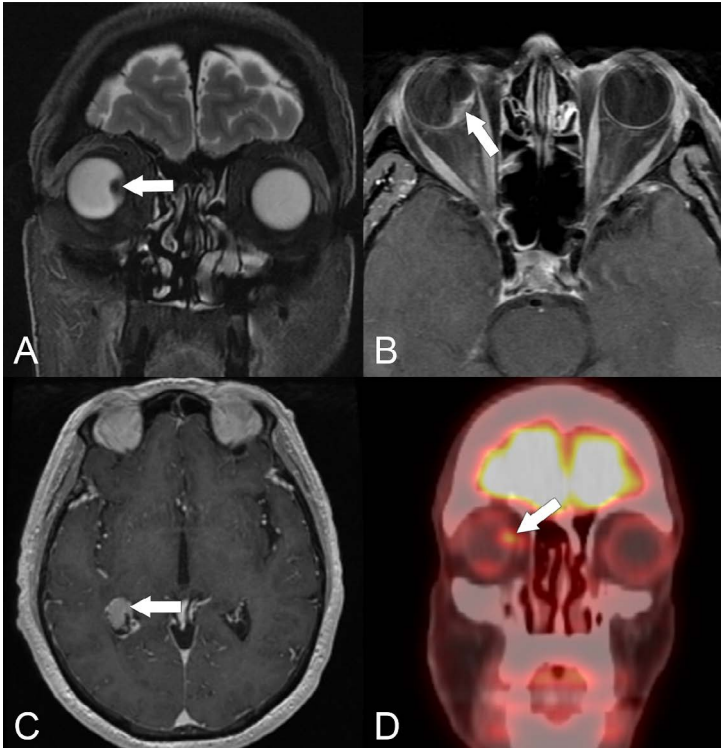


Figure 4: A 67-year-old male with a pituitary metastasis from papillary thyroid carcinoma-follicular variant (PTC-FV). (A) Coronal T2 MRI shows a hypointense mass involving the choroid of the right eye (arrow). (B) Axial T1 post-contrast MRI shows the enhancing right choroidal metastasis (arrow). (C) Axial T1 post-contrast MRI shows a metastasis involving the choroid plexus in the atrium of the right lateral ventricle (arrow). (D) Coronal PET/CT shows an FDG-avid right choroidal metastasis (arrow).

PATIENT SUMMARY TABLE

	Case 1	Case 2	Case 3
Age	61	20	67
Gender	Male	Male	Male
Primary thyroid cancer	PTC	MTC	PTC-FV
Clinical presentation (pituitary metastasis)	Polydipsia, polyuria, headache	Panhypopituitarism	Blurred vision (pituitary metastasis discovered on subsequent imaging)
Diagnostic imaging	MRI sella	MRI sella	MRI brain
Treatment	WBRT with sella boost	Resection of perceived pituitary adenoma	NA
Disposition	Surveillance	Surveillance	Hospice
PTC: papillary thyroid carcinoma			
MTC: medullary thyroid carcinoma			
fv: follicular variant			
WBRT: whole brain radiation therapy			

KEYWORDS

Thyroid cancer; pituitary; metastasis; cavernous sinus; optic chiasm; magnetic resonance imaging

ABBREVIATIONS

MRI = MAGNETIC RESONANCE IMAGING
PTC-FV = PAPILLARY THYROID CARCINOMA-FOLLICULAR VARIANT
US-GUIDED FNA = ULTRASOUND-GUIDED FINE NEEDLE ASPIRATION
DTC = DIFFERENTIATED THYROID CANCER (DTC)
MEN = MULTIPLE ENDOCRINE NEOPLASIA

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