Case Report

Pituitary Metastasis from Renal Cell Carcinoma: A Case Report with Literature Review

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A 52-year-old man suffered from visual disturbance for 5 months. He then developed malaise, constipation and anorexia with significant weight loss. Physical examination showed noticeable signs of hypothyroidism, such as slurred speech, dry skin, macroglossia, myoedema and slow relaxation of ankle reflexes. In addition, eye exam showed abnormal visual acuity with left homonymous hemianopia. A large mass was found at right scapular region. Endocrinologic investigation results were compatible with secondary hypothyroidism with adrenal insufficiency. Subsequent CT brain revealed an enhancing mass at pituitary gland and also a mass at right occipital lobe with surrounding edema. CT of chest demonstrated multiple lung nodules, right scapular mass and incidentally revealed 8.7-cm hypervascular mass at left kidney. The final diagnosis was renal cell carcinoma with bone, lung, brain and pituitary metastasis. He received hormone replacement therapy as well as bisphosphonate and brain radiation. Following treatments, he was able to return to work with recovery of visual impairment.

Pituitary metastasis is a rare condition. Our patient presented with symptoms of hypothyroidism which may mimic pituitary adenoma, but had other clues of malignancy such as significant weight loss and scapular mass. The most common cancers that occasionally metastasize to pituitary gland are breast and lung cancer. Previously, renal cell carcinoma with pituitary metastasis has been reported. Unlike our patient, most of these cases developed metachronous pituitary metastasis.

Keywords: *Pituitary metastasis, Renal cell carcinoma, Hypopituitarism*

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A 52 year-old previously healthy man presented with progressive blurry vision for five months. Over the past month, he had developed profound fatigue, constipation, anorexia and 7-kg weight loss. He was a heavy smoker and had previous history of alcohol abuse. Physical examination revealed noticeably slurred speech, dry skin, macroglossia, clubbing of fingers and a 20 x 10 cm subcutaneous mass at the right scapular region. Eye examination showed significant impairment of visual acuity. He was able to count fingers in two-foot distance and see hand movement in one-foot distance by his right and left eye, respectively. The perimetry test for visual field showed left homonymous hemianopia. There was no limitation of extraocular eye movements. Myoedema and blunted Archiles tendon reflexes with slow relaxation were detected, whereas other neurological examination results were normal. The testes and pubic hair were normal. Endocrinologic evaluations showed free T4 of 0.59 ng/mL (normal, 0.9-1.9 ng/mL), T3 of 85.9 ng/dL (normal, 80-180 ng/mL), serum TSH of 2.4 mIU/L (normal, 0.23-4.0 mIU/L), and low level of 8 a.m. cortisol of 0.41 μg/dL, compatible with central hypothyroidism with adrenal insufficiency. Blood chemistry showed blood urea nitrogen of 8 mg/dL, creatinine of 1.2 mg/dL, total calcium of 14.4 mg/dL (normal, 8.1-10.4 mg/dL) and normal electrolytes. Urine analysis was normal with the urine specific gravity of 1.020.

Initial imaging including plain film of skull revealed widening of sella turcica (Fig. 1). Computed tomographic (CT) scan of brain demonstrated a 1.6 x 1.3 cm enhancing mass at the infundibulum with cavernous sinus involvement and a right parieto-occipital lobe enhancing lesion with surrounding brain edema, suggestive of brain metastasis (Fig. 2). Plain film of right scapula showed osteolytic lesion (Fig. 3),

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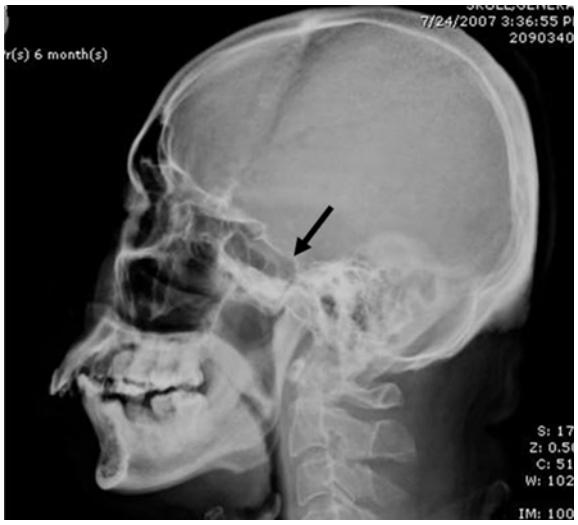

Fig. 1 Plain film of the skull showed widening of sella turcica (arrow) without evidence of bony destruction

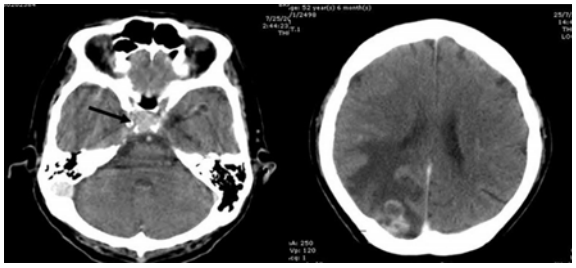

Fig. 2 Representative CT scan of the brain demonstrated an infundibular mass (arrow) and an enhancing lesion at right occipital lobe with surrounding brain edema. There was no midline shift

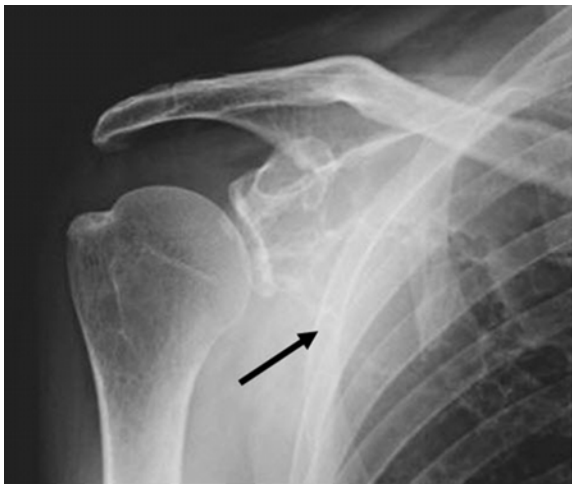

Fig. 3 Plain film of the right shoulder showed osteolytic lesion (arrow) at the right scapula, which corresponded to the area of the palpable mass by physical examination

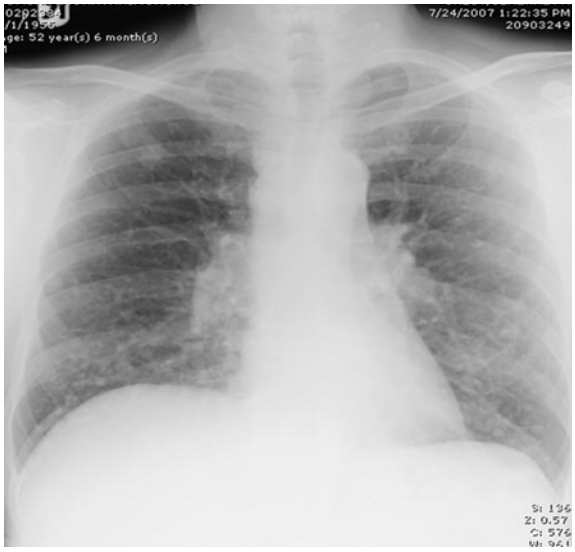

Fig. 4 Reticulonodular infiltration both lungs and bilateral hilar enlargement were demonstrated by CXR

corresponding with abnormal uptake on bone scan which also demonstrated bony metastasis at right scapular, as well as right parietal bone, left coracoid process, 2nd rib and 5th lumbar vertebrae.

There were multiple bilateral small pulmonary nodules with prominent both hilar regions as demonstrated by chest X-ray (CXR) in Fig. 4. Given that this patient had history of heavy smoking with abnormal CXR, provisional diagnosis was primary lung cancer with brain and bone metastasis. Subsequent CT of chest showed multiple pulmonary nodules, a huge right scapular mass, multiple mediastinal lymph nodes enlargement, with incidentally revealed 8.4 x 8.7 cm left renal mass and para-aortic lymphadenopathies (Fig. 5).

Histological examination from the right scapular mass revealed clusters of clear cells, suggestive of metastatic carcinoma as shown in Fig. 6A (x100). Immunostainings were positive for cytokeratin (AE1/AE3), vimentin, CD10 (Fig. 6B) and negative for melan-A, synaptophysin, which was suggestive of kidney in origin. The final diagnosis was renal cell carcinoma with bone, lung and brain metastasis.

On admission, the patient received intravenous dexamethasone to reduce brain edema and

replacement therapy for adrenal insufficiency. Thyroid hormone was replaced subsequently. Whole brain radiation, total dose of 20 Gray in 10 fractions was given. He received intravenous pamidronate every 3 weeks as treatment of hypercalcemia. Three months after starting treatment, symptoms of hypothyroidism disappeared. He was able to go back to work as previously. Thyroid function tests were normal. Unfortunately, he did not receive any specific systemic treatment either interferon or angiogenesis inhibitor due to limited affordability. He died of disseminated disease at 9 months after diagnosis.

Discussion

The authors reported a patient with a typical presentation of a rare condition, pituitary metastasis (PM), in a patient with no previous history of known cancer. In autopsy series, latent PM was revealed approximately 5 percent of patients with known malignancy. In two large series of sellar and parasellar lesions treated with transphenoidal surgery, there was only approximately 0.8-1 percent of metastatic cancer to pituitary gland[1,2]. Pituitary metastasis usually develops during terminal phase of malignant disease. As a result, most patients do not have any symptoms from PM (only 2.5-18% of cases)[3]. Most patients have suffered from symptoms of disseminated disease and do not survive long enough to allow symptoms from pituitary deficiency to become evident. In addition, constitutional and neurological symptoms of cancer may mask symptoms of anterior pituitary deficiency.

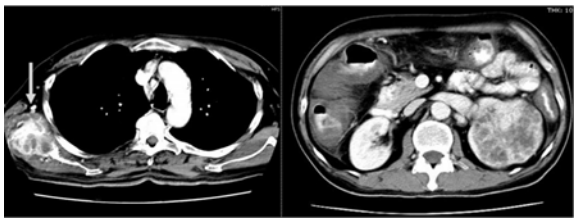

Fig. 5 CT of the chest revealed a right scapular mass (arrow), small pulmonary nodules as well as incidental finding of a hypervascular mass of the left kidney

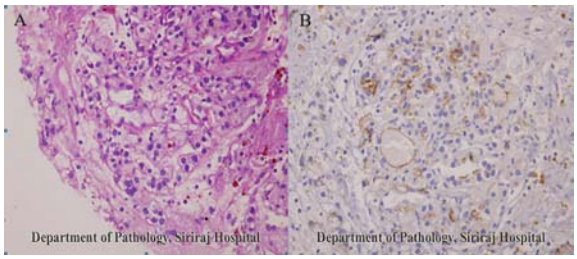

Fig. 6 Histological examination showed clusters of clear cells with positive for CD10, AE1/AE3 and vimentin which was compatible with renal cell carcinoma

Neoplasm from almost every tissue has been reported to metastasize to pituitary gland. Breast and lung cancer account for two-third of pituitary metastasis. Renal cancer (RCC) was found 2.6% in pituitary metastasis series[3]. Symptomatic pituitary metastasis from RCC is extremely rare. To date, there are only 24 cases reported in literatures[4-22]. Two-third of these patients were diagnosed renal cell carcinoma for years prior to onset of PM. Among these patients, interval between first diagnosis of primary cancer and diagnosis of PM varied from only one year up to as high as 27 years. However, some patients were diagnosed of PM as the first presentation of cancer.

Pituitary metastasis more frequently involves posterior lobe than anterior lobe of pituitary gland[2]. Therefore, it often manifests as posterior pituitary syndrome or diabetes insipidus. Only 15-20 percent of PM patients have anterior pituitary hormones deficiency[2,3,6]. However, symptoms of panhypopituitarism and visual impairment are more frequent in reported cases of RCC with PM[4]. Hypopituitarism was more prevalent in RCC with PM (88%) compared with other malignancies, whereas diabetes insipidus was less common (30%)[23]. This finding suggests that RCC preferentially involves anterior pituitary gland than posterior pituitary gland. These may due to the invasive growth and the predilection of RCC to extend into suprasellar region[21].

Treatment of PM from RCC is focused on palliation and symptom relief. Choices of treatments depend on symptoms and extension of systemic metastasis. Surgery may be indicated for patients with intractable pain and visual compromise, but surgery does not usually improve symptoms of pituitary hormone deficiency. Radiotherapy is beneficial, either as primary modality or adjuvant treatment after surgery in order to lengthen control of disease. Systemic treatments such as sunitinib, sorafenib, bevacizumab plus interferon or mTOR inhibitors are potential treatments with expectations to improve survival.

Conclusion

The authors present a patient of RCC with PM, who had apparent symptoms and signs of hypothyroidism at first presentation. Central

hypothyroidism and adrenal insufficiency, combining with visual symptoms lead us to diagnosis of pituitary tumor. Although there is very low incidence of pituitary metastasis compared with pituitary adenoma, finding of huge scapular mass and clubbing of fingers leaded us to a suspicion of metastatic cancer to pituitary gland rather than pituitary adenoma. Subsequent investigations confirmed the diagnosis and disclosed primary site of cancer.

Potential conflicts of interest

None.

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รายงานผู้ป่วยไทยหนึ่งรายที่เป็นโรคมะเร็งที่ไตกระจายไปที่ต่อมใต้สมอง

ศุทธินี อิทธิเมฆินทร์, ปานเทพ สุทธินนท์, จารุวรรณ เอกวัลลภ

ภาวะโรคมะเร็งกระจายไปที่ต่อมใต้สมองเป็นภาวะที่พบได้น้อยมาก ผู้ป่วยอาจมาด้วยอาการของการขาดฮอร์โมนดังเช่นในผู้ป่วยที่นำเสนอ ซึ่งอาจมีอาการคล้ายคลึงกับเนื้องอกของต่อมใต้สมอง (pituitary adenoma) ซึ่งมีอุบัติการณ์สูงกว่ามาก โรคมะเร็งที่กระจายไปที่ต่อมใต้สมองที่มีรายงานมากที่สุด ได้แก่ มะเร็งปอด และมะเร็งเต้านม สำหรับมะเร็งไตพบได้น้อยมาก และมักจะพบภายหลังจากที่ทราบว่าเป็นมะเร็งไตมากกว่าที่จะเป็นอาการนำไปสู่การวินิจฉัย

รายงานนี้นำเสนอผู้ป่วยชายไทยอายุ 52 ปีที่มาด้วยอาการอ่อนเพลีย เบื่ออาหาร น้ำหนักลด ทำงานได้ช้าลงในระยะเวลา 1 เดือนก่อนมาโรงพยาบาล มีอาการตามัว 5 เดือน การตรวจร่างกายพบว่าผู้ป่วยมีผิวแห้งมาก พูดช้ามาก ลิ้นมีขนาดใหญ่ นิ้วปุ้ม และมีก้อนที่สะบักข้างขวาขนาด 20 เซนติเมตร ต่อมทัยรอยด์ไม่โต การตรวจทางตาพบ left homonymous hemianopia การตรวจเลือดการทำงานของไทรอยด์เข้าได้กับการทำงานของไทรอยด์ต่ำชนิดทุติยภูมิ (secondary hypothyroidism) และตรวจพบว่ามีภาวะต่อมหมวกไตทำงานบกพร่อง (adrenal insufficiency) การตรวจ CT brain แสดงว่ามีก้อนที่ต่อมใต้สมองและที่สมองบริเวณ occipital lobe ข้างขวา การตรวจ CT chest พบว่ามีก้อนที่ปอดขนาดเล็กทั้งสองข้างกระจาย พบก้อนที่กระดูกสะบักด้านขวา และก้อนที่ไตด้านซ้าย ร่วมกับการตรวจชิ้นเนื้อจากก้อนที่สะบัก เข้าได้กับมะเร็งไต และมีการกระจายไปที่สมอง กระดูก และปอด ผู้ป่วยมีอาการดีขึ้นหลังได้รับการรักษาด้วยการทดแทนฮอร์โมนไทรอยด์และสเตียรอยด์ การฉายรังสีที่สมอง และได้รับยาในกลุ่ม bisphosphonate