Hypophysitis Caused by Rathke’s Cleft Cyst
—Case Report—

Tomofumi NISHIKAWA*,***, Jun A. TAKAHASHI*, Akira SHIMATSU**.†, and Nobuo HASHIMOTO*

Departments of *Neurosurgery and **Medicine, Kyoto University Hospital, Kyoto; ***Department of Neurosurgery, Shizuoka General Hospital, Shizuoka; †Department of Pathology, National Kyoto Hospital, Kyoto

Abstract

A 62-year-old woman presented with general malaise persisting for 2 months and narrowing of her visual field. T1-weighted magnetic resonance (MR) imaging showed swelling of the pituitary gland and stalk, and a homogeneous isointense intra- and suprasellar mass enhanced by gadolinium. During outpatient follow up, her condition deteriorated rapidly and she developed diabetes insipidus and panhypopituitarism. T1-weighted MR imaging demonstrated shrinkage of the lesion and disappearance of the central hypointense area indicating the cyst cavity, especially in the pituitary stalk. She underwent surgical exploration via the transsphenoidal approach under a provisional diagnosis of lymphocytic hypophysitis. Histological examination revealed ciliated columnar cells and squamous metaplasia on the inner surface of the cyst wall, with many foamy cells, infiltration by many lymphoid cells and some eosinophils, and fibrosis in the adenohypophysitis and inflammatory hypophysitis in the anterior and posterior pituitary gland. The present neuroimaging findings of cyst shrinkage associated with rapid clinical deterioration strongly support the suggestion that rupture of Rathke's cleft cyst causes inflammatory hypophysitis.

Key words: hypophysitis, Rathke's cleft cyst

Introduction

Inflammatory hypophysitis, a rare but important cause of hypopituitarism, can be classified as lymphocytic or granulomatous.23) Lymphocytic hypophysitis may be an autoimmune disease, as supported by the detection of antibodies.3,14,15,24,25) Granulomatous hypophysitis is mainly associated with syphilis, tuberculosis, and sarcoidosis. Granulomatous lesions of the pituitary gland may be caused by inflammatory reaction originating from a tumor or meningitis.2,19,26) Therefore, many causes of inflammatory hypophysitis are subsumed under lymphocytic hypophysitis8,12,13,17,27 and granulomatous hypophysitis.8,20) Five cases of inflammatory anterior pituitary lesions due to craniopharyngioma and prolactinoma suggested that this entity can be differentiated from lymphocytic and granulomatous hypophysitis.19) Inflammation originating from Rathke’s cleft cyst may also cause granulomatous hypophysitis.1,5,8,10,11,21–23,28,29) However, only one case of Rathke’s cleft cyst presented pathological evidence of cyst rupture.5)

We report a rare case of inflammatory hypophysitis attributable to rupture of a Rathke’s cleft cyst as documented by neuroimaging findings.

Case Report

A 62-year-old woman had suffered general malaise for 2 months. A local physician made a diagnosis of autonomic ataxia. One month later, she noticed narrowing of her visual field and visited an ophthalmologist who referred her to us under a diagnosis of bitemporal upper quadrantanopsia and pituitary gland lesion. T1-weighted magnetic resonance (MR) imaging showed swelling of the pituitary gland and stalk, and a homogeneous isointense intra- and suprasellar mass enhanced by gadolinium (Fig. 1). During outpatient follow up, her condition deteriorated rapidly and she developed diabetes insipidus (urine specific gravity 1.000, urine volume/day <5000 ml) and panhypopituitarism.
Comparison of MR images obtained before deterioration and on admission to our hospital revealed shrinkage of the mass (Fig. 2). On admission, examination confirmed decreased visual acuity and diabetes insipidus. Endocrinological study showed hypopituitarism with serum levels of follicle-stimulating hormone 2.6 mIU/ml, luteinizing hormone >0.5 mIU/ml, growth hormone 0.9 ng/ml, adrenocorticotrophic hormone 15.5 pg/ml, prolactin 63 ng/ml, somatomedin C 67 g/ml, cortisol 1.9 μg/dl, T3 141 ng/dl, and T4 4.9 μg/dl. Dynamic MR imaging disclosed continuous and heterogeneous enhancement from the pituitary stalk to the intra- and suprasellar mass.

She underwent surgical exploration via the transsphenoidal approach under a provisional diagnosis of lymphocytic hypophysitis. The lesion was yellowish and slightly solid. Cutting the surface caused spillage of turbid white fluid. Bacteriological examination returned negative results. Histological examination revealed ciliated columnar cells and squamous metaplasia on the inner surface of the cyst (Fig. 3A), with many foamy cells (Fig. 3B), infiltration by many lymphoid cells and some eosinophils, and fibrosis in the adeno- and neurohypophysis (Fig. 3C, D). No giant cells were observed. The final diagnosis was Rathke’s cleft cyst and inflammatory hypophysitis in both the anterior and posterior pituitary gland.

Based on the neuroimaging and histological findings, we concluded that her hypophysitis was induced by rupture of the Rathke’s cleft cyst. There were no postoperative complications and 5 years after the operation she was doing well with steroid replacement therapy for panhypopituitarism and diabetes insipidus.

### Discussion

Our previous autopsy study of patients with Rathke’s cleft cyst associated with hypopituitarism showed inflammatory reaction in areas surrounding
the pituitary gland, although patients with asymptomatic Rathke’s cleft cysts showed no inflammatory reaction.\textsuperscript{23} The observed epithelial stratification may be attributable to extension of the inflammation into the adjacent adenohypophysis or neurohypophysis.\textsuperscript{7} These findings suggest that the inflammatory reaction is induced by leakage of the cyst contents. Cyst rupture is only one of the possible causes of leakage.

Various cases of rupture of Rathke’s cleft cyst have been reported. An autopsy case showed that rupture of Rathke’s cleft cyst had led to panhypopituitarism and hydrocephalus.\textsuperscript{21} Other cases suggested that spillage of the cyst content induced sterile inflammatory response or foreign body reaction.\textsuperscript{1,\textsuperscript{28}} Secretion of mucus by goblet cells in the cyst wall may lead to the formation of granulation tissue in the epithelium surrounding the cyst.\textsuperscript{16} Chronic inflammatory hypophysitis may be attributable to extravasation of the cyst content into the adjacent gland, as the material contained within granulomas consisted of the mucins produced by the columnar cells lining the cyst wall.\textsuperscript{18} One patient had infected Rathke’s cleft cyst which led to aseptic meningitis that spread to the pituitary gland and resulted in hypophysitis.\textsuperscript{29} These cases all presented with leakage of the cyst contents, which is suggestive of rupture of Rathke’s cleft cyst but provides no direct evidence for cyst rupture. The most convincing proof of cyst rupture was documented as focal dehiscence of the cyst wall.\textsuperscript{9} However, such focal dehiscence is difficult to detect and was not found in the present and other cases. Computed tomography and MR imaging confirmed the spontaneous rupture of an unknown suprasellar cystic tumor.\textsuperscript{20} This report indicated that neuroimaging change can provide convincing evidence of cyst rupture.

Clinical deterioration in most previous patients with inflammatory hypophysitis seemed to be due to cyst rupture with acute clinical presentation and short morbidity period (0–8 months).\textsuperscript{1,\textsuperscript{4,\textsuperscript{8,\textsuperscript{11,\textsuperscript{20}}} However, no MR imaging was performed before the manifestation of acute deterioration. Our patient underwent MR imaging before and after the onset of clinical deterioration, which was clearly attributable to the rapid cyst shrinkage, although previous enlargement might have caused the visual disturbance. Rapid clinical deterioration implies rupture of the Rathke’s cleft cyst. We could not clearly explain why our patient presented with general malaise before acute clinical deterioration, but enlargement of the Rathke’s cleft cyst or minor leakage may have occurred. The present neuroimaging findings of cyst shrinkage associated with rapid clinical deterioration strongly support the suggestion that rupture of Rathke’s cleft cyst causes inflammatory hypophysitis.

References

15) O’Dwyer DT, Smith AI, Matthew ML, Andronicos NM, Ranson M, Robinson PJ, Crock PA: Identification of the 49-kDa autoantigen associated with

Neurol Med Chir (Tokyo) 47, March, 2007


Address reprint requests to: Jun A. Takahashi, M.D., Department of Neurosurgery, Kyoto University Hospital, 54 Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan.

e-mail: jat@kuhp.kyoto-u.ac.jp