Letter to the Editor

IgG4-related hypothalmo-hypophysitis

Keywords
IgG4-related hypothalmo-hypophysitis
Neurohypophysitis
Optic tract edema
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Dear Editor,

IgG4-related disease is an immune-mediated fibroinflammatory condition with high serum IgG4 levels, that affects multiple organs such as autoimmune pancreatitis, sclerosing cholangitis, Mikulicz disease, orbital disease, and retroperitoneal fibrosis [1,2]. IgG4-related hypophysitis has been established as a cause of lymphocytic hypophysitis [3,4]. We report a rare case of isolated IgG4-related hypothalmo-hypophysitis that rapidly responded to steroids and markedly improved on MRI within 4 days.

1. Case report

A 79-year-old man developed syncope and low blood pressure (BP) one month before admission. He was aware of fatigue, appetite loss, and nausea. As he was unable to ingest food except for water for several days, he was admitted to our hospital. He was alert. His body temperature was 36.8 °C, BP was 98/61 mmHg, and heart rate was 71 beats/min, being regular. His general appearance and medical examination findings were normal. There was no lymph node swelling or struma. Neurological examination revealed normal cranial nerves, motor and sensory systems, and reflexes. Marked orthostatic hypotension was confirmed by a pillow test. Pollikuria was observed 10–20 times/day and the urine volume was 2000–4000 mL/day. Urine osmolality was 279 mOsm/kgH₂O and blood osmolality was 283 mOsm/kgH₂O. There was no abnormality in routine blood chemistry, including electrolyte levels.

Endocrine assessment revealed a reduction in ACTH (3.3 pg/mL), cortisol (1.6 μg/dL), LH (<0.1 mIU/mL), FSH (1.02 IU/mL), estradiol (<10 pg/mL), and testosterone (<0.04 mg/mL), and an increase in prolactin (29.83 μg/dL). Serum ACE, anti-AQP4 antibody, sIL-2R, T-SPOT, MPO-ANCA, PR3-ANCA, antinuclear antibody, antithyroid antibodies, and autoantibodies against Ro/SS-A and La/SS-B were normal, but the serum IgG4 level increased to 157 μg/dL.

No tumefactive lesions in the face, neck, lung, pancreas, or retroperitoneal spaces were found on whole-body CT. Prominent high-signal areas of swelling were observed in the hypothalamus, tuber cinereum, infundibulum (Fig. 1A), and bilateral optic tracts on MRI FLAIR images (Fig. 1B). The bottom of the third ventricle was suppressed, and high-intensity signals in the optic tract extended to lateral geniculate bodies and optic radiations (Fig. 1C). MRI T1WI with contrast media demonstrated a swollen hypothalamus and tuber cinereum, cystic infundibulum expansion, and suppressed anterior pituitary on the floor of the sella turcica (Fig. 1D, E).

On the next day after methylprednisolone pulse therapy (1 g/day, 2 days), fatigue and loss of appetite improved. On the 4th day after sequential oral hydrocortisone administration (30 mg/day), the hypothalamus, tuber cinereum, and infundibulum shrank markedly (Fig. 1F, G, H). Hypothalamo-hypophysial contrast enhancement also improved (Fig. 1I, J). As the urine volume did not improve, oral desmopressin was administrated. At the 9-month follow-up examination, endocrine values remained unchanged. The patient remained in a good condition while orally receiving 15 mg/day of hydrocortisone and 2.5 μg/day of DDAVP.

2. Discussion

IgG4-related hypophysitis represents a rare etiology of hypophysitis (less than 5% of cases), and it can present as isolated primary hypophysitis or as part of IgG4-related multi-systemic disease, which is noted in 60–90% of cases [4]. The proposed diagnostic criteria consist of 1) pituitary histopathology with rich IgG4-positive lymphocytes and plasma cell infiltration, 2) sellar mass and thickened pituitary stalk on MRI, 3) positive biopsy findings in another organ, 4) increased serum IgG4 (>140 mg/dL), and 5) improvement with steroids [3,4]. Our case fulfilled criteria 2 + 4 + 5. The present case was diagnosed as rare primary IgG4-related hypothalmo-hypophysitis and exhibited markedly rapid recovery of symptoms and MRI findings within 4 days after treatment [5].

Typical MRI findings of IgG4-related hypothalmo-hypophysitis and exhibited markedly rapid recovery of symptoms and MRI findings within 4 days after treatment [5].

Abbrivations: MRI, magnetic resonance imaging; BP, blood pressure; CT, computed tomography; FLAIR, fluid attenuated inversion recovery; T1WI, T1 weighted image; T2WI, T2 weighted image; ACTH, adrenocorticotropic hormone; LH, luteinizing hormone; FSH, follicle stimulating hormone; ACE, angiotensin converting enzyme; AQP4, aquaporin-4; sIL-2R, soluble interleukin 2 receptor; MPO-ANCA, myeloperoxidase-antineutrophil cytoplasmatic antibody; PR3-ANCA, proteinase-3-antineutrophil cytoplasmatic antibody; DDAVP, 1-desamino-8-D-arginine vasopressin.

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and pituitary stalk enlargement, 32% had isolated pituitary stalk swelling, 18% had isolated anterior pituitary enlargement, and 7% had chiasma compression [4]. Cystic enlarged anterior pituitary, empty sella after treatment, loss of normal T1WI hyper-intensity in the posterior pituitary and pituitary stalk, and dark parasellar signals on T2WI have been also reported [5–7]. Our case exhibited enhanced hypothalamic and tuber cinereum lesions, cystic enlargement of the infundibulum, and compressed anterior pituitary. Complexed edema of the optic tract - lateral geniculated body - optic radiation has not been reported in IgG4-related hypophysitis. Contrast-enhanced T1WI suggested that the primary lesion in this case was located in the hypothalamus and tuber cinereum, and may have caused the cystic infundibulum expansion and compression of the anterior pituitary, which are characteristic of neurohypophysis. As edema of optic nerve systems is often reported in craniopharyngioma due to neurohypophysis [8], neurohypophysis swelling may cause extensive edema of optic tract systems. (759 words).

Fig. 1. MRI images of IgG4 related hypothalamo-hypophysitis Prominent high-signal areas of swelling in the hypothalamus, tuber cinereum, infundibulum (A: red arrows), bilateral optic tracts (B: yellow arrows), and lateral geniculate bodies (C: white arrows). Contrast media-enhanced swelling of the hypothalamus and tuber cinereum, and closed bottom of the third ventricle (D: red arrow), cystic infundibulum expansion, and suppressed anterior pituitary on the floor of the sella turcica (E: red arrow). At the 4th day after treatment, swelling of the hypothalamus, tuber cinereum and infundibulum improved markedly (F, G, H). Contrast enhancement areas also improved (I, J). A – E: On admission; F – J: 4th day after steroid treatment; A – C and F – H: FLAIR images; D, E, I, and J: T1WI with contrast media enhancement. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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