Natural course of lymphocytic infundibuloneurohypophysitis

M. Amagasa¹, F. Yuda², H. Kojima³, N. Noshita¹ and S. Sato¹

Departments of ¹Neurosurgery and ²Pathology, Yamagata City Hospital Saiseikai, Yamagata, and ³Department of Clinical Neuropathology, Tokyo Metropolitan Institute for Neuroscience, Tokyo, Japan

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Abstract. Natural course of lymphocytic infundibuloneurohypophysitis is poorly understood. A 49-year-old male had noticed being unnaturally thirsty since about two years previously. An enlargement of the pituitary stalk and pituitary gland was thus observed by MR at that time. However, no medical care had been given. Two years later, he was admitted to our hospital due to headache in addition to panhypopituitarism. The histologic features included T cell dominant lymphocytes infiltrating predominantly the entire pituitary gland with a small amount of multinucleated giant cells, focal and small necrosis, cholesterin crystals and granuloma. Neither tuberculosis nor Langerhans histiocytosis were observed. In addition, the patient was found to have a unique massive well-encapsulated lesion in the sphenoid sinus, just below the pituitary fossa, consisting of serous fluid, normal columnar epithelium and submucosal fibrosis. This patient had a fairly typical clinical manifestation of lymphocytic infundibuloneurohypophysitis with invasion of the posterior lobe and the stalk. The lesion became chronic and leaked to the sphenoid sinus. As a result, chronic hypophysitis with granuloma formation thus occurred. This case may show the course of this disease if not treated.

Introduction

Hypophysitis is classified as lymphocytic and granulomatous [Honegger et al. 1997]. It is well-known that granulomatous hypophysitis is difficult to identify as a clinical entity [Higuchi et al. 1993, Honegger et al. 1997, Miyamoto et al. 1988]. The coexistence of lymphocytic hypophysitis and granulomatous hypophysitis has also been reported [Higuchi et al. 1993, Honegger et al. 1997, Miyamoto et al. 1988]. There is speculation that the difference between both may be a difference in the stage regarding the process of inflammation [Higuchi et al. 1993, Honegger et al. 1997, Miyamoto et al. 1988]. We observed a patient showing a unique course with chronic infundibulohypophysitis and discuss the diagnosis and the pathogenesis.

Case report

A 42-year-old man became aware of an unnaturally strong thirst, excessive water intake and polyuria in about September 1995. An MRI was done at a hospital and was estimated normal. A retrospective analysis showed the stalk of the pituitary gland in the MRI to be thick. The sphenoidal sinus was normal. Because the patient felt generalized fatigue, he retired from his job. As the symptoms did not improve, he was hospitalized in the medical department of our hospital in January, 1996 and underwent various tests. The endocrinological examinations were almost normal, he was diagnosed to have psychogenic polydipsia. The pituitary gland and the stalk on MRI views were diagnosed to be within the normal limits (Figure 1a). However, their images were, in retrospect, clearly abnormal. Frontal and ethmoidal sinusitis was present. No sinusitis of the sphenoid sinus was detected. By restricting the water intake, he stabilized for a while. Headache appeared from the frontal to parietal region in October 1996. The headache was continuous, although the degree of pain changed. He was hospitalized due to headache symptoms in January 1997.

His neurological tests including visual acuity and visual fields were normal. How-
ever, hypopituitarism was observed. The volume of urine was in the normal range. The serum antipituitary antibodies were negative. MRI revealed the pituitary gland and the stalk to be enlarged. T1 images showed isointensity with a prominent enhancement (Figure 1b,c). T2 images showed from is to high intensity. A lesion in the sphenoid sinus was connected with the pituitary fossa (Figure 1d). A sagittal image of the bone tomography of the pituitary fossa revealed the defect clearly. The pituitary lesion was partially
evacuated by an intracranial approach on April 22, 1997. The pituitary gland was enlarged, white and tight (Figure 2a). Microscopically (Figure 2b), T cell predominant lymphocytic infiltration was observed along with the formation of granulation accompanied with focal and small necrosis, cholesterin crystals, leukocytes, Schaumann bodies, deposition of hemosiderin and foreign body type giant cells. These turned out to be macrophages confirmed immunohistochemically positive for CD68 and negative for S100 protein. The histological diagnosis was chronic hypophysitis with granulation.

Postoperatively, both diabetes insipidus and hypopituitarism became aggravated. Steroid therapy was performed. The sphenoid sinus lesion (Figure 2c) was removed by otolaryngologists on May 19. A well-defined mass with semitransparency and encapsulating membrane was cut, and serous exudate was recognized. Fistulation to the pituitary fossa could not be detected. Histologically, submucosal conjunctive tissue and bone fragments were recognized (Figure 2d). The lesion was diagnosed to be a scar, different from that of common chronic sinusitis or mucocele. A postoperative MRI showed a reduction of lesions in the pituitary gland and the stalk. Panhypopituitarism and diabetes insipidus were treated by hormonal therapy. The patient was discharged on August 31, 1997. He is now leading a normal life.
Discussion

The initial symptoms of this patient were surely diabetes insipidus and the initial lesion was inflammation at the stalk and the posterior lobe of the pituitary gland. Two years later, clinical manifestations and radiological characteristics looked very similar to "necrotizing infundibulo-hypophysitis" as reported by Ahmad et al. [1993]. Lymphocytic hypophysitis, which is not related to pregnancy and appears in men, has been reported to damage the posterior lobe and the stalk [Imura et al. 1993, Nishioka et al. 1996, Sautner et al. 1995]. Kojima et al. [1989] in his report on chronic infundibuloneurohypophysitis pointed out that the inflammation was localized in the stalk and posterior lobe, but several reports showed the anterior lobe to be also damaged following extension from the posterior lobe. Kojima’s case appeared to show a shorter duration than most other similar cases. The clinical and radiological characteristics of our case are same as those of the recently reported lymphocytic infundibuloneurohypophysitis [Imura et al. 1993, Miyamoto et al. 1988, Nishioka et al. 1996, Sautner et al. 1995].

The major pathological findings of our case were granuloma formation with giant cells and massive T cell dominant lymphocytic infiltration. In addition, focal and small necrosis and cholesterol crystals were also observed. The giant cells were of macrophage type and not a specific finding indicating a characteristic pathogenesis. The diagnosis may be cholesterol granuloma. If the discovery of this disease is delayed and the process becomes chronic, the lymphocytic hypophysitis might change into non-specific granulation resembling cholesterol granuloma of the middle ear [Shirataki et al. 1988]. The progression of our case demonstrates the pathogenesis of the so-called "granulomatous hypophysitis" [Scanarini et al. 1989].

Our patient showed, in addition, a sphenoid sinus lesion which did not exist at the initial stage, and the lesion had a connection to the pituitary gland lesion in the radiological images. The mucosal enhancement of the sphenoid sinus was reported to be one of the main characteristics of hypophysitis [Honegger et al. 1997, Sautner et al. 1995]. The MRI findings suspecting a connection between sphenoid sinus lesions and pituitary lesions have been reported [Honegger et al. 1997, Sautner et al. 1995]. The possibility that hypophysitis leaked from the upper lesion may also be possible. The dura mater and the bone of the floor of the sella turcica is very tight. However, active hypophysitis could destroy the structure. Since radiologically the lesion of the pituitary gland developed first in our patient, sphenoid sinusitis could thus be ruled out as the cause of hypophysitis. The histology of the sphenoid sinus lesion is very unique and also proved this relation.

Our case shows that the stage of inflammation is very important regarding the pathology of hypophysitis.

References


