A case of relapsed autoimmune hypothalamitis successfully treated with methylprednisolone and azathioprine

Xian Ling Wang, Ju Ming Lu*, Li Juan Yang, Zhao Hui Lü, Jing Tao Dou, Yi Ming Mu, Chang Yu Pan

Department of Endocrinology, Chinese PLA General Hospital, Beijing, China.

Correspondence to: Ju Ming LU, Department of Endocrinology, Chinese PLA General Hospital, Fuxing Road 28, Beijing, 100853 China. tel: +86 10-66936213; fax: +86 10-68168631 e-mail: wangxianling1972@sohu.com

Submitted: 2008-05-13 Accepted: 2008-09-09 Published online: 2008-12-29

Key words: autoimmunity; hypothalamus; pituitary; glucocorticoid; diabetes insipidus

Abstract
Autoimmune hypothalamitis is a rare autoimmune neuroendocrine disease. A case of a 70-year-old female with autoimmune hypothalamitis was reported. The chief clinical characteristics were diabetes insipidus and adenopituitary function deficiency. Cranial magnetic resonance imaging (MRI) scan indicated a mass in the hypothalamus. The diagnosis of autoimmune hypothalamitis was presumed. After treatment with prednisone, there was a marked reduction in the mass and the hypothalamus-adenopituitary function partially improved. However, after glucocorticoid therapy was withdrawn, the hypothalamic lesion relapsed progressively. High dose methylprednisolone pulse therapy (HDMPT) in combination with azathioprine was initiated thereafter. During follow-up, MRI scan indicated the lesion shrank strikingly, and the patient's clinical condition improved as well. In view of the good response of the hypothalamic lesion to glucocorticoid and immunodepressant, the putative diagnosis of autoimmune hypothalamitis was confirmed. This case report suggested that HDMPT in combination with azathioprine therapy might be an effective trial for autoimmune hypothalamitis treatment.

INTRODUCTION
Autoimmune hypothalamitis is a rare autoimmune neuroendocrine disease. To our knowledge, only one such case was reported [Stelmachowska et al. 2006]. It has been suggested that hypothalamus may be infiltrated by lymphocytes and plasma cells in autoimmune hypothalamitis. In this report, we described a case with relapsed autoimmune hypothalamitis successfully treated with high dose methylprednisolone pulse therapy (HDMPT) in combination with azathioprine therapy.

CASE REPORT
The patient was a 70-year-old female. The chief complaints were thirsty, polydipsia and polyuria for 1 year. The symptoms of weakness and feeling chilly were also present. In the local hospital, after desmopressin administration, the symptoms of thirst, polydipsia and polyuria were all relieved.

On physical examination, blood pressure was 120/70mmHg. l0 goiter but no nodules were palpated in thyroid. Visual fields were normal. The remainder of the examination was unremarkable.
A case of relapsed autoimmune hypothalamitis successfully treated with methylprednisolone and azathioprine

Abbreviations:
- ACTH: adrenocorticotropic hormone
- FSH: follicle-stimulating hormone
- HDMPT: high-dose methylprednisolone pulse therapy
- LH: luteinizing hormone
- MRI: magnetic resonance imaging
- T\(_3\): triiodothyronine
- T\(_4\): thyroxine
- TGAb: antithyroglobulin antibodies
- TPOAb: antithyroperoxidase antibody
- TSH: thyrotropic stimulating hormone

Laboratory investigations showed plasma and urine osmotic pressure were 286 mOsm/L and 176 mOsm/L respectively during desmopressin administration. Thyroid function test showed TSH 15.37 mU/L (0.35–5.5), free T\(_3\) 2.36 pmol/L (2.76–6.30), and free T\(_4\) 1.57 pmol/L (10.42–24.32). Antithyroglobulin antibody (TGAb) was 343.1 IU/mL (<60), and antithyroperoxidase antibody (TPOAb) was >1300 IU/mL (<60). Serum adrenocorticotropic hormone (ACTH) and free cortisone at 8 am were <2.2 pmol/L (2.2–10.12) and <25.7 nmol/L (160.0–797.5) respectively. Sexual hormones examination showed LH <0.07 IU/L (5.9–54.0), FSH 0.48 IU/L (3.0–116.3) estradiol <36.7 pmol/L (<83.7), and prolactin 45.8 μg/L (0.8–29.2).

In cranial magnetic resonance imaging (MRI) sagittal T\(_1\)-weighted image, a hypothalamic mass (oval-shaped, 12 × 7 mm) (Fig 1A) which could be enhanced homogeneously after gadolinium injection, partial empty sella and loss of 'bright spot' in the postpituitary were revealed.

As to the hypothalamic mass, the diagnosis of autoimmune hypothalamitis was presumed, and the glucocorticoid was then administrated. The proposal was prednisone 20 mg tid × 2 weeks, tapered by 5 mg every 2 weeks to withdrawal. 1–6 months later, MRI scan showed the mass shrank (Fig 1B,C). Serum ACTH (<2.2 pmol/L) and free cortisone (343.8 nmol/L) at 8 am both increased to the normal range.

16 months after prednisone withdrawal, MRI scan showed the hypothalamic mass relapsed to a size of 20 × 13 mm (Fig 2A). Serum ACTH (<2.2 pmol/L) and free cortisone (<25.7 nmol/L) at 8 am both decreased again. Then HDMPT in combination with azathioprine therapy was administrated. The proposal was methylprednisolone 200 mg/d × 3 d iv, 100 mg/d × 3 d iv, then changed to oral prednisone 15 mg/d in combination with azathioprine 100 mg/d. 1–10 months later, MRI scan showed the lesion shrank (Fig 2B,C). Currently the patient remains in remission on prednisone 10 mg/d in combination with azathioprine 100 mg/d.

---

Figure 1. MRI sagittal T\(_1\)-weighted image. A: Before prednisone therapy. B: 1 month later. C: 6 months later.

Figure 2. MRI sagittal T\(_1\)-weighted image. A: Before HDMPT combination with azathioprine therapy. B: 1 month later. C: 10 months later.
DISCUSSION

The hypothalamus is a very critical center in the nervous system. The majority of hypothalamus masses are tumors, while autoimmune hypothalaminis was rarely reported.

As to this patient, the symptoms of polydipsia and polyuria, as well as the good response to desmopressin acetate administration all indicated the diagnosis of central diabetes insipidus. Thyroid function examination showed TG (+) and TPO (+), which supported the diagnosis of Hashimoto’s thyroiditis. Hormone assessment showed adenopituitary function deficiency and MRI scan indicated a hypothalamic mass.

According to the patient’s clinical presence and radiological examination, the possibility of hypothalamic tumors (craniopharyngioma germinoma etc) and a lot of nonadenomatous lesions (sarcoïdosis, tuberculosis etc) could be excluded, and the diagnosis of autoimmune hypothalaminis was presumed. The tentative therapy with glucocorticoid was therefore initiated. 1–6 months after treatment, a good response in hypothalamic lesion shrinkage supported the putative diagnosis. However the lesion relapsed after glucocorticoid therapy withdrawal. Later on, HDMPT in combination with azathioprine therapy got even more marked effect than before. This further supported the putative diagnosis.

Histopathology remains the gold standard for diagnosis of autoimmune hypothalaminis, but the hypothalamus biopsy or surgery is impractical. Till now, its pathophysiological mechanism is presumed to be similar to the pathophysiology of lymphocytic hypophysitis [Bensing et al. 2007, Gutenberg et al. 2006, De Bellis et al. 2007]. As to this case, we considered that even without pathological confirmation, the clinical diagnosis of autoimmune hypothalaminis could still be defined. The reasons were:

1) Hypothalamic mass. The possibility of tumors, infectious diseases and tuberculosis were all excluded.
2) Adenopituitary function deficiency and central diabetes insipidus.
3) Hypothalamic mass relapsed after glucocorticoid therapy withdrawal and showed a good response to glucocorticoid and immunodepressant therapy.
4) The coexistence of Hashimo’s thyroiditis was an adjuvant diagnosis.

As for the therapy of autoimmune hypothalaminis, the information and knowledge are very limited. Previously, only one 69-year-old case treated with glucocorticoid was described [Stelmachowska et al. 2006]. It has been reported that therapy with high dose glucocorticoid was more effective in producing lesion shrinkage and hypophysis function improvement in patients with lymphocytic hypophysitis [Bensing et al. 2005, Lecube et al. 2003].

For this patient, 1–6 months after prednisone therapy, the lesion shrank and the adenopituitary function was partially recovered, but after prednisone withdrawal, the lesion relapsed. HDMPT in combination with azathioprine therapy could extensively inhibit cell proliferation which exacerbates most inflammatory processes, while its adverse events were fewer than that of conventional glucocorticoid therapy. To this case, after HDMPT in combination with azathioprine therapy, the shrinkage of hypothalamic lesion was marked, and the physical status was improved greatly.

CONCLUSION

In summary, we reported a rare case with autoimmune hypothalaminis, and suggested that HDMPT in combination with azathioprine therapy might be an effective attempt for mass reduction and hypothalamus-pituitary function recovery.

REFERENCES