CASE REPORT

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

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Abstract

Autoimmune hypothalamitis is a rare autoimmune neuroendocirne 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 However, after glucocorticoid therapy was withdrawn, the hypothalamic lesion relapsed progressively.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 neuroendocirne 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. I^0 goiter but no nodules were palpated in thyroid. Visual fields were normal. The remainder of the examination was unremarkable.

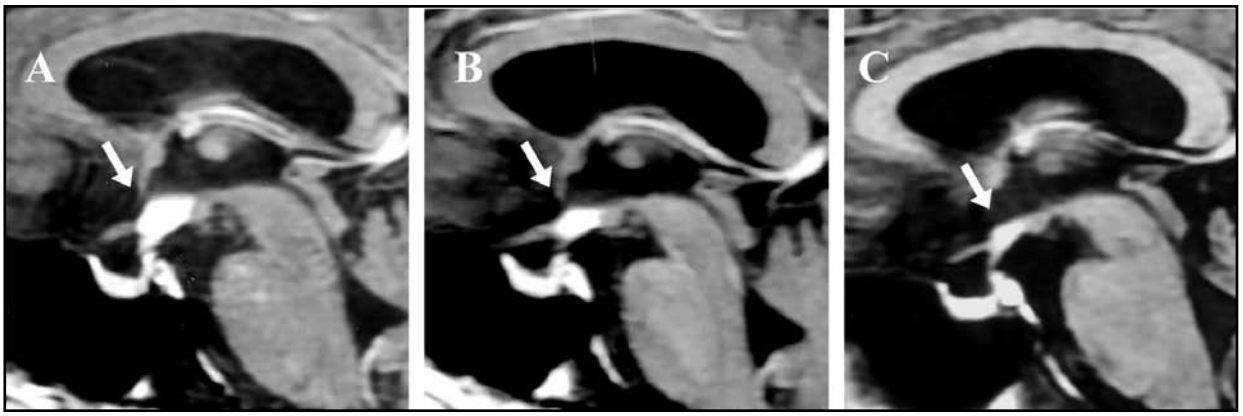

Figure 1. MRI sagittal Tl-weighted image. A: Before prednisone therapy. B: 1 month later. C: 6 months later.

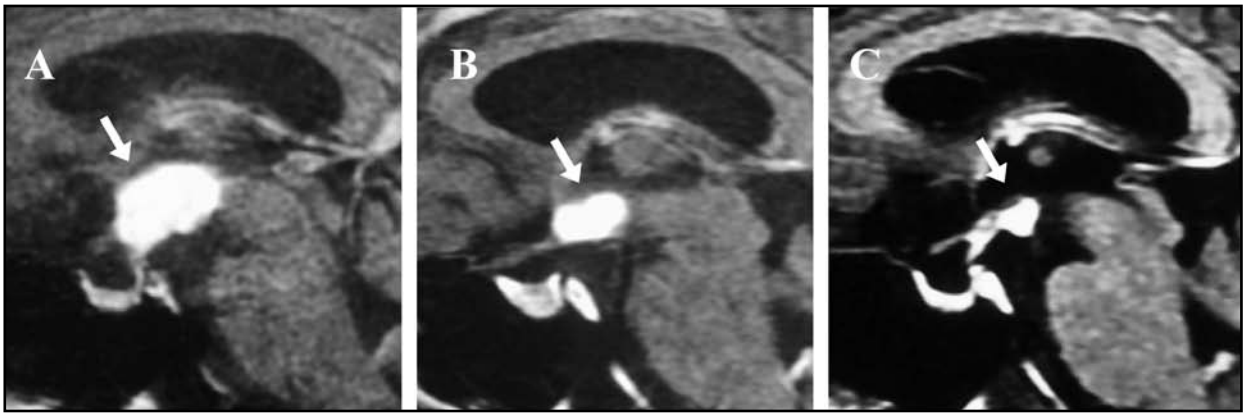

Figure 2. MRI sagittal Tl-weighted image. A: Before HDMPT combination with azathioprine therapy. B: 1 month later. C: 10 months later.

Abbreviations:

ACTH	– adrenocorticotrophic hormone
FSH	– follicle stimulating hormone
HDMPT	– high dose methylprednisolone pulse therapy
LH	– luteotrophic hormone
MRI	– magnetic resonance imaging
T_4	– thyroxine
T_3	– triiodothyronine
TGAb	– Antithyroglobulin antibodies
TPOAb	– Antithyroperoxidase antibody
TSH	– thyrotropic stimulating hormone

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

In cranial magnetic resonance imaging (MRI) sagittal Tl-weighted image, a hypothalamic mass (oval-shaped,12 × 7mm) (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 20mg tid × 2 weeks, tapered by 5 mg every 2 weeks to withdrawal. 1–6 month later, MRI scan showed the mass shrank (Fig 1B,C). Serum ACTH (7.66pmol/l) and free cortisone (343.8nmol/l) at 8am both increased to the normal range.

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

DISCUSSION

The hypothalamus is a very critical center in the nervous system. The majority of hypothalamus masses are tumors, while autoimmune hypothalamitis 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 (sarcoidosis, tuberculosis etc) could be excluded, and the diagnosis of autoimmune hypothalamitis was presumed. The tentative therapy with glucocorticoid was therefore initiated. 1–6 months after treatment, a good response in hypothalamus 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 hypothalamitis, but the hypothalamus biopsy or surgery is impractical. Till now, its pathophyisological 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 hypothalamitis 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 Hashimoto's thyroiditis was an adjuvant diagnosis.

As for the therapy of autoimmune hypothalamitis, 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 glucocoritcoid 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 glucocoticoid therapy. To this case, after HDMPT in combination with azathioprine therapy, the shrinkage of hypothalamus lesion was marked, and the physical status was improved greatly.

CONCLUSION

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

REFERENCES

1 Bensing S, Hulting AL, Höög A, Ericson K, Kämpe O. (2007). Lymphocytic hypophysitis: report of two biopsy-proven cases and one suspected case with pituitary autoantibodies. J Endocrinol Invest. **30**: 153–162.
2 Bensing S, Kasperlik-Zaluska AA, Czarnocka B, Crock PA, Hulting A. (2005) Autoantibodies against pituitary proteins in patients with adrenocorticotropin-deficiency. Eur J Clin Invest. **35**: 126–132.
3 De Bellis A, Colao A, Pivonello R, Savoia A, Battaglia M, Ruocco G, et al. (2007). Antipituitary antibodies in idiopathic hyperprolactinemic patients. Ann N Y Acad Sci . **1107**: 129–135.
4 Gutenberg A, Hans V, Puchner MJ, Kreutzer J, Brück W, Caturegli P,et al. (2006) . Primary hypophysitis: clinical-pathological correlations. Eur J Endocrinol. **155**: 101–107.
5 Lecube A, Francisco G, Rodríguez D, Ortega A, Codina A, Hernández C, et al. (2003). Lymphocytic hypophysitis successfully treated with azathioprine: first case report. J Neurol Neurosurg Psychiatry. **74** : 1581–1583.
6 Stelmachowska M, Bolko P, Waśko R, Kosiński D, Towpik I, Sowiński J. (2006). Lymphocytic hypophysitis and hypothalamitis-case report. [In Polish] Endokrynol Pol. **57**: 648–653.