Lymphocytic infundibulo-neurohypophyseitis associated with recurrent optic neuritis

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Abstract
A 35-year-old woman presented with diabetes insipidus. The T1-weighted images showed a loss of the hyperintense signal of the posterior pituitary and thickening of the pituitary stalk. DDAVP was started with the diagnosis of lymphocytic infundibulo-neurohypophyseitis (LINH). Three months later, she complained of right visual acuity loss. MRI revealed right optic nerve swelling, compatible with the diagnosis of the retrobulbar optic neuritis. She had two other such episodes in the next 3 months. She developed a transient oculomotor and abducens nerve palsies as well. Each time the symptoms disappeared with corticosteroid therapy. The pituitary stalk became normal in size 6 months later. LINH and recurrent optic neuritis occurred in a short duration. Accordingly, a common causative background is suspected. Since the auto-immune process has been hypothesized as a cause of optic neuritis, our case may present further clinical evidence to support the hypothesis of an auto-immune mechanism for LINH.

Key words: Diabetes insipidus, lymphocytic infundibulo-neurohypophyseitis, magnetic resonance image, optic neuritis.

Introduction
Lymphocytic infundibulo-neurohypophyseitis (LINH) is a chronic inflammatory process at the infundibulum and neurohypophysis. It is an important clinical entity among pituitary lesions presenting with diabetes insipidus (DI). Although an autoimmune process has been hypothesized as a cause, its mechanism has yet to be elucidated. This is a rare case report of LINH that accompanied recurrent optic neuritis during its clinical course. Association of LINH and eye signs is reviewed, and its pathomechanism is discussed.

Case report
A 38-year-old woman suddenly developed polydipsia and polyuria for 3 months, and visited a local physician in September 1997. MRI revealed a small mass lesion in the sella and suggested the presence of a pituitary tumour. She was then referred to our department. She had been free of diseases including endocrinological or auto-immune disorders. She had experienced two normal deliveries 14 and 12 years previously. On admission in December 1997, her general physical condition was normal. No visual acuity, visual field defects or other neurological deficits was detected on the examinations. Routine laboratory examinations showed normal results. Urine volume was about 7000 ml/day, as much as her intake. The plasma antidiuretic hormone level was 0.7 pg/ml and demonstrated low response to hypertonic saline loading test. With a diagnosis of central DI, desmopressin acetate (DDAVP) was initiated. Results of basal serum levels of pituitary hormones were as follows: GH 0.58 ng/ml (0.66-
prolactin 58.87 ng/ml (1.4–14.6), ACTH 16.7 pg/ml (9–52), TSH 1.4 mici/ml (0.34–3.5), LH 0.14 mIU/ml (5–20), FSH 6.6 mIU/ml (10–40). Triple stimulation test was normal. Anti-nuclear, anti-smooth muscle, anti-RNP, anti-SM, anti-mitochondria and anti-thyroglobulin antibodies were all negative. Anti-pituitary antibody (indirect fluorescent antibody method; SRL Company, Tokyo) was positive. Skull radiographs and CT showed no apparent lesion. Magnetic resonance imaging (MRI) disclosed a mass lesion which was enhanced by GdTA, at the root of the infundibulum. On the T1-weighted image, loss of the hyperintense signal of the posterior pituitary was noted with thickening of the pituitary stalk (Fig. 1). No other intracranial lesions were visible on MRI.

LINV was strongly suspected based on the MRI findings and the presence of anti-pituitary antibody. We chose to observe closely in the outpatient clinic with MRI follow-up. In December 1997, she started to have difficulty in seeing well with her right eye. Ophthalmological examination showed loss of visual acuity on her right eye (VD:0.15, VS:1.2) as well as mydriasis and central visual defect on the same side. A pattern VEP was almost extinguished on the affected side and the response from the fellow eye was normal. Coronal MRI revealed a hyperintense signal from the whole optic nerve on T1-weighted image, and on enhanced image, hyperintense signal of the outer rim of the nerve with hypointense signal of the central part (Fig. 2). No mass lesion was noted in the sellar area to compress the optic pathway. In the CSF the cell count and protein were 2/3 mm³ (monocyte only) and 37 mg/dl, respectively. Other CSF findings were non-specific including oligoclonal band and MBP. With a diagnosis of optic neuritis, the patient was treated with prednisolone 240 mg in the first day and 180 mg in the next 2 days. Her visual acuity and central visual defect rapidly improved in a few days (VD:0.9, VS:0.9). In January and February 1998, she developed loss of visual acuity in her right eye (VD:0.15, VS:0.5), and left eye (VD:1.2, VS:0.1), respectively. Prednisolone 80 mg was begun in the
first 4 days, 40 mg in the next 4 days, and 20 mg in the last 4 days. Each time prednisolone was effective.

In March, 1998, 6 months after the onset of DI, MR images showed a normalized pituitary stalk (Fig. 3) and the basal serum levels of the anterior pituitary were normal including prolactin.

In May 1998, she suddenly developed double vision in all directions. Neurological examination revealed incomplete right oculomotor and abducens nerve palsy. MRI revealed no apparent lesion in the subarachnoid space or in the cavernous simul. Steroid therapy was begun again with 180 mg prednisolone for the first day and tapering gradually in the next 15 weeks. Thereafter, despite lasting DI, no ophthalmological symptoms recurred during the 27 months out-patient follow-up period.

Discussion

We report a patient who presented with DI. Since MRI revealed loss of the hyperintense signal of the posterior pituitary with thickening of the pituitary stalk, LINH was strongly suspected. During the follow-up period, she presented retrobulbar optic neuritis verified by MRI 3 times and an episode of double vision, all of which responded to corticosteroid treatment. Except for transient use of the medication, we managed our patient conservatively. Although DI did not improve, MRI revealed a normal-size pituitary stalk 6 months later.

To our knowledge, 16 cases of histopathologically proven LINH have been reported, with adequate description of clinical courses.1-14

Essential clinical features of LINH are summarized as follows:

1. DI as an initial cardinal sign, although there may be other symptoms and signs such as headache and anterior pituitary dysfunction.
2. The characteristic MRI findings.
3. Chronic inflammatory changes in histology.
4. A self-limited clinical course.

Although our case possessed the 3 clinical features but no histological confirmation, we believe that the diagnosis is LINH. Because other conditions have not been fully excluded without histological examination, a long-term outpatient follow-up is mandatory.

Since this disorder takes a benign self-limited clinical course, the initial assessment with MRI is important in determining a therapeutic choice. Imura et al. reported the features of LINH on MRI, which were: (1) enlargement of the pituitary gland; (2) thickening of the pituitary stalk; and (3) lack of hyperintense signal of the normal posterior pituitary.1 These MRI findings were essential diagnostic criteria suggestive of the disease. Once we suspect the diagnosis, we believe that a therapeutic policy of medical control with DDAVP without surgical intervention is justified. We need regular MRI follow-up every 3–6 months till the pituitary stalk decreases its size. The pituitary stalk in reported patients became normalized in 3 weeks to 18 months, averaging 8.0 months.1-14

A unique feature in our case is an association of recurrent ophthalmological signs. Eye symptoms associated with LINH have been rarely reported. As far as we know, such incipient symptoms were
only reported by Nussbaum et al.\textsuperscript{1} and Imura et al.\textsuperscript{1} Nussbaum et al. reported bilateral abducens nerve palsy caused by a MRI-verified mass lesion invading the cavernous sinus. Imura et al. showed loss of the visual acuity without a corresponding mass lesion on MRI, which was similar to our case. They did not specify a cause of the eye symptom. We succeeded in obtaining MR images of swollen optic nerve with abnormal enhancement effect. CT and MRI excluded mass lesions compressing the optic pathway. Since the optic neuritis is a term used to refer to inflammation of the optic nerve, these clinical findings coincide with the diagnosis of optic neuritis in our case.\textsuperscript{15} The exact cause of optic neuritis is not clear in our case. Although multiple sclerosis is one of the most common causes of optic neuritis, we think that this is unlikely, because of the clinical presentation limited to pituitary gland and optic nerves and nonspecific CSF findings. To confirm this, a long-term follow-up is essential.

The pathogenesis of the optic neuritis is presumed to be demyelination. One hypothesis postulates that oligodendrocytes undergo primary autoimmune attack resulting in demyelination. The other theory holds that it results from an aberrant response to a viral infection. It is important that in either theory the final pathogenesis is auto-immune.\textsuperscript{16}

The pathomechanism of LINH has been suspected as autoimmune as well, based on an inflammatory process of self-limited and spontaneous regression, predominance of women and presence of T-cell infiltration in the biopsied tissue.\textsuperscript{1} Other clinical evidence to support the hypothesis is scarce. Since the LINH and recurrent optic neuritis in our case occurred in the CNS and with short duration, a common causative background is suspected, and our case may present further evidence to support the hypothesis of the autoimmune mechanism as a cause of LINH.

Cases of LINH may have an atypical clinical course such as recurrence\textsuperscript{6,17} or associated neurological sign (as seen in our case), a long-term and regular endocrinological and neuroradiological assessment is required.

Conclusions

We report a patient who presented with diabetes insipidus as an initial manifestation and MRI revealed typical images of LINH. She showed recurrent optic neuritis, which responded to corticosteroid therapy. MRI became normal in 6 months. Association of LINH and recurrent optic neuritis has never before been reported. Since both disorders occurred in the CNS and with short duration, a common causative background is suspected. Since the autoimmune process has been hypothesized as a cause of optic neuritis, our case presents further clinical evidence to support the hypothesis of autoimmune mechanism as a cause of LINH.

References