Hypothalamic Histiocytosis X with Diabetes Insipidus and Korsakoff's Syndrome
—Case Report—

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Abstract

A 54-year-old female presented with apparent isolated hypothalamic histiocytosis X associated with diabetes insipidus and Korsakoff's syndrome. Computed tomographic and magnetic resonance imaging demonstrated a single hypothalamic mass. A craniotomy for biopsy found granulation tissue of unknown cause. Further investigation discovered genital bleeding before admission. Biopsy of the cervix uteri revealed histiocytosis X. Further studies showed the disease was restricted to the hypothalamus and the endometrium of the cervix uteri. Low-dose irradiation led to partial regression of the hypothalamic mass and improvement of Korsakoff's syndrome. Even when a diagnosis of isolated hypothalamic histiocytosis X is confirmed, the possibility of another histiocytosis X lesion in an unexpected region must be considered.

Key words: histiocytosis X, hypothalamic tumor, biopsy, radiation therapy

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Introduction

Histiocytosis X in the central nervous system frequently involves the hypothalamus. Accurate diagnosis of a histiocytic granuloma in the hypothalamus when cutaneous, visceral, or skeletal forms of the disease are absent, is difficult both clinically and histologically.1,4 We describe a case of hypothalamic histiocytosis X associated with diabetes insipidus and Korsakoff's syndrome, which later was identified as disseminated histiocytosis X. We discuss the diagnosis of this disease by computed tomographic (CT) scanning, magnetic resonance (MR) imaging, and biopsy, and review the literature.

Case Report

A 54-year-old female presented on May 8, 1989, with a 26-month history of thirst, polydipsia, and polyuria, and a 2-month history of impaired recent memory. Physical examination on admission revealed a well-developed, slightly obese woman.

Neurological examination demonstrated poor recent memory, disorientation, and confabulation (Korsakoff's syndrome). She underwent a water deprivation test. The initial serum osmolarity was 286 mOsm/l, and the urine osmolarity was 150 mOsm/l. After 4 hours of water deprivation, the urine osmolarity had increased to 164 mOsm/l only, and the serum osmolarity to 290 mOsm/l. Ten-µg of 1-deamino-8-D-arginine vasopressin (DDAVP) was given. One hour later the urine osmolarity had increased to 449 mOsm/l. From these results, diabetes insipidus of central origin was diagnosed. Hematological levels including complete blood count, electrolytes, blood urea nitrogen, creatinine, and
blood glucose were within normal limits, but the erythrocyte sedimentation rate was 57.5 mm/hour. The cerebrospinal fluid (CSF) contained protein 89 mg/dl, glucose 71 mg/dl, and neutrophils 4.7/mm³. No abnormal cytology was found in the CSF. Endocrinological tests revealed the following values: tetraiodothyronine, 5.1 µg/dl; thyroid-stimulating hormone, 3.27 µU/ml; prolactin, 71.3 ng/ml; luteinizing hormone, 0.5 mIU/ml; follicle-stimulating hormone, 4.5 mIU/ml; estradiol, 6.4 pg/ml; growth hormone, 1.5 ng/ml; and cortisol in the morning, 9.4-13.9 µg/dl. An insulin tolerance test showed neither cortisol nor growth hormone response to hypoglycemia.

Plain skull x-ray films and cerebral angiograms disclosed no abnormalities. However, CT scans revealed a suprasellar isodense mass with post-contrast homogeneous enhancement (Fig. 1). MR imaging demonstrated this suprasellar mass as an isointense area on both T₁- and T₂-weighted images (Fig. 2). Coronal and sagittal MR images showed this mass lesion to be mainly in the third ventricular floor, that is the tuber cinereum.

On May 24, the hypothalamic mass was explored via a right frontotemporal craniotomy. The pituitary gland, optic nerves, and optic chiasma appeared uninvolved. A light yellow mass, which was elastic hard and bled easily, was found in the third ventricular floor. The mass was only partially removed to avoid possible hypothalamic dysfunction. The histological diagnosis was a granulation tissue of unknown etiology. Further investigation of her history revealed a small amount of genital bleeding that began 1 week or so before admission.

She was then referred to the Department of Gynecology. A lesion of the cervix uteri was completely removed, and the genital bleeding ceased. Biopsy of the cervix uteri revealed histiocytosis X.
Photomicrographs of the cervix uteri. *left:* A polymorphous collection of histiocytes (arrowhead), lymphocytes, and occasional eosinophils with bilobular nuclei (arrow) is shown. HE stain, × 600. *right:* Immunohistochemical staining for S-100 protein shows the histiocytes are positive. Avininon biotin complex method, × 400.

Fig. 4 *upper:* T₁-weighted MR images (left and center, SE 500/28 msec) and T₂-weighted image (right, SE 2000/90 msec) after irradiation. T₁-weighted images demonstrate a high-intensity area in the third ventricular floor (arrowheads). T₂-weighted image shows the mass as an isointense area (arrowheads). *lower:* T₁-weighted images with Gd-DTPA demonstrating homogeneous enhancement.

(Fig. 3). We therefore administered a total of 2000 rad irradiation in 10 fractions over 2 weeks to the hypothalamic area. Within 6 months MR imaging demonstrated partial regression of the hypothalamic...
mass (Fig. 4). The Korsakoff's syndrome also started to improve. Diabetes insipidus remained unchanged, although vasopressin therapy was unnecessary.

**Discussion**

Histiocytosis X, which Lichtenstein considered a single nosological entity, is a non-neoplastic disorder of unknown etiology characterized by masses of proliferating histiocytes, plasma cells, and eosinophilic inflammatory cells forming granulomas within any organ system in the body. Granulomas of histiocytosis X can be distinguished from reactive or infectious granulomas by immunohistochemical staining. The histiocytes of the former are positive for S-100 antigen, but those of the latter are negative. Sites in the central nervous system include the cerebrum, cerebellum, optic chiasma, pituitary gland, hypothalamus, etc. Histiocytic histiocytosis X is often found in disseminated histiocytosis X, but is rarely an isolated lesion. The present case emphasizes the necessity to consider the possibility of other histiocytosis X lesions in unexpected regions, even if a diagnosis of isolated hypothalamic histiocytosis X has strong support. In one case of disseminated histiocytosis X, irradiation of the hypothalamic-hypophyseal area resulted in complete regression of all mucocutaneous lesions, including the vulva. There are also reports of spontaneous regression of disseminated histiocytosis X.

The present case might have been diagnosed as isolated hypothalamic histiocytosis X if the biopsy had revealed histiocytosis X. The cervix uteri lesion might have then been overlooked, or might have resolved by hypothalamic irradiation, spontaneous regression or an unknown cause. In our case, diabetes insipidus, Korsakoff's syndrome, and genital bleeding appeared sequentially. Probably the lesion was initially located only in the hypothalamus but eventually invaded the endometrium of the cervix uteri. Therefore, an isolated hypothalamic histiocytosis X lesion became disseminated histiocytosis X. This possibility has been reported previously.

Table 1 summarizes the clinical data for the 18 cases of hypothalamic histiocytosis X.

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author (Year)</th>
<th>Age, Sex</th>
<th>Chief complaint</th>
<th>Diagnostic method</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gagel (1941)</td>
<td>39, F</td>
<td>polydipsia</td>
<td>autopsy</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>Hewer and Heller (1949)</td>
<td>10, M</td>
<td>polydipsia</td>
<td>autopsy</td>
<td>none</td>
</tr>
<tr>
<td>3</td>
<td>Cureton (1949)</td>
<td>17, M</td>
<td>polydipsia</td>
<td>autopsy</td>
<td>none</td>
</tr>
<tr>
<td>4</td>
<td>Weitzman and Friedman (1960)</td>
<td>27, F</td>
<td>confusion</td>
<td>autopsy</td>
<td>none</td>
</tr>
<tr>
<td>5</td>
<td>Ezrin et al. (1963)</td>
<td>43, M</td>
<td>polydipsia</td>
<td>autopsy</td>
<td>irradiation</td>
</tr>
<tr>
<td>6</td>
<td>Kepes and Kepes (1969)</td>
<td>63, F</td>
<td>weakness, nausea</td>
<td>autopsy</td>
<td>none</td>
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<tr>
<td>7</td>
<td></td>
<td>31, M</td>
<td>polydipsia</td>
<td>delayed biopsy of temporal bone</td>
<td>none</td>
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<tr>
<td>8</td>
<td></td>
<td>19, F</td>
<td>polydipsia</td>
<td>autopsy</td>
<td>none</td>
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<tr>
<td>9</td>
<td></td>
<td>20, M</td>
<td>polydipsia</td>
<td>hypothalamic biopsy</td>
<td>none</td>
</tr>
<tr>
<td>10</td>
<td>Bernard and Aguilar (1969)</td>
<td>20, M</td>
<td>progressive weakness</td>
<td>autopsy</td>
<td>irradiation</td>
</tr>
<tr>
<td>11</td>
<td>Beard et al. (1970)</td>
<td>31, M</td>
<td>delayed biopsy of temporal bone</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Pressman et al. (1975)</td>
<td>18, F</td>
<td>polydipsia</td>
<td>delayed biopsy of lymph node</td>
<td>irradiation (5000 rads), chemotherapy</td>
</tr>
<tr>
<td>13</td>
<td></td>
<td>21, F</td>
<td>amenorrhea</td>
<td>hypothalamic biopsy (insufficient) and delayed biopsy of mandible</td>
<td>irradiation (5000 rads)</td>
</tr>
<tr>
<td>14</td>
<td>Schneider and Guthert (1975)</td>
<td>47, F</td>
<td>polydipsia</td>
<td>autopsy</td>
<td>none</td>
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<tr>
<td>15</td>
<td>Tibbs et al. (1978)</td>
<td>10, M</td>
<td>malaise</td>
<td>hypothalamic biopsy</td>
<td>irradiation (1500 rads), chemotherapy</td>
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<tr>
<td>16</td>
<td>Ibayashi et al. (1983)</td>
<td>29, M</td>
<td>polydipsia</td>
<td>hypothalamic biopsy</td>
<td>irradiation (3000 rads)</td>
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<tr>
<td>17</td>
<td>Ober et al. (1989)</td>
<td>18, F</td>
<td>visual disturbance</td>
<td>hypothalamic biopsy</td>
<td>irradiation (2000 rads)</td>
</tr>
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<td>18</td>
<td>Present case</td>
<td>54, F</td>
<td>polydipsia</td>
<td>hypothalamic biopsy (insufficient) and biopsy of cervix uteri</td>
<td>irradiation (2000 rads)</td>
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</table>
cases of isolated hypothalamic histiocytosis X and those diagnosed as such at the early stage. This disease has no characteristic symptom. Diabetes insipidus is found as in other suprasellar masses, and was present in 67% of cases as the initial symptom and 83% during the whole course. No previous case of this disease associated with Korsakoff’s syndrome has been reported. Korsakoff’s syndrome was probably caused by dysfunction of the mammillary bodies.

The hypothalamic histiocytosis X lesion appears as an iso- or high-density area on precontrast CT scans and as a homogeneously enhanced area on postcontrast scans. T1-weighted MR images usually demonstrate isointense or slightly high-intensity areas. MR imaging demonstrates the topography of the lesion better than CT with the arbitrary plane selection. However, there is no characteristic appearance on CT or MR imaging. Biopsy is therefore the optimum method for correct diagnosis. Table 1 shows early biopsy of the hypothalamus in six cases, and correct diagnoses in four cases. Biopsy does not always achieve the correct diagnosis because: 1) The hypothalamus is deeply situated and is the most important center of the autonomic nervous system, so sufficient tissue for histological diagnosis cannot always be obtained (Case 13 and our case). 2) Frequently astrocytic gliosis surrounds the focus of cerebral histiocytosis X, so there may also be hypertrophic or bizarre astrocytes, resulting in a false diagnosis of neoplasm (Cases 9 and 11).

The therapy of histiocytosis X is controversial. Chemotherapy, irradiation, or a combination have been reported. Previous cases diagnosed as isolated histiocytosis X achieved total regression after irradiation or chemotherapy with irradiation. Histiocytosis X, in particular isolated histiocytosis X, is very sensitive to radiation therapy compared with gliomas.

References


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