LETTER TO THE EDITOR

Meningioma-induced Cushing’s syndrome due to ectopic production of corticotropin-releasing hormone: A case study of clinical presentation

Dear Editor,

Ectopic synthesis of corticotropin-releasing hormone (CRH) outside the hypothalamus has been identified in both neuroendocrine and non-neuroendocrine tissues, including anterior pituitary, skin, and ovary [1]. We report a rare case of meningioma-induced Cushing’s syndrome (CS) due to ectopic production of CRH.

A 57-year-old woman was admitted for Cushingoid appearance and hypokalemia in June 2003. She had a history of diabetes mellitus and hypertension during the preceding 3 years. Physical examination revealed moon face, buffalo hump, abdominal obesity and striae, and ecchymosis of four limbs. Her height was 150 cm, weight 59 kg, and blood pressure 170/90 mmHg. Plasma potassium was 2.5 mEq/L. Endocrinological studies revealed adrenocorticotropic hormone (ACTH)-dependent CS. Baseline plasma ACTH was 427 pg/mL. Magnetic resonance imaging (MRI) of the sella turcica showed no evidence of pituitary nodule, but did find a left high frontoparietal meningioma (3.5 cm in diameter, Fig. 1A). Cerebral angiography demonstrated a hypervascular tumor stain at the left high frontoparietal region, supplied mainly by the right middle meningeal artery (Fig. 1B). Spasm of this artery was found while performing a procedure to embolize the meningioma 4 days after cerebral angiography. The peripheral plasma ACTH level fell to 131 pg/mL 2 days after spasm.

Two weeks after spasm, the patient had symptoms and signs of adrenal insufficiency. Baseline plasma cortisol and ACTH levels were low (3.72 μg/dL and 45.8 pg/mL, respectively). Four weeks after spasm, the baseline plasma ACTH level was reduced to 3.92 pg/mL. Brain MRI revealed ischemic change and partial regression of the tumor (Fig. 1C). Left parietal craniotomy and total excision of the brain tumor were performed in August 2003, 6 weeks after spasm. Pathology proved the tumor was a meningioma. The immunohistochemical (IHC) stain for ACTH was negative (Fig. 1D). Eleven months after resection, circadian rhythm of the baseline plasma cortisol was normal. Twenty-seven months after resection, an overnight low-dose dexamethasone suppression test failed to suppress plasma cortisol (36.0 μg/dL). Twenty-eight months after resection, brain MRI demonstrated recurrent meningioma (1.5 cm in diameter). The patient refused any further surgical intervention for the recurrent meningioma. She died in December 2007. One hundred and two months after resection, there was positive IHC staining for CRH in paraffin-embedded block of meningioma (Fig. 1E).

This is the first case report of positive IHC stain for CRH in meningioma-induced CS. Lokich et al [2] reported a case of islet cell carcinoma metastasis to liver with ectopic ACTH-dependent CS. After hepatic artery embolization, plasma ACTH decreased rapidly. ACTH was not identified in the excised primary tumor or metastatic liver lesion. The authors explained that this was probably related to the inadequacy of the assay system [2]. However, ectopic ACTH-dependent CS can be caused by either ACTH- or CRH-secreting tumors. Possibly, the ACTH-negative tumor could have elaborated CRH [3].

A normal-sized pituitary gland has been found in imaging (MRI or CT) or autopsy studies in patients with an ectopic CRH secreting tumor. Undetectable or normal plasma CRH levels have also been reported [1,4,5]. Adrenal insufficiency should be kept in mind after embolization of an ectopic CRH-secreting meningioma-induced CS.
Figure 1. (A) Magnetic resonance imaging (MRI) of the sella turcica reveals a left high frontoparietal meningioma (arrow); (B) cerebral angiography of the brain demonstrates a hypervascular tumor stain at the left high frontoparietal region (arrow) supplied mainly by the right middle meningeal artery (arrowhead); (C) MRI of the brain shows ischemic change and partial regression (arrow) of the meningioma 4 weeks after spasm of the right middle meningeal artery; (D) immunohistochemical (IHC) stain for adrenocorticotropic hormone (ACTH) from the resected meningioma is negative (100×); (E) IHC stain for corticotropin-releasing hormone from the paraffin-embedded block of meningioma is positive (200×).

References


Jui Lan
Department of Anatomic Pathology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

Chun-Chung Lui
Department of Radiology, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

Tao-Chen Lee
Division of Neurosurgery, Department of Surgery, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan

*Corresponding author.
Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, 123 Ta-Pei Road, Niao-Sung District, Kaohsiung City 83301, Taiwan.

E-mail addresses: tungqq44112@yahoo.com.tw, q44112@adm.cgmh.org.tw (S.-C. Tung)

Shih-Chen Tung*
Division of Endocrinology and Metabolism, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan