

# A Rare Cause of Pituitary Stalk Enlargement and Panhypopituitarism

SHEHZAD BASARIA, M.D.<sup>1</sup>, JULIE S. KROP, M.D.<sup>1</sup>, AND MILENA BRAGA-BASARIA, M.D.<sup>2</sup>

## Abstract

Pituitary stalk involvement is seen in a variety of medical conditions such as infectious diseases, infiltrative diseases and tumors (intracranial and metastatic). Metastatic cancer has a greater propensity to involve the infundibulum and neurohypophysis. We report a case of a 68-year-old man who presented with thickening of the stalk, panhypopituitarism, diabetes insipidus and generalized lymphadenopathy. Lymphoma was diagnosed on axillary lymph node biopsy and lymphomatous involvement of the infundibulum was suspected. Although infundibular thickening resolved and diabetes insipidus improved after chemotherapy, panhypopituitarism persisted.

**Key Words:** Panhypopituitarism, lymphoma.

## Introduction

THE PITUITARY GLAND AND INFUNDIBULUM can be involved in a variety of medical conditions, such as infiltrative diseases (hemochromatosis, sarcoidosis, Wilson's disease), infections (tuberculosis, fungal infections) and tumors (intracranial and metastatic) (1, 2). Metastatic cancers have a predisposition to spread to the posterior pituitary and the infundibulum, with diabetes insipidus (DI) being a common pathology at presentation. Lymphomas are known to metastasize to the pituitary gland (2). Infundibular thickening is the most common finding on the magnetic resonance imaging (MRI) in these patients. We report a middle-aged man who presented with DI, pituitary stalk thickening and generalized lymphadenopathy. Axillary lymph node biopsy showed high-grade B-cell

lymphoma. Lymphadenopathy and infundibular thickening resolved after chemotherapy, and DI improved. However, anterior pituitary function did not improve.

## Case Report

A 68-year-old man was admitted with a 6-week history of polyuria, polydipsia, postprandial nausea and emesis. The patient had been well until 6 months previously, when he developed anorexia and early satiety. He lost 20 lbs over this period of time. He denied any abdominal pain, but six weeks before admission he developed emesis, which occurred 60–90 minutes after a meal. He denied any dysphagia, odynophagia, fever, night sweats, headaches, head trauma, or visual symptoms. He was not taking any medications. He did complain of polyuria (6–8 times, both diurnal and nocturnal) and polydipsia, decreased libido, impotence and muscle weakness. There was no history of hyperpigmentation. His medical history and family history were unremarkable.

On physical examination, a 3.5 cm left axillary lymph node was palpable. There was no cervical lymphadenopathy. The visual fields were normal and there was no organomegaly. Both testes were atrophic. Neurological exami-

<sup>1</sup> Division of Endocrinology and Metabolism, Johns Hopkins University School of Medicine, Bayview Medical Center, and <sup>2</sup>SEMPR — Serviço de Endocrinologia e Metabologia do Hospital de Clínicas da Universidade Federal do Paraná, Curitiba, Brazil.

Address all correspondence to Shehzad Basaria, M.D., 4940 Eastern Avenue, B-Building, Suite 114, Baltimore, MD 21224; E-mail: sbasaria@jhmi.edu

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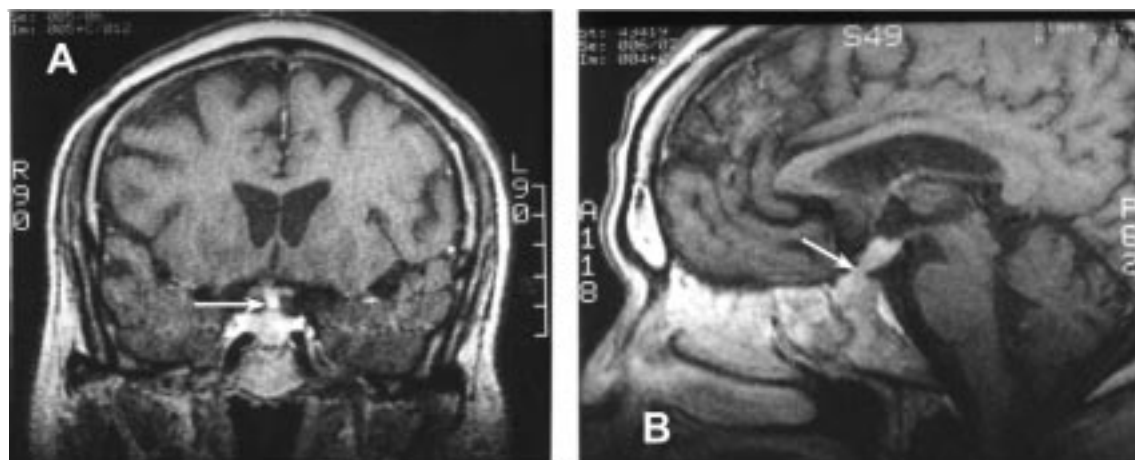
nation was significant for decreased muscle bulk and power. Pertinent laboratory values are as follows: sodium 149 meq/L, potassium 3.9 meq/L, creatinine 0.9 mg/dL, glucose 92 mg/dL, calcium 7.9 mg/dL, LDH 241 IU/L, uric acid 9.2 mg/dL, hematocrit 33.2%, and WBC  $4.1/\text{mm}^3$ . Serum osmolality was 304 mOsm/kg with a concomitant urine osmolality of 67 mOsm/kg and specific gravity of 1.004. A comprehensive endocrine work-up was performed, revealing the following: luteinizing hormone (LH)  $<0.1$  mIU/mL, follicle-stimulating hormone (FSH) = 0.7 mIU/mL, testosterone  $<20$  ng/dL (normal 400–1000), TSH = 1.09 mIU/L (0.5–4.50), free T4 = 0.6 ng/dL (0.7–1.6), prolactin = 18 ng/mL (0–20), insulin-like growth factor-1 (IGF-1)  $\leq 16$  ng/mL (normal 71–290), and random cortisol = 5.5  $\mu\text{g}/\text{dL}$ . Cosyntropin stimulation test (250  $\mu\text{g}$  of adrenocorticotropic hormone [ACTH] administered intravenously resulted in a serum cortisol level of 10.3  $\mu\text{g}/\text{dL}$  (normal 20  $\mu\text{g}/\text{dL}$ ) at 60 minutes. Urine electrolytes were normal. MRI of the pituitary showed thickening of the pituitary stalk without any other lesions (Figs. 1a and 1b).

Excisional biopsy of the 3.5 cm axillary lymph node was performed. Histopathology was consistent with diffuse, large B-cell lymphoma. The computerized tomography (CT) scan of the chest showed mediastinal and pre-tracheal adenopathy. Abdominal CT scan showed significant celiac adenopathy resulting in compression of the gastric pylorus (explaining patient's post-prandial emesis). Serum angiotensin-converting enzyme (ACE) level (15 IU/L [normal 10–34]) and 1.25 vitamin D level (31 pg/mL [normal 15–60]) were normal (thus excluding sarcoidosis). Serum and urine protein elec-

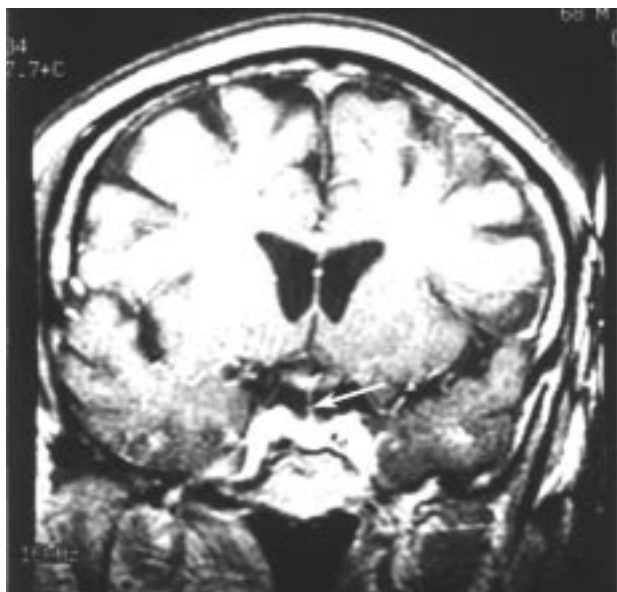
trophoresis were normal. It was concluded that the patient's hypophyseal involvement most likely represented metastatic lymphoma. The patient was started on vasopressin analogue (DDAVP) at a dose of 10  $\mu\text{g}$  twice daily intranasally and replacement doses of hydrocortisone (10 mg twice daily), levothyroxine (0.1 mg once daily) and testosterone enanthate (200 mg intramuscularly every two weeks). The patient underwent four cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP). After the fourth cycle, his appetite improved significantly, with resolution of his postprandial nausea and vomiting. The patient's polyuria also improved, resulting in a reduction in his DDAVP dose (10 g once daily). A follow-up CT scan showed complete resolution of the mediastinal and abdominal lymphadenopathy. Follow-up MRI of the pituitary gland showed complete resolution of the pituitary stalk thickening (Fig. 2). However, hormonal evaluation of the anterior pituitary showed persistent panhypopituitarism (testosterone  $<20$  ng/dL, LH = 9.6 mIU/mL, FSH = 3.2 mIU/mL, IGF = 22 ng/mL, cortisol after cosyntropin stimulation test = 16  $\mu\text{g}/\text{dL}$  [normal  $>20$ ] and TSH = 0.11  $\mu\text{IU}/\text{mL}$ ). He continued on stable replacement doses of DDAVP, hydrocortisone, levothyroxine and testosterone. Six months later, his disease recurred and the patient failed to respond to additional cycles of chemotherapy. He died 3 months later.

## Discussion

In an adult, the diagnosis of pituitary stalk enlargement is entertained when the stalk diameter exceeds 4 mm (1). The differential diagno-



**Fig. 1.** Coronal (a) and sagittal (b) view of the pituitary stalk (arrows), showing significant enlargement on magnetic resonance imaging.



**Fig. 2.** Coronal view of the infundibulum, which has returned to its normal size (after) after chemotherapy.

sis of pituitary stalk enlargement includes infiltrative diseases like hemochromatosis and sarcoidosis, infectious diseases like tuberculosis and fungal infections, vascular compromise, metastatic solid tumors (including lymphomas) and leukemias (2). According to various reports, pituitary metastases have been reported to occur in 1–27% of patients with cancer (2). Breast cancer in women and lung cancer in men are the most common cancers involving the infundibulum and the posterior pituitary. The presence of DI is an important feature differentiating metastatic lesions from adenomatous lesions of the pituitary gland. Metastatic deposits are lodged more frequently in the neurohypophysis than in the adenohypophysis, due to the nature of the vascular supply of the posterior pituitary. The posterior lobe is supplied by the hy-

pophysial arteries, which are branches of the internal carotid artery. This systemic circulation predisposes the posterior pituitary to become a haven for metastatic deposits compared to the anterior pituitary, which is relatively protected by the sealed circulation of the portal venous system. In patients with lymphoma, DI occurs due to infiltration of the pituitary stalk and/or neurohypophysis. In the majority of these patients, the pituitary function does not recover, despite treatment of the underlying condition. Although our patient did not have any recovery of his anterior pituitary function after chemotherapy, the dose of DDAVP decreased, suggesting an improvement in DI. Diffuse large cell lymphoma of B-cell immunophenotype is known to be the most common lymphoma metastasizing to the pituitary gland and the pituitary stalk. This type of lymphoma is often extremely aggressive and is associated with a high mortality rate. Angiocentric T-cell lymphoma has also been reported to metastasize to the infundibulum (3–5).

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