CASE REPORT

Rheumatoid Factor Positive Hypertrophic Cranial Pachymeningitis in Association with Hypopituitarism and Multiple Cranial Nerve Palsies

Yasuhiro Manabe, Hisashi Narai, Hitoshi Warita, Takeshi Hayashi, Kenichi Sakai and Koji Abe

Abstract

This is the first report of a patient presenting with rheumatoid factor (RF) positive hypertrophic cranial pachymeningitis (HCP) in association with hypopituitarism and multiple cranial nerve palsies. Our patient developed palsies of the left II and III, bilateral VI and VII, and right IX, X, and XII cranial nerves. A stimulation test showed hypopituitarism due to hypothalamic failure. The patient was seropositive for RF but had no multiple joint pain or deformities. Magnetic resonance imaging (MRI) showed thickened dura of the sellar and parasellar region, hypothalamus, bilateral cavernous sinuses and the tentorium all of which were enhanced by gadolinium (Gd). Treatment with prednisone improved clinical symptoms and MRI findings concomitant with reduction of RF titer. Although the exact mechanism of HCP has not been clearly elucidated, the present case suggests an autoimmune mechanism associated with RF.

Key words: inflammatory disease, central nervous system, MRI

Introduction

Hypertrophic cranial pachymeningitis (HCP) is a rare chronic inflammatory disease that causes thickening of the dura mater. Only a few clinical cases were reported before the advent of computed tomography (CT), but the number reported has recently increased (1-3). Among them, HCP in association with hypopituitarism and multiple cranial nerve palsies was reported in two of the cases, but both were negative for rheumatoid factor (RF) (4, 5). Here, we report a unique case of RF positive HCP in association with hypopituitarism and multiple cranial nerve palsies.

Case Report

A 75-year-old man who had been complaining of headaches since age 69 noticed general fatigue, loss of appetite, left eyelid ptosis, diplopia, and ataxia at age 72. He was shown to be RF seropositive and have hypopituitarism. Steroid therapy was commenced at an initial dose of 3.75 mg/day. At age 74 he developed left visual loss. His other symptoms improved and the RF serum level decreased with steroid administration, but the symptoms reappeared along with increasing RF level whenever treatment was tapered. On admission to our hospital, he was obese, but not arthritic. Neurological examination revealed left visual loss, left eyelid ptosis, bilateral abducens nerve palsy, bilateral facial nerve palsy, dysphagia, hoarseness, and tongue deviation to the right side, indicating palsies of the left II and III, bilateral VI and VII, and right IX, X, and XII cranial nerves. Deep tendon reflexes were hyporeactive throughout and Babinski’s response was absent.

Routine studies, including blood cell counts, blood chemistry and enzymes, were normal. The erythrocyte sedimentation rate was 57 mm/h. Serum test for RF was 156 IU/ml (normal, <60). Titers for common viruses (HIVs, Epstein-Barr, cytomegalovirus, herpes zoster, and herpes simplex), bacteria, and toxoplasmosis were negative. Tests for autoantibodies (antineural, anti-deoxyribonucleic acid, and anti-ribonucleoprotein antibodies), lupus erythematosus factor, syphilis serology, p and c ANCA were all negative. His serum angiotensin-converting enzyme level was normal. Lumbar puncture showed cerebrospinal fluid (CSF) pressure at 120 mmH₂O. Queckenstedt’s test was negative. CSF cell count was 10/mm³, all lymphocytes. The CSF protein level was elevated at 84 mg/dl (normal, <40) and glucose was normal at 91 mg/dl (blood glucose; 113 mg/dl). Cytology and culture of the CSF for bacteria, tuberculous bacillus, and fungi were negative. CT of the chest and abdomen showed no evidence of lymphadenopathy. Electromyography and nerve conduction studies did not indicate peripheral neuropathy. Endocrinological evaluation before steroid therapy revealed hypopituitarism with slight hyperprolac-
HCP with Hypopituitarism and Multiple Cranial Nerve Palsies

Table 1. Endocrinological Evaluation before Steroid Therapy

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Serum level</th>
<th>Normal range</th>
</tr>
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<tbody>
<tr>
<td>Pituitary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>6</td>
<td>9-52</td>
</tr>
<tr>
<td>GH (ng/ml)</td>
<td>0.57</td>
<td>0.34-3.50</td>
</tr>
<tr>
<td>PRL (ng/ml)</td>
<td>13.2</td>
<td>&lt;10.0</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>0.7</td>
<td>1.8-5.2</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>2.3</td>
<td>2.9-8.2</td>
</tr>
<tr>
<td>ADH (pg/ml)</td>
<td>1.1</td>
<td>0.3-3.5</td>
</tr>
<tr>
<td>TSH (μU/ml)</td>
<td>0.53</td>
<td>0.5-4.0</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FT4 (ng/dl)</td>
<td>0.73</td>
<td>0.71-1.85</td>
</tr>
<tr>
<td>Cortisol (μg/dl)</td>
<td>1.6</td>
<td>4.0-18.3</td>
</tr>
</tbody>
</table>


Figure 1. A) ACTH showed a normal response to the stimulation of CRF. B) LH and FSH also showed a normal response to the stimulation of LH-RH.

Discussion

HCP is a rare, chronic inflammatory disorder characterized by marked dural thickening, typically involving the cranial dura mater and the skull base dura. Long histories of headaches and progressive cranial nerve paresis are the common clinical symptoms, and cavernous sinus syndrome is also common (6). In addition to multiple cranial nerve paresis caused by fibrous entrapment or ischemic damage of the nerve, adjacent tissue involvement such as encephalitis (7), hydrocephalus (8), sinus thrombosis (9), and pituitary lesions have been reported. Pituitary involvement has been observed in seven cases (4–8, 10). However, apparent hypopituitarism and multiple cranial nerve...
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Figure 2. A) A gadolinium (Gd) enhanced T1-weighted sagittal image shows diffuse enhancement of the dura mater in the cranial convexity (arrowheads). B) A Gd enhanced T1-weighted coronal image shows diffuse enhancement of the tentorium (arrowheads). C) A Gd enhanced T1-weighted axial image at the level of the Meckel’s cave shows high signal intensity along the clivus. The lesion shows thickening the dura of the cavernous sinus and the tentorium (arrowheads), extending superiorly into the region of the diaphragma sella and the anterior cranial fossa. D) A Gd enhanced T1-weighted coronal image shows high signal intensity in the cavernous sinus and the pituitary gland (arrowheads). E) Magnification of Fig. 2A. A midline Gd enhanced T1-weighted sagittal image shows high signal intensity in the pituitary gland, hypothalamus and an extensive linear enhancing lesion posterior to the clivus (arrowheads).

Palsies were observed in only two cases apart from the present case (Table 2). This is the first case of RF positive HCP in association hypopituitarism and multiple cranial nerve palsies. Diffuse dural thickening has been found in pachymeningitis accompanying various conditions, such as syphilis (11), tuberculosis (12), fungal infection (13), Wegener’s granulomatosis (2), sarcoidosis (14), mixed connective tissue disease (15), intracranial hypotension (16), Tolosa-Hunt syndrome (17), and lymphoma or other neoplastic lesions (18). However, none of the above matched the findings of the present patient.

HCP is considered to be an autoimmune disorder because of its association with other autoimmune disorders. HCP is associated with disorders such as, mixed connective tissue disorder and rheumatoid arthritis (RA) (15, 19, 20). The present patient had a seropositive rheumatoid factor, but no multiple joint deformities. The patient did not satisfy the usual criteria.
of RA. Because our patient’s symptoms improved and RF was reduced with steroid administration but reappeared several times whenever the steroid was decreased, the disorder in this patient is most likely due to an autoimmune mechanism associated with RF. The natural course of HCP is poorly understood, and its management is not well defined. However, steroid therapy has been shown to be most effective in improving the symptoms and arresting the progression of HCP (21). In our patient, steroid pulse therapy improved clinical symptoms and MRI findings concomitant with a reduction in RF titer.

Although the previous two cases of hypopituitarism showed pituitary failure (4, 5), test results of our patient suggest hypothalamic failure resulting in secondary pituitary. In the hypothalamus, nerve cells secreting thyrotropin-releasing hormone (TRH) and growth hormone-releasing hormone (GH-RH) are located medially, while the CRF and LH-RH releasing cells are located in the outer side. Therefore, the secretion of CRF and LH-RH may be more easily affected than that of TRH or GH-RH. Firstly, the endocrine abnormalities of our patient might be due to the hypothalamic parenchymatous involvement. Secondly the inflammed pituitary stalk seen in Gd-MRI might indicate that the pituitary portal system was compromised functionally, thereby resulting in a dysfunctional anterior lobe. This report extends the spectrum of neurologic and endocrinologic manifestations of HCP. Although the exact mechanism of HCP has not been clearly elucidated, the present case suggests an autoimmune mechanism associated with RF.

References