Metastatic renal cell carcinoma to the pituitary presenting with hyperprolactinemia

S. Basaria¹, W.H. Westra², H. Brem³, and R. Salvatori¹
¹Department of Medicine, Division of Endocrinology; ²Department of Pathology; ³Department of Neurosurgery, Johns Hopkins University School of Medicine, Baltimore, USA

ABSTRACT. Metastases to the pituitary gland from systemic cancers is a rare phenomenon and usually occurs in patients with disseminated disease. The neurohypophysis is the most commonly involved site, and diabetes insipidus is the most common presentation in these patients. Breast and lung cancer are the most common cancers metastasizing to the pituitary. Involvement of the pituitary by renal cell carcinoma (RCC) is exceedingly rare. Mild-to-moderate degree of hyperprolactinemia is a rare presentation of pituitary metastases. We report the case of a woman with metastatic RCC to the pituitary presenting an unusually high degree of hyperprolactinemia.

INTRODUCTION
Metastases to the pituitary from systemic cancers is a rare phenomenon and usually occurs in patients with widely disseminated disease (1). The majority of systemic cancers involve the posterior pituitary (due to its systemic blood supply), making diabetes insipidus (DI) the major manifestation in these patients (2). Amongst the systemic cancers that metastasize to the pituitary, breast cancer is most common in women and lung cancer in men (3). Renal cell carcinoma (RCC) with metastasis to the pituitary is extremely rare. Hyperprolactinemia is a rare manifestation of pituitary metastasis and if encountered, it is generally mild. We report the case of a woman with metastatic RCC to the pituitary masquerading as a macroadenoma.

CASE REPORT
A 77-yr-old woman was referred to the endocrine clinic in October 2001 for the evaluation of a pituitary mass. The patient was asymptomatic until April 2001, when she developed blurred vision without headache or diplopia. Her poor vision was attributed to cataract. Over the next 4 months she underwent bilateral cataract surgery without any improvement in her vision. Furthermore, she developed intermittent diplopia. In August 2001, she underwent visual field testing that showed bitemporal hemianopsia. Magnetic resonance imaging (MRI) of the pituitary gland was performed and revealed a 2x2 cm pituitary mass with suprasellar extension compressing the optic chiasm and invading cavernous sinuses bilaterally (Fig. 1). The patient reported a several month history of reduced appetite, weight loss, and fatigue. She denied a history of galactorrhea, polyuria or polydipsia or nocturia. She was on no medication. Her past history was significant for breast cancer diagnosed in 1987 for which she underwent left mastectomy. She did not receive chemotherapy or radiation. In February 2001, she had been diagnosed with RCC for which she had undergone left nephrectomy. She was considered cured from both these cancers, as chest, abdomen and pelvis computed tomography (CT) had shown no evidence of metastatic disease 2 weeks prior to the diagnosis of the sellar mass. She had undergone menopause at the age of 50 and never received estrogen therapy. Her family history was significant for brain cancer (unknown type) in two brothers, one dying at the age of 17 and the other the age of 68. Her physical examination revealed right ptosis. Visual fields on direct confrontation confirmed bitemporal hemianopsia. The rest of her examination was normal, with the exception of evident kyphosis.
Her initial laboratory evaluation was as follows: sodium=141 meq/l (135-148), potassium=4.5 meq/l (3.5-5.0), creatinine=1.3 mg/dl (0.5-1.2), TSH=1.96 ulU/ml (0.5-4.5), free T4=0.4 ng/dl (0.7-1.6), LH=<0.2 mIU/ml (14-62), FSH=<0.3 mIU/ml (25-160), IGF-1=66 ng/ml (71-290), cortisol=4.7 ug/dl (drawn at 11 am) (6-26), PRL=210 ng/ml (0-18) (confirmed after serum dilution). PRL was assayed by a two site monoclonal antibody immunoenzymometric assay (AlA-PACK PRL on the Tosoh AlA NexIA) (Tosoh Biosciences, Inc., S. San Francisco, CA). The differential diagnosis included macroprolactinoma, non-secreting pituitary tumor, or sellar mass of other nature. The possibility of metastatic disease was considered unlikely due to lack of symptoms of diabetes insipidus and no evidence of metastatic disease elsewhere. She was started on hydrocortisone (10 mg in am and 5 mg in pm) and levothyroxine (75 mcg/dl) with dramatic improvement of her constitutional symptoms. Although an 11 AM serum cortisol of 4.7 ug/dl is not diagnostic of adrenal insufficiency, because of the high likelihood of adrenal insufficiency (sellar mass and failure of the other pituitary hormones), and of the clinical response to hydrocortisone therapy, no dynamic evaluation of her adrenal function was deemed necessary. The decision was made to send the patient in for pituitary surgery. The day before surgery, serum PRL was confirmed to be elevated at 186 ng/ml. On 10/23/01, the patient underwent transphenoidal resection of the mass. The tumor was highly vascular and the patient required intraoperative blood transfusion. Debulking of the tumor was performed, however, complete excision was deemed impossible due to the degree of invasiveness. Pathology showed metastatic RCC (Fig. 2). Immunostaining for PRL was negative.

In May 2002, a repeat MRI of the brain showed a slight increase in the suprasellar mass along with new metastatic lesions in the left lateral ventricle (1.4x1.2x1 cm) and in the left temporal bone (2.5x1.5 cm) near the left orbit. PRL remained elevated at 148.3 ng/ml. A CT scan of the body showed three 1 cm nodules in the lungs and one lesion in the spleen, consistent with metastatic disease. She underwent stereotactic radiosurgery in July 2002 receiving 3000 cGy in 6 fractions to the sella. In August 2002, she received

Fig. 1 - Coronal view of gadolinium-enhanced magnetic resonance imaging of the sellar mass.

Fig. 2 - Renal cell carcinoma (RCC) metastatic to the anterior pituitary. Typical of renal cell carcinoma, the tumor cells have prominent nucleoli, abundant granular cytoplasm and a nested growth pattern (A). The tumor cells are immunoreactive for RCC (B) but not PRL (not shown).