Ectopic Pituitary Adenoma in the Cavernous Sinus Causing Oculomotor Nerve Paresis  
—Case Report—

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Abstract

A 24-year-old woman presented with a rare adrenocorticotropic hormone (ACTH)-positive pituitary adenoma in the cavernous sinus, manifesting as sudden onset of oculomotor nerve paresis. Neuroimaging revealed a tumor in the cavernous sinus bulging into the subdural space. There was no continuity between the tumor and the pituitary gland in the sella turcica. Gross total removal of the tumor was performed through the orbitozygomatic approach followed by stereotactic radiosurgery. The oculomotor nerve paresis was resolved. Histological examination revealed an adenoma positive for ACTH. Ectopic pituitary adenoma occurs mostly in the sphenoid sinus or the suprasellar region. This extremely rare case of ectopic macroadenoma in the cavernous sinus manifested as oculomotor nerve paresis without signs of Cushing’s syndrome.

Key words: adrenocorticotropic hormone-secreting adenoma, cavernous sinus, ectopic pituitary adenoma, empty sella, oculomotor nerve paresis, silent corticotroph adenoma

Introduction

Ectopic pituitary adenoma is an adenoma that occurs outside the sella without continuity to the normal pituitary gland. Intracranial and extracranial locations are known, most often in the suprasellar region or the sphenoid sinus. Only four of 65 (6.2%) reported ectopic pituitary adenomas have been found in the cavernous sinus. We present a case of adrenocorticotropic hormone (ACTH)-positive ectopic pituitary adenoma in the cavernous sinus manifested as sudden onset of oculomotor nerve paresis and did not cause Cushing’s syndrome. This symptom gradually resolved after removal of the tumor and stereotactic radiosurgery.

Case Report

A 24-year-old woman woke one morning and found that she could not open her left eye. She also suffered from double vision when she forced the left eye open. On admission 4 days after onset, neurological examination revealed no deficit except for complete left oculomotor nerve paresis manifesting as mydriasis, fixed abducent ocular position, and absence of light reflex. Physical examination revealed no definite clinical signs of endocrinological dysfunction.

Skull radiography showed the sella configuration was normal without bone erosion or hypertrophy. Computed tomography showed a well-enhanced mass lesion occupying the left cavernous sinus, and partially bulging into the subdural space. Magnetic resonance (MR) imaging demonstrated that the mass was isointense on both T1- and T2-weighted images. The sagittal view showed that the pituitary gland located at the bottom of the sella, which was enhanced gradually and uniformly in a dynamic study (Fig. 1). No continuity of the mass to the sella was recognized.

High-dose dexamethasone therapy was carried...
out under a diagnosis of suspected inflammatory lesion, but this did not bring any clinical improvement. Unfortunately, the pituitary hormonal study was not available before the administration of dexamethasone. Levels of the anterior lobe hormones measured after this therapy were normal: growth hormone (GH) 0.15 ng/ml, prolactin 1.0 ng/ml, thyroid-stimulating hormone (TSH) 0.308 mIU/l, luteinizing hormone (LH) 3.8 IU/l, follicle-stimulating hormone (FSH) 5.5 IU/l, and ACTH 23 pg/ml.

Ten days after onset, surgery was performed through the left orbitozygomatic approach (combined extra- and intradural approach) under a diagnosis of intracavernous sinus tumor such as meningioma, cavernoma, or pituitary adenoma. Removal of the anterior clinoid process exposed the anterior portion of the tumor in the cavernous sinus. Then, the convexity dura was cut and the sylvian fissure was widely opened. The intradural part of the tumor was observed around the supraclinoid portion of the internal carotid artery, and the oculomotor nerve was hidden by the tumor. The lateral wall of the cavernous sinus was hyperemic and markedly bulged laterally. The intradural tumor at the oculomotor trigone was first removed, then the dura between the internal carotid artery and the oculomotor nerve, namely the clinoid space, was incised and the intracavernous tumor was curetted. Parkinson’s triangle was then opened and gross total removal of the tumor was achieved without sacrificing any structures in the cavernous sinus, including the oculomotor nerve. The whitish tumor was elastic hard and fibrous. Pulsation of the cavernous portion of the internal carotid artery was observed after tumor removal. The oculomotor nerve was totally surrounded by the tumor along the intradural and intracavernous course, and there was no continuity between the tumor and the pituitary gland in the sella turcica (Fig. 2).

Histological examination of the tumor revealed monotonous proliferation of polyclonal cells with round nuclei and relatively abundant eosinophilic cytoplasm, forming trabeculae, solid nests, and a focally papillary growth pattern (Fig. 3A). These findings were compatible with a pituitary adenoma. Few mitotic events were found, and the MIB-1 proliferation index was low. Some infiltration to the dura was found. Immunohistochemical examination showed most tumor cells were reactive for ACTH and synaptophysin (Fig. 3B). No reactivity was

Fig. 1 Axial T1-weighted magnetic resonance (MR) images showing a well-enhanced mass occupying the left cavernous sinus (upper left), and bulging into the subdural space superolaterally (upper right). Coronal (lower left) and sagittal (lower right) T1-weighted MR images showing the pituitary gland located at the bottom of the bottom.

Fig. 2 Intraoperative photographs showing an elastic hard, fibrous, whitish mass (T: tumor) protruding from the cavernous sinus and surrounding the oculomotor nerve (CN III) at the oculomotor trigone (upper row: before removal, lower row: after removal). CN II: optic nerve, FL: frontal lobe, ICA: internal carotid artery, PcomA: posterior communicating artery, TL: temporal lobe.
found for GH, prolactin, TSH, LH, FSH, epithelial membrane antigen, or glial fibrillary acidic protein.

Her postoperative course was uneventful. MR imaging performed after surgery revealed no residual tumor (Fig. 4). Levels of pituitary hormones were normal again postoperatively: GH 0.05 ng/ml, prolactin 1.0 ng/ml, TSH 1.86 mIU/l, LH 3.9 IU/l, FSH 7.6 IU/l, and ACTH 14 pg/ml. After stereotactic radiosurgery in the left cavernous sinus, she was discharged from the hospital. The oculomotor nerve paresis gradually improved and finally subsided completely after one year. She has been followed up for 3 years with no signs of recurrence.

Discussion

Invasion of the cavernous sinus and resultant cranial nerve dysfunction is not uncommon in cases of intrasellar pituitary adenoma. In contrast, the present case showed no change in pituitary function after removal of the tumor, no neuroimaging or intraoperative evidence of connection between the tumor and the inside of the sella, and an apparently normal pituitary gland in the sella by conventional and dynamic MR imaging. These findings suggest that the tumor originated from within the cavernous sinus, rather than from inside the sella. Intracavernous metastasis of ectopic ACTH-producing tumor, such as carcinoid or small cell carcinoma, may be suggested as a differential diagnosis. However, this can be excluded in our case because ACTH produced by such tumor is not depressed by dexamethasone administration, and because no ‘original’ lesion or other metastatic lesions were discovered for 3 years after resection of the intracavernous tumor. ACTH-secreting ectopic pituitary microadenoma originating in the cavernous sinus may manifest as Cushing’s syndrome, but this case of an ectopic pituitary macroadenoma in the cavernous sinus manifested as oculomotor nerve paresis due to the mass effect.

There are two main theories regarding the origin of ectopic pituitary adenomas. Adenoma in the suprasellar region may arise from anterior lobe cells attached to the supradiaphragmatic portion of the pituitary stalk. Adenoma occurring along the path of the embryonal development of Rathke’s pouch, such as the sphenoid sinus, nasal cavity, and
suprasellar region, is thought to originate from the embryologic remnants of pituitary tissue.\textsuperscript{11,12} Suprasellar ectopic pituitary gland cells were found in 75% of normal adult brains, and pituitary tissue remains in the pharyngeal roof area for life, so may be called the pharyngeal pituitary.\textsuperscript{2,3} The tumor in the present case had no attachment to the pituitary stalk and was distant from the embryonal pathway for Rathke’s pouch. Therefore, the present case seems to be distinct from the usual type of ectopic pituitary adenomas accounted for by these two theories. Ectopic pituitary adenomas in association with an empty sella may be the result of incomplete migration of Rathke’s pouch and incomplete adenohypophyseal development.\textsuperscript{17} This hypothesis might be applicable in the present case.

The tumor cells in the present case were immunohistochemically positive for ACTH, but the patient did not manifest any symptoms of Cushing’s syndrome. Her preoperative serum ACTH level was normal, but this was measured after high-dose dexamethasone therapy. An ACTH-producing ectopic pituitary adenoma can function as its intrasellar counterpart, retaining feedback inhibition by high-dose dexamethasone.\textsuperscript{21} Therefore, it is possible that the serum level of ACTH in the present case was high before high-dose dexamethasone therapy. However, the present case is more likely to be ‘silent corticotroph adenoma.’ This clinical entity is now widely accepted and is defined by the following characteristics: absence of clinical signs of Cushing’s disease, immunoreactivity for ACTH, no or minor increases in serum ACTH levels, high frequency of symptoms attributable to mass effects, large tumor size, and sphenoid or cavernous sinus invasion.\textsuperscript{5,20} The clinical characteristics of the present case meet these criteria.

Another characteristic of the present case was the sudden onset of isolated oculomotor nerve paresis without other cranial nerve disturbance. A previous case of pituitary adenoma also invaded the cavernous sinus, which bulged farther into the subdural space.\textsuperscript{9} The dural pocket of the third cranial nerve is a weak point of the meningeal wall of the cavernous sinus and a tumor can easily extend through this point.\textsuperscript{9} Since the location of the subdural part of the tumor in our case was similar, we surmise that subdural extension of the tumor through the dural pocket caused kinking of the oculomotor nerve.

The rapid clinical course in the present case strongly suggests pituitary apoplexy. Although no necrosis or hemorrhage was found in the specimen, apoplexy could not be excluded. It is possible that apoplectic foci were located in unexamined tissues, since the tumor was removed piecemeal and some fragments were sucked away.

Ectopic pituitary adenoma is an important differential diagnosis for an intracavernous tumor, but is extremely rare compared to meningioma, cavernoma, or neurinoma. The present case indicates that ectopic pituitary adenoma should be considered in the differential diagnosis of a tumor located in the cavernous sinus, even there are no clinical signs of endocrine dysfunction.

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References


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