Case Report

Pituitary Metastasis of Papillary Thyroid Carcinoma: The First Case in Thailand

Wasawat Muninthorn, MD[1], Arunee Singhsnaeh, MD[2], Arunrat Auttara-atthakorn, MD[3], Chutintorn Sriphrapadang, MD[3], Ake Hansasuta, MD[1]

[1] Division of Neurosurgery, Department of Surgery, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.
[2] Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.
[3] Division of Endocrinology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Pituitary metastasis (PM) is uncommon. Papillary thyroid carcinoma (PTC) causing PM is very rare, with only 16 case reports around the world. The authors present a case of PM from PTC who also harbored lung and bone metastases. At the same time as PTC diagnosis, a sellar mass with suprasellar extension, compressing the optic pathway, and a precentral sulcus leptomeningeal lesion were identified. Although the patient had no complaint of related symptoms other than panhypopituitarism, eye examination demonstrated a typical visual field defect. Surgical decompression by endoscopic transsphenoidal surgery encountered a highly vascularized tumor. Histopathology confirmed the diagnosis of the PM from PTC. The patient received subsequent radiation and radioactive iodotherapy. At six months after surgery, she was able to live independently. A short summary of previous case reports of PTC to pituitary gland is provided.

Keywords: Thyroid carcinoma; Papillary; Pituitary; Sellar; Metastasis; Pituitary gland; Endoscopic transsphenoidal surgery

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Malignancy of the thyroid gland, or thyroid carcinoma (TC), consists of 4 subtypes. Papillary and follicular are the well-differentiated forms that have longer survival than the poorly differentiated, medullary and anaplastic subtypes. Papillary TC (PTC) accounted for 90% of all TCs. This subtype has a favorable prognosis with a 10-year relative survival rate of 93%[1,2]. Local spreading to nearby structures and regional lymph nodes are the usual form of PTC spread. Seldomly, distant metastasis can develop, with lung and bone being the most frequently involved organs (10 to 15%)[3]. In contrast, intracranial metastasis is largely uncommon (0.87 to 1%)[4,5]. Furthermore, pituitary metastasis (PM) from PTC is extremely rare. Excluding reports from autopsy cases, to date, there were 16 previously published literature of living patients with PTC that had PM[6-19]. The authors describe the first patient with PTC metastasis to pituitary gland (PG) in Thailand. A short summary of the other 16 reports is furnished.

The present study was approved by ethics committee, Faculty of Medicine Ramathibodi Hospital, Mahidol University (No. MURA2021/18).

Correspondence to:

Hansasuta A.

Division of Neurosurgery, Department of Surgery, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Phone: +66-2-2012571 ext. 256

Email: ake.han@mahidol.ac.th

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Case Report

The patient was a 64-year-old woman who had rapidly enlarging neck mass for just over 2 months. The mass caused progressive compression of the nearby structures. Upon radiographic work-up, with the same computerized tomography (CT) scans that revealed the thyroidal mass, a lesion at pituitary fossa with suprasellar extension was also detected (Figure 1). After a total thyroidectomy, pathological examination confirmed PTC. She was also diagnosed with lung and bone metastases by subsequent CT scans of the chest and abdomen. Furthermore, magnetic resonance imaging (MRI) scans of the brain and pituitary detailed an intrasellar mass, with suprasellar extension and intra-tumoral hemorrhage, resulting in compression of the optic apparatus. PM from the PTC was suspected. In addition, a small enhancing leptomeningeal nodule at the left precentral sulcus was noted, representing PTC metastasis to the brain (Figure 2). Despite the lack of patient's visual complaints, she was found to have a bitemporal field deficit along with abnormal visual acuity, 20/50 on the Snellen chart. Pituitary hormone studies showed central hypothyroidism, adrenal insufficiency, and slightly elevated prolactin level from stalk effect (Table 1). However, the patient did not have clinical or laboratory evidence of diabetes insipidus (DI). She was prescribed oral levothyroxine along with corticosteroid replacement, since the discovery of panhypopituitarism.

Due to the specific concern of potential intra-tumoral hemorrhage with the administration of radioactive iodine-131 (RAI), surgical excision of the PM was deemed

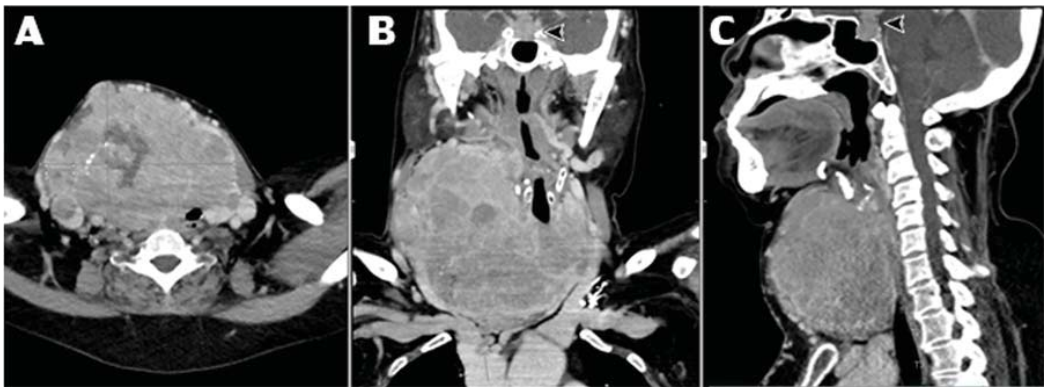

Figure 1. Computerized tomography with contrast, axial (A), coronal (B), and sagittal (C), scans revealed a large lobulated solid-cystic thyroidal mass, 9.9x12.8x11 centimeters, with internal calcification and necrotic portion mainly centered at right thyroid with involvement of isthmus and left thyroid gland. Note an intrasellar contrast-enhanced lesion with suprasellar extension (dark arrowhead).

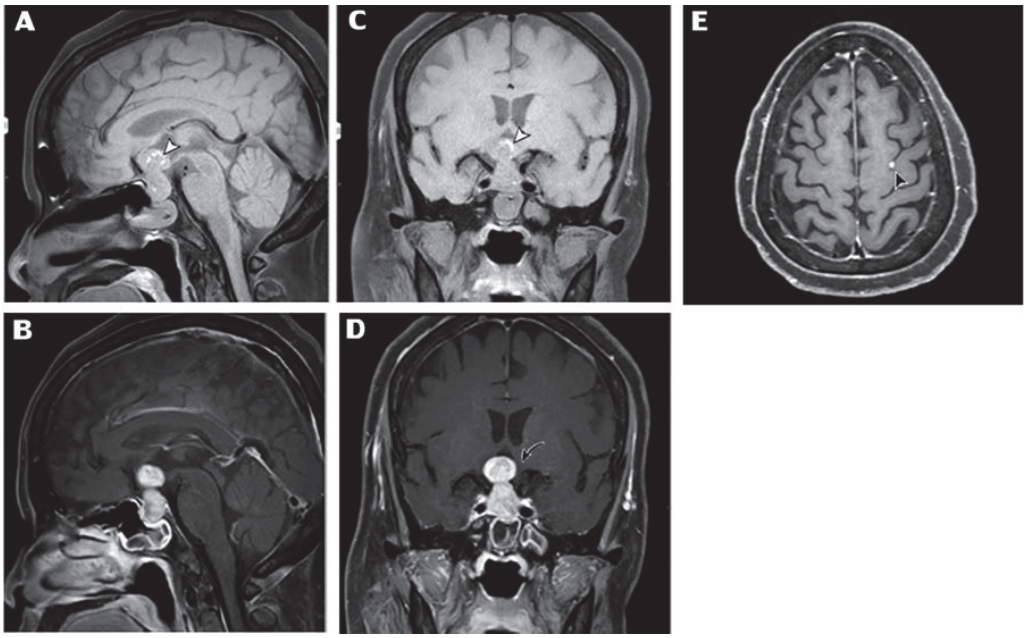

Figure 2. Magnetic resonance imaging, sagittal T1-weighted (T1W) (A), sagittal T1W with contrast (B), coronal T1W (C), coronal T1W with contrast (D), and axial T1W with contrast (E), scans of the patient showing gadolinium-enhanced 1.8x1.9x3.1 centimeters, dumbbell shape, intra-, and suprasellar lesion. Posterior bright spot and pituitary stalk are not clearly seen. The white arrowheads (A&C) indicate hemorrhagic changes within the lesion. Note the optic chiasmal compression by the pituitary metastasis (curve arrow in D). Another small leptomeningeal enhancing nodule at the left-sided precentral sulcus is shown on the axial scan (dark arrowhead in E).

necessary. She underwent an endoscopic transsphenoidal surgery (ETSS) in which a highly vascularized PM, with a small area of sellar floor erosion, was encountered. The normal pituitary gland (PG) could not be distinguished from the

PM. Its consistency was rather firm, neither soft nor suckable as one would expect from a typical pituitary adenoma (PA), hence, piecemeal resection was undertaken. With the estimated blood loss of 800 milliliters and the frozen section revealing PM, surgery was concluded without the attempt for total resection. The final histopathology confirmed metastatic PTC to the PG (Figure 3). The patient had an uncomplicated hospital stay without DI. A few weeks later, she received adjuvant radiotherapy and RAI without event. Six months after surgery, at the time of this manuscript preparation, the patient lived independently with an improvement of her visual field. Figure 4 shows shrinkage of the PM on the follow-up MRI scans.

Discussion

Pituitary metastasis, sometimes referred to as sellar metastasis, is diagnosed by primary malignancy spreading into PG. From a recent review by Shahein et al, PM accounted for 0.87% of overall intracranial metastases[4]. This rare condition is predominately found in the 60 to 70 years of age and is often discovered with varying intervals, from months to years, after primary cancer's diagnosis[6,8,10-13,15-17,20-26]. Breast and bronchopulmonary carcinoma are the most common primary sources[4]. Because the hematogenous route is the most common type of metastasis, the posterior PG is more frequently involved by PM than the anterior PG. The direct connection with systemic arterial circulation to posterior PG could be the probable explanation, unlike the anterior PG which is supplied by the portal hypophyseal system. Hence, DI is one of the most common presentations of PM. Another frequent symptom, associated with a larger size of PM, is the optic pathway compression. Bitemporal hemianopsia, caused by suprasellar extension of the PM's pressure to optic chiasm, can be found. The incidence of such visual decline is 50 to 60%[27]. Furthermore, if the PM extends laterally into cavernous sinus, it can bring about ophthalmoplegia, ptosis, or facial anesthesia. Due to the invasive growth pattern of PM, it often results in extensive bone erosion of the skull base[24,25].

Panhypopituitarism can be caused by a combination of the direct cancerous damage of PG, or hypothalamus, and/or the disruption between hypothalamus and PG via pituitary stalk compression. From a review by Javanbakht et al, the incidence of panhypopituitarism from all PM was estimated to be 37%[25]. Hyperprolactinemia, usually not exceeding 200 nanograms/milliliter, is common, indicating pituitary stalk effect. Nevertheless, the literature review by Habu et al, could not correlate hyperprolactinemia and the presence of either panhypopituitarism or DI[2]. In benign and slow-growing neoplasms such as PA, DI is a rare presentation (<1%)[4,28]. On the contrary, per the aforementioned pathophysiology, DI is considerably more frequent in PM, with a reported incidence of 27 to

Table 1. Pituitary hormone work-up panel

Serum hormones	Results	Normal
FT3	1.89 ng/dl	1.88 to 1.48 ng/dl
FT4	0.49 ng/dl	0.7 to 1.48 ng/dl
TSH	1.31 µIU/ml	0.3 to 5.0 µIU/ml
Morning cortisol	<1 µg/dl	5 to 25 µg/dl
ACTH	5 pg/ml	0 to 46 pg/ml
Prolactin	64.07 ng/ml	5.18 to 26.53 ng/ml
IGF-1	50 ng/ml	37 to 219 ng/ml

FT3 = free triiodothyronine; FT4 = free thyroxine; TSH = thyroid stimulating hormone; ACTH = adrenocorticotrophic hormone; IGF-1 = Insulin-like growth factor; ng = nanogram; dl = deciliter; µIU = microinternational unit; ml = milliliter; µg = microgram; pg = picogram

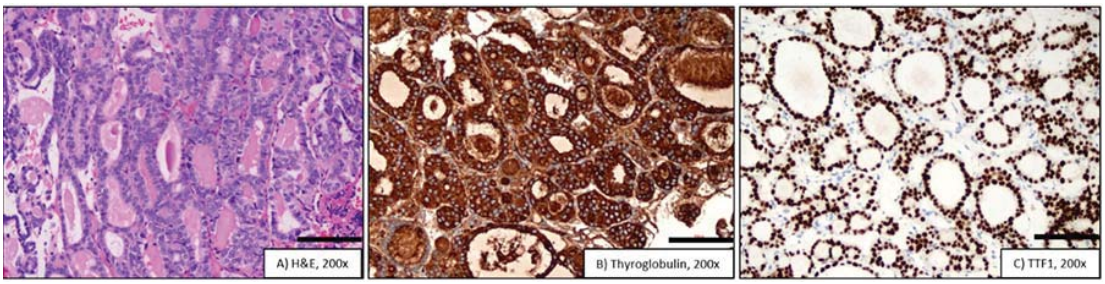

Figure 3. Histopathological specimens of the sellar mass at 200 magnification power. Hematoxylin and eosin (H&E) stain (A), there are follicles of thyroid with characteristic nuclear features of papillary carcinoma of thyroid gland which are enlargement, oval shape, elongation and overlapping, clearing or ground glass appearance, irregularity of nuclear contours, including grooves and nuclear pseudo-inclusions. Immunohistochemistry stain for thyroglobulin shows positive in the cytoplasm (B). Immunohistochemistry stain for thyroid transcription factor 1 (TTF1) shows positive in the nucleus (C).

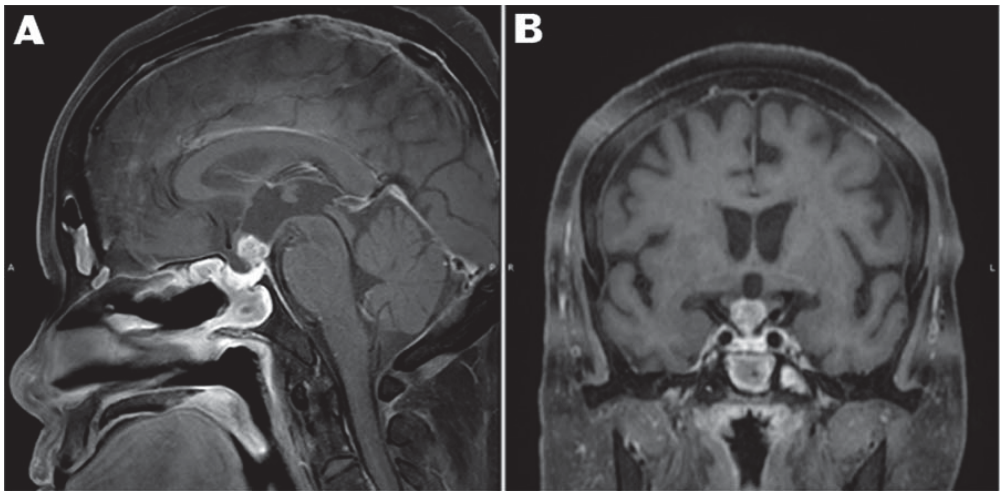

Figure 4. Contrasted T1-weighted magnetic resonance imaging, sagittal (A) and coronal (B), scans of the patient, at six months after treatments of the pituitary metastasis (PM), demonstrating shrinkage of the PM.

71%[2,6,25,29,30].

Pituitary metastasis commonly appears on MRI scans as hypo-to-iso signal intensity on T1-weighted (T1W) and iso-to-hyper signal on T2-weighted (T2W) images. In addition, homogenous gadolinium-enhanced sellar mass on T1W is typical. Therefore, at times, it cannot be distinguished from PA solely by radiographic appearances[2,29]. Because of this limitation, pathological confirmation is often required for definitive diagnosis. The finding of heterogeneous T1W and T2W signal intensities is usually indicative of intra-tumoral bleeding. In general, PM has 8.5% overall incidence of intra-tumoral hemorrhage[2].

The current treatments for PM comprise surgical resection, radiotherapy, and chemotherapy. The goal of surgery is to obtain definitive histopathology and/or to alleviate the mass effect caused by the PM. Subsequent to a surgical procedure, adjuvant radiotherapy is typically prescribed. Specifically for PM with PTC, RAI is instrumental by way of another adjunct, as in the present case. Patients with PM's survival is largely influenced by their primary malignancy and systemic disease status. Either surgical resection of PM alone or in combination with adjuvant treatments does not affect the overall mortality rate[25,31]. The median survival of PM is reported to be 6 to 12 months[25].

Discoverable English-language literature search via PubMed, Scopus, Web of Science, and Google Scholar identified 16 case reports of PM from PTC with pathological confirmation while patients were still alive[6-19]. Table 2 summarizes the cases of such entity including this report, the 17th patient. The most frequent presentation was visual symptoms from optic pathway compression[4,6-19,24,25]. With 12 of 17 patients (70.6%) from these reports, PM from PTC produced a slightly higher incidence of visual decline than the overall PM. The rate of panhypopituitarism in, 10 of 14 (71.4%), PM from PTC is almost double comparing to 37% from the review by Javanbakht et al[25]. In contrast, only 2 of 13 case reports (15.4%), PTC had a uniquely lower incidence of DI, similarly to an observation by Lim et al[32]. Additionally, worth mentioning is the fact that there is a higher rate of radiographic intra-tumoral hemorrhage in PM from PTC (23.1%) compared to other PM (8.5%)[2,6-19,33,34]. Indeed, we did come across the highly vascularized PM during the ETSS. Although primary PTC has excellent survival, the life expectancy of its PM actually is as short as other PM[2,6-20,25]. There were 8 patients, in Table 2, who had died at the time of publication. They had 39 days to 4 years (median = 11 months) to live. Other cases from 8 reports, and ours, were still living at 2 months to 3 years (median = 12 months). This is not significantly different from the average PM's survival.

Our patient was similar to the majority of PTC with PM in that she was in the typical age group. Also comparable with other case reports were the status of her secondary organ involvement and panhypopituitarism without DI. Nevertheless, her presentation was uncommon. Only 6 of 17 patients were diagnosed with PM at the same time of PTC discovery. Other 11 cases had PM development that varied widely from 2 months to 25 years after PTC. With ETSS and subsequent adjuvant treatments, the reported patient was living independently at 6 months after surgery.

In summary, PM from PTC is very rare. Despite the similarity between PM's and PA's imaging, understanding the differences in clinical manifestation ought to improve clinicians' early detection of PM. This is paramount since such condition required thorough workup as well as timely and aggressive treatments[27]. Although there were 16 existing

Table 2. Summary of the 16 case reports of pituitary metastasis from papillary thyroid carcinoma and the presented case

Year of publication	First author	Patient's age/sex	Time from PTC diagnosis to PM diagnosis	Other secondary organ involvement	Symptoms and signs	Intra-tumoral hemorrhage	Panhypopituitarism/ DI/Prolactin elevation	Surgery of PM/Adjuvant treatment(s)	Alive or dead at the time of case report	Length of Survival
1965	Johnson[9]	56 F	14 y	-	VFD, diplopia	NR	+/NR/NR	-/RAI, RT	Alive	20 m
1977	Pelosi[14]	32 M	Same time	NR	Painful diplopia	NR	+/NR/NR	TCS/RAI	Dead	39 d
1982	Ozanne[13]	66 F	2 y	NR	VFD, diplopia	NR	NR/NR/NR	-/-	Dead	2 m
1985	Sziklas[18]	44 M	25 y	Bone chest wall	-	-	+/+/NR	TSS/RAI	Dead	13 m
1999	Masiukiewicz[11]	56 M	5 y	Lungs, Right orbit	VFD, diplopia, ptosis	-	+/-/NR	-/RAI, CMT	Dead	1 y
1999	Masiukiewicz[11]	55 F	20 y	Lungs, Bone	VFD	-	+/-/NR	NS/RAI, RT	Dead	7 m
2001	Bell[7]	35 F	25 y	Lungs	VFD	+	+/+/+	TSS/RAI	Alive	NS
2010	Simmons[16]	48 M	Same time	-	VFD, seizures	-	NR/-/+	NS/RAI	Alive	3 y
2010	Xia[19]	56 F	7 y	-	VFD, ophthalmoplegia	NR	NR/NR/NR	TSS/NR	Alive	1 y
2011	Madronio[10]	53 F	Same time	-	VFD, headache	-	+/-/+	TSS/RAI	Alive	13 m
2012	Stojanovic[17]	67 F	Same time	Brain	VFD	-	+/-/+	TCS/-	Dead	10 m
2013	Barbaro[6]	63 F	Same time	Rib	Ptosis, diplopia	-	Normal/-/+	-/ RAI, RT	Alive	NS
2013	Barbaro[6]	65 F	2 m	-	Diplopia	-	Normal/-/-	NS/RT	Alive	2 m
2013	Chikani[8]	70 F	15 y	T1 vertebral metastasis	VFD	+	+/-/+	TSS/RAI,RT	Dead	4 y
2021	Meltzer[12]	56 F	17 y	Lymph nodes	Headache, diplopia	-	Normal/-/-	TSS/RT	Alive	6 m
2021	Poplawska-Kita[15]	68 F	4 y	-	VFD, headache, diplopia, facial paresthesia	-	Normal/-/NR	TSS/-	Dead	1 y
2021	Our case	64 F	Same time	Lungs, bone, brain	VFD	+	+/-/+	TSS/RAI, RT	Alive	6 m

F = Female; M = Male; NR = Not reported; NS = Not specified; VFD = Visual field defect; TCS = Transcranial surgery; TSS = transsphenoidal surgery; RAI = radioactive iodine I-131 ablation; CMT = Chemotherapy; RT = radiotherapy; PTC = papillary thyroid carcinoma; PM = Pituitary metastasis; d = day(s); m = month(s); y = year(s); + = present; - = absent

case reports from around the world, none was from Thailand. Hence, this is the first case report of PM from PTC of the country.

Conclusion

Papillary thyroid carcinoma metastasis to pituitary gland is very rare. In contrast to other pituitary metastasis, diabetes insipidus is a less common presentation while panhypopituitarism and intra-tumoral hemorrhage on imaging are more frequent.

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What is already known on this topic?

1) PTC metastasis to pituitary gland is extremely rare.

2) Visual field defect and DI are the common presentations in PM.

What this study adds?

1) This is the first case report of PTC with PM from a Thai patient.

2) This condition has a higher incidence of panhypopituitarism than other PM.

3) DI is uniquely less common in PM from PTC.

4) PTC with PM shows intra-tumoral hemorrhage on imaging more often than other PM.

Potential conflicts of interest

The authors declare no conflict of interest.

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