**Idiopathic Hypertrophic Cranial Pachymeningitis of the Cavernous Sinus Mimicking Lymphocytic Hypophysitis**

—Case Report—

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**Abstract**

A 56-year-old female presented with idiopathic hypertrophic cranial pachymeningitis manifesting as headache, hypopituitarism, and diabetes insipidus, mimicking lymphocytic hypophysitis. Five months later, she complained of double vision and unusual right facial sensation. The diagnosis was based on magnetic resonance imaging, angiography, and meningeal biopsy via transsphenoidal surgery, and exclusion of other known causes of pachymeningitis. Despite initial response to steroid treatment, her symptoms recurred repeatedly and she became steroid-dependent. Repetition of short-term steroid pulse therapy restrained the deterioration of her condition. The clinical presentation of idiopathic hypertrophic cranial pachymeningitis is variable, and it may develop with signs of adjacent tissue involvement. Resultant secondary hypophysitis must be differentiated from lymphocytic hypophysitis. Initial steroid therapy is effective in improving symptoms, but should be carefully considered since the natural course of this disease seems to be self-limited.

Key words: hypertrophic cranial pachymeningitis, cavernous sinus, pituitary gland, secondary hypophysitis, lymphocytic hypophysitis

**Introduction**

Idiopathic hypertrophic cranial pachymeningitis (IHCP) is a rare chronic inflammatory lesion of the cranial dura mater and mainly affects the skull base dura. Modern neuroimaging methods are detecting this disease with increasing frequency. However, the clinical presentation of this lesion varies, and the natural course is still unknown.

We report a unique case of IHCP of the cavernous sinus involving the pituitary gland and the internal carotid arteries (ICAs), manifesting as hypopituitarism, diabetes insipidus, and cavernous sinus syndrome, which recurred repeatedly despite an initial response to steroid treatment.

**Case Report**

A 56-year-old post-menopausal female presented with headache and central diabetes insipidus in December 1995. She had had no medical problems before 1995. In March 1996, she developed hypopituitarism, and magnetic resonance (MR) imaging demonstrated a sellar lesion, which yielded a tentative diagnosis of lymphocytic hypophysitis. In addition to hormone replacement with thyroid hormone and desmopressin acetate (DDAVP), corticosteroid therapy was initiated. This treatment achieved transient improvement of headache and adenohypophysial dysfunction. Five months later, she was referred to our department because of recurrent hypopituitarism, uncontrolled diabetes insipidus, and cavernous sinus syndrome.

On admission, she complained of headache, double vision, right facial numbness, general fatigue, polydipsia, and polyuria. She appeared lethargic. Her urine volume was 5600–6300 ml/day (density
1.002–1.005 g/ml) when receiving 10 µg per day DDAVP. Neurological examination revealed bitemporal inferior quadrantopnia, right abducens nerve palsy, and right trigeminal nerve dysesthesia. Routine laboratory test results were normal apart from a slight elevation of C-reactive protein level and leukocytosis. Titers for common viruses (Epstein-Barr, cytomegalovirus, enteric cytopathogenic human orph-an, influenza, parainfluenza, herpes zoster, and herpes simplex), bacteria, and toxoplasmosis were negative. Serum tests for rheumatoid arthritis and syphilis, and anti-human immunodeficiency virus-1 antibody were negative. In addition, test for antipituitary antibodies, other autoantibodies (antineuronal, anti-deoxyribonucleic acid, antiribonucleoprotein antibodies), and lupus erythematous factor were all negative. Her serum angiotensin-converting enzyme level was normal. Chest radiography and abdominal and thoracic computed tomography (CT) showed no abnormalities. Examination of the cerebrospinal fluid showed normal cell numbers and levels of proteins, and the cytological examination and culture were negative. Endocrinological evaluation revealed hypopituitarism with slight hyperprolactinemia: adrenocorticotropic hormone (ACTH) < 5 pg/ml (normal 9–52), cortisol <1.0 µg/dl (normal 4–18.3), luteinizing hormone (LH) < 0.5 mIU/ml (normal 9–38), follicle-stimulating hormone (FSH) 0.7 mIU/ml (normal 26–113), thyroid-stimulating hormone (TSH) 0.09 µU/ml (normal 0.34–3.5), growth hormone (GH) 0.42 ng/ml (normal 0.66–3.68), and prolactin 16 ng/ml (normal 1.4–14.6). These adeno-hypophysial hormones showed low or no response to the triple stimulation (thyrotropin-releasing hormone, LH-releasing hormone, insulin) test. The plasma antidiuretic hormone level was <0.3 pg/ml (normal 0.3–3.5).

Skull radiography and brain CT were normal. MR imaging disclosed a sellar and parasellar lesion involving the pituitary gland and the bilateral cavernous sinuses particularly on the right side. T₁-weighted MR imaging showed the pituitary gland and the cavernous sinuses were ill-defined (Fig. 1 left), and loss of the hyperintense signal of the neurohypophysis was observed (Fig. 1 right). T₂-weighted MR imaging showed the cavernous sinus lesion as hypointense. The lesion and the stalk were well enhanced by gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) (Fig. 1 center). These MR imaging findings were identical to those of the initial study. On the other hand, cerebral angiography showed prominent stenosis of the bilateral extradural ICAs, in the intracavernous (C₄) portion of the left ICA and the intrapetrosal (C₅) portion of the right ICA (Fig. 2). In addition, the bilateral cavernous sinuses were poorly filled in the venous phase. Thallium-201 single photon emission computed tomography showed a high accumulation on the early scan in the lesion.

Biopsy of the lesion was performed via transsphenoidal surgery to establish the diagnosis. After removal of the sella floor, which appeared normal, a firm, dull-gray dural lesion was exposed. The lesion extended continuously inside the sella and no pituitary tissue could be identified. A small biopsy specimen was excised but no further removal of the lesion was performed. Histological examination disclosed fibrotic and collagenous tissue with inflammatory infiltrates composed of lymphocytes and a few neutrophils indicating granulomatous pachymeningitis of unknown etiology (Fig. 3). No caseous necrosis or

Fig. 1 Coronal T₁-weighted magnetic resonance images demonstrating an isointense lesion involving the cavernous sinus and the pituitary gland (left), and enhancement of the lesion and stalk by gadolinium-diethylenetriaminepenta-acetic acid (center). Sagittal T₁-weighted image showing loss of the hyperintense signal of the neurohypophysis (right).
epitheloid granuloma was present. Specific stains were negative for fungi and acid-fast bacilli. Immunohistochemical staining for GH, prolactin, ACTH (DAKO, Carpinteria, Calif., U.S.A.), and α- and β-subunits of LH, FSH, and TSH (supplied by the National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, Md., U.S.A.) demonstrated that no adenohypophysial cells were present in the specimen. Furthermore, immunohistochemical staining for UCHL-1 (DAKO, Glostrup, Denmark) and L-26 (DAKO, Kyoto) showed that the infiltrating lymphocytes were polyclonal. The diagnosis was IHCP. The postoperative course was uneventful. Her headache and double vision improved and diabetes insipidus became controllable with 10 μg per day DDAVP. In addition, slight improvements in the facial dysesthesia and adenohypophysial dysfunction were observed.

One month after biopsy, she suffered recurrence of intense headaches, facial paresthesia, and disturbance of left visual acuity. Visual field and ocular movements were normal. Follow-up MR imaging with Gd-DTPA revealed no change. Steroid therapy was commenced with an initial dose of 16 mg/day of betamethasone, which was subsequently tapered. This therapy achieved immediate improvement of symptoms, but she became steroid-dependent; her symptoms improved with steroid administration but reappeared whenever treatment was tapered or discontinued. In addition, aseptic epiphyseal necrosis of the bilateral femurs developed, probably as a complication of the steroid therapy. Therefore, high-dose short-term pulse steroid therapy was initiated at a daily dose of 1000 mg of methyl prednisolone and tapered within a week. This regimen was repeated until her symptoms gradually improved without any other complication. Sixteen months after biopsy, she remained in good condition without steroid treatment, but still required hormone replacement therapy. On the follow-up study, MR imaging appearance remained unchanged except for reduction of the pituitary mass lesion (Fig. 4).

Discussion

Previous cases of IHCP have demonstrated clinical features similar to those in the present case. The 47
patients, including ours, were aged from 19 to 75 years (mean 50.3 years) with no sex predominence (24 males and 23 females). The location of the lesion showed three distinct patterns: the most frequent pattern mainly affected the falco-tentorial and posterior fossa dura mater (20 cases),\textsuperscript{2,3,7,8,10,17,18,24,31,34} the lesion was localized in the parasellar and cavernous sinus dura mater (9 cases),\textsuperscript{10-12,14,25,27,30,36} or the lesion affected both regions or diffuse cranial dura and, on occasion, the upper cervical spine (14 cases).\textsuperscript{6,10,11,15,16,18,20,21,31,33} Therefore, IHCP tends to originate in the midline dura producing symmetrical lesions.\textsuperscript{31} Long histories of headaches and progressive cranial nerve paresis (30 cases) were the most common clinical symptoms, and cavernous sinus syndrome was also common (15 cases).\textsuperscript{10,11,14-16,21,23,25,27,30,31,36} In addition to multiple cranial nerve pareses caused by fibrous entrapment or ischemic damage of the nerve, adjacent tissue involvement such as encephalitis (6 cases),\textsuperscript{15,20,22,23,29} hydrocephalus (5 cases),\textsuperscript{3,10,22,23,54} sinus thrombosis (3 cases),\textsuperscript{10,17,28} and the pituitary lesion were reported. Pituitary involvement was observed in six cases,\textsuperscript{15,18,23,30,36} but apparent hypopituitarism and diabetes insipidus were only observed separately in one case each\textsuperscript{15,30} apart from the present case. The initial presentation of our case mimicked lymphocytic hypophysitis although inflammation of the pituitary gland was not histologically identified. It was suggested that visual defect in our case was also caused by either ischemic or direct inflammatory damage of the optic nerve. Involvement of the ICA in IHCP has also been reported.\textsuperscript{30}

Lymphocytic hypophysitis is a distinct entity involving a chronic inflammatory lesion mainly affecting the adenohypophysis. This disease commonly affects females during late pregnancy or in the postpartum period, and can cause visual disorders and hypopituitarism. However, the clinical presentation of lymphocytic hypophysitis is also variable.\textsuperscript{1,13,28,35} This disease can also affect males and post-menopausal females. In addition to neurohypophysial involvement manifesting as diabetes insipidus, presentations with hyperprolactinemia, cavernous sinus syndrome, and occlusion of the bilateral carotid arteries have been described. A case of recurrence has also been reported.\textsuperscript{20} Consequently, although IHCP and lymphocytic hypophysitis are quite different entities, they may exhibit similar clinical features.

Hypophysitis originating from various associated pathological processes, also called secondary hypophysitis,\textsuperscript{22} should be differentiated from original lymphocytic hypophysitis. Secondary hypophysitis is associated with various sellar lesions including craniohypophyriangioma, Rathke’s cleft cyst, and other vascular events in the pituitary. Lymphocytic hypophysitis lacks specific and reliable clinicopathological diagnostic markers,\textsuperscript{1,26,28,32} so various atypical cases reported as lymphocytic hypophysitis may be secondary hypophysitis. Inflammation of lymphocytic hypophysitis, probably an autoimmune lesion, is essentially limited to the pituitary gland, with infrequent extension to the hypothalamus, but never to the cerebrum, causing encephalitis or basal meningitis. In the present case, lymphocytic hypophysitis is unlikely to have preceded and caused secondary pachymeningitis of the cavernous sinus. MR imaging showed hypertrophic pachymeningitis of the cavernous sinus at the onset of pituitary symptoms, and this remained unchanged during the course and was unrelated to either symptoms or treatments. In addition, angiography showed involvement of the bilateral ICAs. Therefore, the present case indicates that IHCP can involve the pituitary gland and cause associated symptomatic secondary hypophysitis. Furthermore, our case is similar to fibrosing pseudotumor of the sella and parasellar region, a localized form of IHCP.\textsuperscript{4,9,30}

The diagnosis of IHCP is based on exclusion of many other known causes of dural thickening. Various bacterial and fungal infections, some of which are clinically difficult to detect even with biopsy and culture studies, can cause pachymeningitis. Although MR imaging is useful in the tentative diagnosis of hypertrophic pachymeningitis, aggressive efforts to clarify the etiology are important before instituting steroid treatment. Corticosteroid therapy is both therapeutic and diagnostic for IHCP. In most patients (35 of 37 reported cases) initial steroid therapy was effective in improving the clinical symptoms, particularly headaches. However, MR imaging findings did not change after the therapy in 12 of 20 patients, and symptoms recurred despite steroid treatment in 25 of 35 patients. Most patients with recurrent IHCP became steroid-dependent, and side effects of the steroid therapy were reported in some.\textsuperscript{20,22,23,29} Although surgical excision is occasionally necessary to alleviate mass effect of the lesion,\textsuperscript{3,5,21,29} the effectiveness of immunosuppressive drugs and radiation therapy is uncertain. Consequently, IHCP is a slowly progressive disease and the natural history, which seems to be self-limited, may be little modified by these treatments.\textsuperscript{2,21,22} To avoid the risk of steroid dependence, as well as the risk of worsening occult bacterial or fungal infections, unnecessary and unneeded high-dose long-term steroid treatment must be avoided. Short-term steroid pulse therapy, repeated with increased dose when ineffective, may be the best present...
strategy for patients with an accurate diagnosis of IHCP, based on surgical biopsy and decompression of mass lesions.

References


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