Repeated Hemorrhage in Ciliated Craniopharyngioma
—Case Report—

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Abstract

A 49-year-old female presented with a ciliated craniopharyngioma manifesting as repeated intratumoral hemorrhage. Histological examination suggested that the hemorrhage originated from the many thin blood vessels in the cyst wall stroma associated with inflammation. Symptomatic hemorrhage in cystic craniopharyngioma may mimic pituitary apoplexy but the etiology is quite different. Minor hemorrhage may recur unless the cyst wall is totally removed.

Key words: craniopharyngioma, intratumoral hemorrhage, pituitary apoplexy, Rathke’s cleft cyst

Introduction

Symptomatic pituitary hemorrhage is usually associated with adenoma, particularly with large adenomas, and more rarely with other sellar tumors. Acute hemorrhagic infarction and necrosis of a pituitary adenoma may lead to fulminant tumor expansion and result in sudden severe headache, visual disturbances, cranial nerve paresis, and rarely disturbance of consciousness. The definition of pituitary apoplexy remains ambiguous, but is generally recognized as such rare but abrupt neurological deteriorating conditions associated with adenomas. Although subclinical hemorrhage may not be rare, symptomatic hemorrhage associated with craniopharyngioma is very rare. We report a unique case of ciliated craniopharyngioma that manifested as repeated spontaneous hemorrhage.

Case Report

A 49-year-old female suddenly suffered severe headache, nausea, and left visual disturbance. Twenty-two years previously, she had undergone surgical treatment for craniopharyngioma manifesting as gradual onset of visual disturbance. A cystic tumor containing a yellow fluid and some hematoma clots was subtotally removed via a right frontotemporal approach. Since the initial admission, she had lost her right visual function. However, no signs of recurrence had been observed and her pituitary function had remained normal, so she had not been examined for the last 10 years.

On admission, she complained of general fatigue, excessive sleep requirement, nausea, anorexia, cold intolerance, and dizziness, suggestive of hypopituitarism. Neurological examination demonstrated left blurred vision and temporal hemianopsia, in addition to the right visual loss. Endocrinological examination of hormone levels confirmed the diagnosis of hypopituitarism: Adrenocorticotropic hormone 7 pg/ml (normal 9–52), cortisol 3.6 μg/dl (4.0–18.3), thyroid-stimulating hormone 1.8 μU/ml (0.2–5.0), free T3 <1.3 pg/ml (2.47–4.34), free T4 0.48 ng/dl (0.65–1.8), luteinizing hormone (LH) <0.5 mIU/ml (8.7–38.0), follicle-stimulating hormone 1.0 mIU/ml (26.2–113.3), growth hormone 0.47 ng/ml (0.66–3.68), and prolactin 17 ng/ml (1.5–9.7). The levels of adrenohypophysial hormones showed no or poor response to the triple stimulation test (thyrotropin-releasing hormone 0.5 mg, LH-releasing hormone 0.1 mg, and regular insulin 6 U). The plasma antidiuretic hormone level was 1.5 pg/ml (0.3–3.5). She also showed hyponatremia of 133 mEq/l (138–148). Other neurological examinations and routine laboratory examinations, including cerebrospinal fluid studies, showed no abnormalities.
Hemorrhage in Ciliated Craniopharyngioma

Fig. 1 Craniogram demonstrating a markedly enlarged sella. No calcification is present.

Fig. 2 Axial computed tomography scans obtained 2 weeks after an apoplectic episode showing a homogeneously isodense sellar mass lesion with suprasellar extension (left), and enhancement of the margin by contrast medium (right).

Craniography showed the sella turcica was remarkably enlarged without destruction (Fig. 1). Computed tomography (CT) showed a homogeneously isodense round sellar mass lesion with suprasellar extension (Fig. 2). No calcification was observed. The lesion was enhanced at the margin. Magnetic resonance (MR) imaging obtained 3 weeks after an apoplectic episode demonstrated an isointense lesion occupying the enlarged sella and compressing the optic chiasm (Fig. 3). T1-weighted MR imaging showed that the lesion contained an irregularly-shaped hyperintense mass.

Replacement therapy with hydrocortisone and thyroid hormone resulted in remarkable improvement of her complaints except for the visual disturbances. Transsphenoidal surgery was performed one month after the apoplectic episode. Incision of the sellar floor dura exposed a partially cystic lesion containing yellow dense fluid and old hematoma clots. Normal pituitary gland was observed posterior to the lesion. Complete excision of the lesion including the cyst wall and drainage of the contents were performed. Her left visual function improved immediately after the surgery.

Histological examination of the specimen revealed papillary type craniopharyngioma. The tumor tissue showed pseudopapillary growth composed of solid sheets of remarkably well-differentiated stratified squamous and prickle epithelial cells interrupted by fibrovascular stroma (Fig. 4A, B). Nodules of wet keratin and foci of calcification were rare. Some cells lining the cyst were associated with foci of ciliated and goblet cells (Fig. 4B). There were some degenerative changes with infiltration of inflammatory cells, edema, and fibrosis (Fig. 4C). The connective tissue stroma contained many thin dilated blood vessels with some hemosiderin-laden macrophages. These findings were basically identical to those of the initial surgical specimen obtained 22 years previously.

Discussion

Craniopharyngioma is a benign epithelial tumor of the sellar region, presumably derived from remnants of the pituitary anlage, and occurs as the adamantinomatus and papillary types. The papillary type usually occurs as noncalcified, partially cystic tumor, often within the third ventricle of adults. A rare type of craniopharyngioma containing ciliated epithelia within the tumor, called ciliated craniopharyngioma, may mimic Rathke’s cleft cyst.

Neurol Med Chir (Tokyo) 40, June, 2000
but is usually of the papillary type.\textsuperscript{1,3,11,12} Distinguishing between ciliated craniohypopharyngioma and Rathke's cleft cyst is of considerable clinical and prognostic importance.\textsuperscript{11} However, craniohypopharyngiomatic tissue and Rathke's cleft epithelium are intermingled in ciliated craniohypopharyngioma, which seems to imply a more intimate histogenetic relationship.\textsuperscript{3,7,12} In addition, papillary craniohypopharyngioma may originate from Rathke's cleft cyst by way of squamous metaplasia.\textsuperscript{3,11,12} Although the present tumor was located in the sella, the diagnosis of ciliated craniohypopharyngioma was based on the vast predominance of remarkably well-differentiated stratified prickle-squamoid epithelium.\textsuperscript{1,11,12}

Symptomatic hemorrhage associated with craniohypopharyngioma has been reported in only three cases in the international literature\textsuperscript{7,10} and in three other cases in the Japanese literature.\textsuperscript{2,5,8} All seven cases, including ours, were surgically treated. The patients were two males and five females aged from 29 to 65 years. None of the seven cases was associated with antecedent events and thus were spontaneous hemorrhage. Sudden onset of headache (7 cases) and visual disturbance (5 cases) were the most common clinical symptoms. The hemorrhage was essentially intratumoral, but also subarachnoid in some cases. None of the six cases, in which the time from hemorrhage to surgery was mentioned, was operated as an emergency, and half were operated on at least a few weeks after the apoplectic episode. There was no mortality and visual outcome was good in all seven cases. In contrast, subclinical or occult hemorrhage within the cystic sellar lesions, including Rathke's cleft cyst and cystic craniohypopharyngioma, may not be rare.\textsuperscript{4,10,17} Apparent hematoma clots were encountered at the initial surgery 22 years previously in the present patient, although there was no apoplectic episode.

The pathological mechanism of the hemorrhage in adenomas has been thoroughly discussed. The most well-known hypothesis suggests that vascular insufficiency due to rapid growth of the adenoma which has outstripped its vascular supply and compression of the stalk and portal vessels at the di-
aphragnostic notch in large adenomas combine to cause hemorrhagic infarction and necrosis.\textsuperscript{15} In contrast, the pathogenesis of hemorrhage in craniopharyngioma is unknown. Blood vessel walls in the tumor and connective tissue stroma may undergo degenerative changes and rupture.\textsuperscript{16} The presence of numerous immature blood vessels suggests that these abnormal vessels may cause hemorrhage.\textsuperscript{17} Similarly, many small blood vessels are present in the tumor stroma. Many thin blood vessels were also present in the tumor stroma of our case. In addition, identical histological findings were observed at the initial surgery, at which subclinical hemorrhage was recognized. We suggest that these small vessels, associated with inflammation and degenerative changes, caused repeated spontaneous hemorrhage in the present case. This pathogenesis may be compatible with the clinical observation of mainly subclinical or minor hemorrhage in this tumor. A similar pathogenesis for intracystic hemorrhage in Rathke’s cleft cyst has been suggested.\textsuperscript{8,10}

CT performed 2 weeks after the apoplectic episode failed to demonstrate hemorrhage, due to either the delay or a relatively small hemorrhage. CT was useful for evaluating the hemorrhage in three of five previous cases of craniopharyngioma with symptomatic hemorrhage, whereas T1-weighted MR imaging demonstrated high signal intensities in all three cases examined, including ours. The MR imaging appearance of craniopharyngiomas is variable and the cyst intensity depends on the content. T2-weighted MR imaging findings of hyperintensity in sellar and parasellar cystic lesions may reflect various factors, including mucopolysaccharide, elevated protein concentration, high content of cholesterol, fat, cell debris from the cyst wall, and subacute or chronic hemorrhage.\textsuperscript{8,10,13,14,17} Elevated protein concentration and hemorrhage may be the likely factors in cystic craniopharyngiomas.\textsuperscript{13,17}

Most cases of spontaneous hemorrhage associated with cystic craniopharyngioma may be subclinical or minor intratumoral hemorrhage. However, the onset may be sudden with visual disturbances mimicking pituitary apoplexy. Visual outcome is good in most cases but incomplete removal of the cyst wall may result in repeated hemorrhage. If the cyst contains hematoma clots or fluid, total removal is essential to avoid recurrent hemorrhage even though no obvious episode of hemorrhage has been observed.

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