LETTER TO THE EDITOR

Cushing's disease due to an ACTH-secreting pharyngeal pituitary tumor

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The pharyngeal pituitary gland is a small embryological remnant derived from Rathke's pouch lying in the mucoperiosteum of the nasopharynx and is almost universally present in humans (1, 2). According to the ultrastructural analysis of the pharyngeal pituitary gland, most of the cells are loaded with secretory granules and display all the characteristics of secretory cells (3). Seven hormone-producing cell types have been identified in the pharyngeal pituitary gland of humans by immunocytochemistry (4, 5).

It is generally agreed that there is a low probability that the pharyngeal pituitary gland contributes appreciably to the overall secretion of adenohypophyseal hormones because of its anatomical isolation from the hypothalamus and its small size relative to the adenohypophysis. Similarly, it seems that the gland is not responsible for clinical disorders, except for very rare cases in which the gland is the site of a functioning tumor.

We report the case of a 43-year-old female patient with Cushing's disease with an adrenocorticotropin (ACTH)-secreting tumor originating from the pharyngeal pituitary gland. Initially she presented with hypertension and diabetes mellitus. Clinically she had the typical features of Cushing's syndrome. Plasma levels of cortisol were elevated with a loss of diurnal variation (0800 h, 1137 nmol/l; 1600 h, 1007 nmol/l). Plasma ACTH was within the normal range (15 pmol/l). Both low-dose and high-dose dexamethasone suppression tests showed no suppression of plasma or urinary cortisol levels. Abdominal computed tomography (CT) showed a 2 cm nodule in the left adrenal gland, and sellar magnetic resonance imaging (MRI) revealed a normal pituitary gland (Fig. 1A). Under the impression that there was ACTH-dependent macronodular adrenocortical hyperplasia, bilateral adrenalectomy was performed. The patient was fine for a few months, but then plasma ACTH levels increased to 99.6 pmol/l and generalized pigmentation developed. One year after bilateral adrenalectomy a follow-up MRI was performed suspecting Nelson's syndrome. It revealed a 3.8 × 2.5 cm sized mass in the nasopharynx and a normal intrasellar pituitary gland (Fig. 1B). The

mass was removed and histologically proved to be a typical densely granulated ACTH cell adenoma. Immunohistochemistry revealed that the tumor tissue was composed entirely of ACTH-immunoreactive cells. There were no luteinizing hormone-, follicle-stimulating hormone-, thyrotropin-, growth hormone-, prolactin- or chorionic gonadotropin-immunoreactive cells in the tumor tissue. On the operation field, the tumor was located at the junction of the nasopharynx and choana. The consistency was soft and somewhat friable like tumors of the pituitary gland. The anterior wall of the sphenoid sinus was partially destroyed by the tumor, but the mucosa and cavity of the sinus were preserved. After the resection of the tumor and post-operative radiation therapy, plasma ACTH was not detected and the patient has now been treated with glucocorticoid substitutive therapy for 4 years.

This case is extraordinary in that Cushing's disease was caused by a rapidly growing ACTH-secreting pharyngeal pituitary tumor. Several problems are apparent in the management of this patient. ACTH-dependent Cushing's syndrome was initially diagnosed but no corticotropin-releasing hormone test and no search for an ectopic ACTH source was performed (e.g. thoracic CT scan, inferior petrosal sinus sampling). Inferior petrosal sinus sampling might have helped to identify the ACTH source earlier. The other point was that we missed the nasopharyngeal lesion which was clearly visible on the initial MRI (Fig. 1A). This was probably due to unawareness of the possibility that a pharyngeal pituitary tumor could be the source of ACTH excess.

Very little is known about functioning tumors of the pharyngeal pituitary gland. Reviewing the literature, there are only few cases of acromegalic patients and one patient with Cushing's disease that originated from a pharyngeal pituitary tumor (6–8). To our knowledge, this is the first case of Cushing's disease due to a pharyngeal pituitary tumor with a more detailed clinical evaluation. In conclusion, in the evaluation of patients with ACTH-dependent Cushing's syndrome, the presence of a functioning pharyngeal pituitary tumor should be kept in mind.

Figure 1 T₁-weighted MRI on initial examination and after adrenalectomy. (A) On sagittal T₁-weighted MRI, a focal soft tissue thickening is noted at the roof of the nasopharynx (arrow). It appears to be confined in the pharyngeal mucosal space. Superiorly, the normal pituitary gland is located in the sella. (B) On sagittal contrast-enhanced MRI, the mass is enlarged in size, as compared with the initial MRI. The mass appears to encroach into the sphenoidal sinus (arrow).

References

- 1 Kovacs K & Horvath E. Morphology of the pituitary in health and disease. In *Principles and Practice of Endocrinology and Metabolism*, pp 109–124. Ed KL Becker. Philadelphia: JB Lippincott Co., 1990.
- 2 Fuller GN & Batsakis JG. Pharyngeal hypophysis. *Annals of Otolaryngology, Rhinology and Laryngology* 1996 **105** 671–672.
- 3 Gonzalez CB, Valdes GF & Ciocca DR. Ultrastructure of the human pharyngeal hypophysis. *Acta Anatomica* 1977 **97** 224–230.
- 4 Ciocca DR, Puy LA & Stati LA. Identification of seven hormone producing cell types in the human pharyngeal hypophysis. *Journal of Clinical Endocrinology and Metabolism* 1985 **60** 212–216.
- 5 Puy LA & Ciocca DR. Human pharyngeal and sellar pituitary glands: differences and similarities revealed by an immunocytochemical study. *Journal of Endocrinology* 1986 **108** 231–238.
- 6 Richards SH & Evans ITG. The pharyngeal pituitary and its surgical significance. *Journal of Laryngology and Otology* 1974 **88** 937–946.
- 7 Warner BA, Santen RJ & Page RB. Growth hormone and prolactin secretion by a tumor of the pharyngeal pituitary. *Annals of Internal Medicine* 1982 **96** 65–66.
- 8 Chandler WF, Schteingart DE, Lloyd RV, McKeever PE & Ibarra-Perez G. Surgical treatment of Cushing's disease. *Journal of Neurosurgery* 1987 **66** 204–212.

Received 15 February 2000

Accepted 17 October 2000