ORIGINAL

Recurrent autoimmune hypophysitis successfully treated with glucocorticoids plus azathioprine: a report of three cases

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Abstract. Recurrent autoimmune hypophysitis is a rare autoimmune endocrine disease involving lymphocytic infiltration and chronic pituitary inflammation. It is even more rare than primary hypophysitis. The objective of the study was to evaluate the efficacy of glucocorticoid treatment combined with azathioprine for treating three cases of recurrent autoimmune lymphocytic hypophysitis encountered within a two-year period. The clinical features and follow-up data of these cases were analyzed, including results of treatment with glucocorticoids combined with azathioprine. All three patients were female and presented with the following clinical characteristics: case 1 was a 22-year-old with headache and diplopia; case 2 was a 70-year-old with dry mouth, polydipsia, and polyuria; case 3, a 32-year-old, with polydipsia, polyuria and menstrual disorders with headache and dizziness. Regarding recurrence, case 1 recurred 4 months after surgery and again 14 months after discontinuing prednisone; case 2 relapsed 16 months after receiving high-dose methylprednisolone pulse therapy; and case 3 recurred during the period of prednisone dose reduction. The patients were treated with glucocorticoids plus azathioprine, and positive responses were seen in all three cases. Symptoms were relieved, and MRI revealed significant reduction of lesions during follow-up. Pituitary function resumed in cases 1 and 3; permanent hypopituitarism was present in case 2. At last follow-up, MRI showed no further recurrence of disease in any patient. Treatment and responses of these patients with autoimmune hypophysitis suggest that glucocorticoid therapy combined with azathioprine is effective treatment for recurrent autoimmune hypophysitis. Endocrine and radiologic studies are an essential part of follow-up.

Key words: Glucocorticoids, Azathioprine, Autoimmune hypophysitis, Recurrence

AUTOIMMUNE hypophysitis (AH), also termed lymphocytic hypophysitis, is a rare autoimmune endocrine disease characterized by lymphocytic infiltration of the pituitary gland and chronic pituitary inflammation [1]. Clinical manifestations of AH include pituitary dysfunction and diabetes insipidus. It affects females far more often than males, is associated with pregnancy, and may present with nausea, vomiting and hyperprolactinemia, which may cause breast milk production and menstrual disturbances in non-pregnant women [2, 3, 4]. Characteristic imaging manifestations of hypophysitis include homogenous pituitary enlarge-

ment and pituitary stalk thickening. Specifically, in lymphocytic adenohypophysitis (LAH) and lymphocytic infundibulopanhypophysitis (LIPH), the following magnetic resonance imaging (MRI) manifestations may be observed: i) intrasellar mass with homogeneous enhancement or ring-like enhancement and triangle and/or saddle diaphragm involvement or ii) diffuse and symmetrical pituitary enlargement with a blurred border; iii) tongue-like changes above the sella turcica; and iv) a delay in total enhance time (> 90 sec) as observed by dynamic contrast-enhanced MRI [5]. For lymphocytic infundibuloneurohypophysitis (LINH) and LIPH the following may be observed: i) diffuse thickening of pituitary stalk (enhanced or not enhanced) and ii) the absence of strong signals in the posterior pituitary as observed in T1-weighted images [5]. Pathological examination is the main basis for diagnosis, but as an autoimmune disease, AH can be confirmed if spontaneous remission occurs or corticosteroid

Received Nov. 5, 2010; Accepted May 18, 2011 as K10E-334

Released online in J-STAGE as advance publication Jun. 10, 2011

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Disclosure: The authors have no conflict of interest or other disclosures to report.

Table 1 Pituitary data—target gland hormone changes in patients before and after treatment

Items	Case 1				Case 2			Case 3			
	At onset	After steroid treatment	At relapse	After healing	At onset	After remission	At relapse	At onset	After remission	At relapse	After healing
TT3 (1.01 ~ 2.95 nmol/L)	1.9	1.78	1.45	1.58	0.76	1.32	0.88	1.72	1.95	2.76	2.93
TT4 (55.3 ~ 160.8 nmol/L)	86.6	95.6	101.4	89.1	34.8	56.2	65.2	101.9	75.7	144.9	113.4
FT3 (2.76-6.30 pmol/L)	4.65	4.67	3.98	4.44	1.71	3.38	2.55	4.34	3.54	6.08	5.81
FT4 (10.4-24.3 pmol/L)	13.22	15.83	17.4	17.33	7.14	7.59	8.95	14.77	12.21	15.26	18.14
TSH (0.35-5.5 mU/L)	2.81	4.77	3.21	3.27	6.14	4.77	9.14	2.42	0.5	0.35	0.8
TGAb (<60 IU/mL)	33.9	-	-	--	343.1	--	--	64	-	-	--
TPOA (<60 bIU/mL)	41.9	-	-	-	>1300	--	--	60.7	-	-	-
LH IU/L [Female (adult): 0.5-76.3 post-menopause: 15.9-54.0]	1.31	3.93	3.67	34.17	<0.07	<0.07	<0.07	4.52	<0.07	1.89	0.5
FSH IU/L [Female (adult): 1.5-33.4 post-menopause: 23.0-116.3]	2.85	3.0	1.94	7.68	0.48	0.3	0.49	6.16	1.49	4.28	1.81
E2 pmol/L [Female (adult): 70.0-1938.0 post-menopause: ≤283.7]	399.4	161.15	265.8	1509.48	<36.7	0.91	81.54	57.4	54.69	44.75	36.7
PRL ((2.8 ~ 29.2) µg/L)	26.53	12.23	40.5	22.82	45.8	54.29	54.0	26.5	16.66	23.56	18.55
ACTH (normal< 10-12 pmol/L) at 8:00	< 2.2	2.4	3.2	-	< 2.2	7.66	< 2.2	2.75	--	5.31	5.2
ACTH (normal< 10-12 pmol/L) at 0:00	< 2.2	< 2.2	< 2.2	-	< 2.2	6.12	< 2.2	2.51	--	2.36	< 2.2
F (198.7 ~ 797.5 nmol/L) 8:00	208.5	365.1	265.9	-	<25.7	343.8	<25.7	227.8	---	188.9	206.4
F (0 ~ 105.7 nmol/L) 0:00	189.8	50.2	147.3	-	<25.7	202.1	<25.7	129.5	--	<25.7	<25.7
UFC (78.6 ~ 589.6 nmol/24h)	230.5	891.8	179.8	-	<25.7	327.1	<25.7	142.9	--		
GH (0.06-5.0 µg/L)	0.33	--	0.56	-	0.17	0.05	0.08	0.33	0.50	0.59	0.07

TT3, total triiodothyronine; TT4, total thyroxine; FT3, free triiodothyronine; FT4, free thyroxine; TSH, thyrotrophin-stimulating hormone; TGAb, thyroglobulin antibody; TPOA, thyroperoxidase antibody; LH, lutenising hormone; FSH, follicle stimulating hormone; E2, 17-β estradiol; PRL, prolactine; ACTH, adrenocorticotrophic hormone; F, cortisol; UFC, urinary free cortisol; GH, growth hormone

teroid treatment is effective [2, 3, 5]. Although primary AH is rare, it has a tendency to recur [2, 3]. However, few studies describe treatment of recurrent autoimmune hypophysitis. Our experience may provide insights to help identify and treat recurrent AH. Herein, we report clinical and treatment data of three recently diagnosed cases of recurrent AH treated with glucocorticoids plus azathioprine, as previously reported [6].

Patients and Methods

Case 1

A 22-year-old female patient was admitted to our hospital on June 17, 2004 due to headache and diplopia. She had sought medical care for similar symptoms at another hospital in January 2004, and “pituitary tumor” was diagnosed based on MRI results.

After resection of the pituitary adenoma at that hospital in February, the patient’s headache and diplopia were significantly relieved. Six months later, headache and diplopia recurred along with appearance of left ptosis, hyperprolactinemia, and menstrual disorders. Physical examination showed left ptosis, limited adduction of eyes and bilateral breast milk discharge triggered by palpation. Laboratory test results were ESR 14mm/h, high-sensitivity C-reactive protein 1.7mg/dL, and blood and urine osmolality 287 mOsm/L and 480 mOsm/L, respectively. Endocrine hormone levels are shown in Table 1. No visual field defects, partial oculomotor nerve paralysis or trochlear nerve palsy was observed. MRI revealed a typical homogenous pituitary enlargement and pituitary stalk thickening as well as abnormal soft tissue signals in the suprasellar cistern, with irregular shape and unclear boundary. Lesions were

Fig. 1 Preoperative and follow-up MRI of Case 1. **A.** Preoperative MRI. Homogenous pituitary enlargement is shown, while the pituitary stalk is not shown clearly. Abnormal soft tissue with irregular shape and unclear boundary is observed in the suprasellar cistern, which pushed the optic chiasm upward. Pituitary stalk is not shown clearly. **B.** MRI after first HDMPT therapy. The pituitary is significantly reduced in size compared to that before surgery. Pituitary stalk is shown clearly. **C.** MRI after recurrence. Bulging pituitary and thickened pituitary stalk are seen with homogeneous enhancement. **D.** MRI after treatment for recurrence (Follow-up at 48th month after admission). Pituitary and pituitary stalk appear normal compared to views in panel C. Signs of disease disappeared.

enhanced significantly after gadolinium, showing the optic chiasm to be pushed upward and wrapping the bilateral internal carotid arteries. The pituitary stalk was not shown clearly (Fig. 1). The Department of Pathology at the Chinese PLA General Hospital reviewed paraffin-embedded sections of pituitary tissue prepared by the hospital where surgery had been performed and found a large amount of lymphocyte infiltration in the pituitary tissue. Autoimmune hypophysitis was diagnosed. High-dose methylprednisolone pulse therapy (HDMPT) was adopted based on that introduced by Kristof *et al.* [7]. To prevent hormone withdrawal syndrome, a modified HDMPT regimen, consisting of intravenous infusion of 100 mg

methylprednisolone daily for 3 days and oral administration of 60 mg prednisone daily for two weeks, was employed by gradually reducing the dosage. The dosage of prednisone was decreased by 5 mg every week after the first two weeks until a 5 mg maintenance dose was reached, which was maintained for 4 weeks. The entire treatment course lasted 16 weeks.

Headache was alleviated on the first day after beginning HDMPT. Diplopia and left ptosis improved significantly after 3 days. MRI showed significant reductions in pituitary size and lesions on the slope of the dorsum sellae and in the cavernous sinus disappeared (Fig. 1). Oral prednisone (2.5 mg /d) was given until the follow-up visit in October 2004 when menstrual

periods were regular and breast discharge disappeared. Prednisone was withdrawn in November. Headache and diplopia occurred again in December 2005. Pituitary function was assessed, and anterior pituitary function was normal (Table 1). Pituitary function was within normal ranges at onset and relapse. MRI showed bulging pituitary and thickened pituitary stalk with homogeneous enhancement. HDMPT was repeated, and all symptoms disappeared. Prednisone (30 mg/d) and azathioprine (100 mg/d) were administered. Prednisone dosage was gradually reduced by 5 mg after 4 weeks and then by 5 mg weekly until 5 mg maintenance dose was reached, which was maintained for 8 weeks. These drugs were withdrawn after 16 weeks. MRI showed decreased lesion size (Fig. 1). Total follow up was 4 years, and the patient's anterior pituitary function remained normal (data not shown). In August 2008, IGF-1 levels were 237 ng/mL. Repeat MRI indicated no recurrence of disease after treatment at 48 months; the recurrence-free follow-up period was 36 months. At last follow-up, normal pituitary function had resumed.

Case 2

A 70-year-old female was admitted to our hospital March 20, 2006 presenting with dry mouth, polydipsia and polyuria experienced for one year. She also experienced fatigue, drowsiness, weight loss and loss of pubic and axillary hair. The patient had a history of "hyperthyroidism" and "osteoarthritis." Physical examination revealed blood pressure of 120/70 mmHg, with dryness of skin and mucous membranes over the entire body. Pubic and axillary hair was thin. Laboratory test results were ESR 32mm/h, high-sensitivity C-reactive protein 1.24 mg/dL, blood osmolality 298 mOsm/L, urinary osmolality 168 mOsm/L and urine specific gravity 1.005. Endocrine hormone levels are shown in Table 1. Anterior pituitary function was decreased at symptom onset and relapse. MRI revealed abnormal signals in the pituitary stalk and hypothalamus, showing homogenous enhancement. Specifically, tongue-like changes were observed above the saddle (hypothalamus). High signals in the posterior pituitary disappeared (data not shown). Autoimmune hypophysitis was diagnosed. The patient was given prednisone (60 mg/d), levothyroxine (100 µg/d), and desmopressin acetate (0.1 mg/d). Symptoms were significantly relieved after 2 weeks. Prednisone dosage was gradually reduced; however, desmopressin treat-

ment continued. Prednisone was withdrawn on August 21st, and repeat lab test results were urine specific gravity 1.015, blood osmolality 295 mOsm/L and urine osmolality 341 mOsm/L. Endocrine hormones are shown in Table 1. MRI showed significantly reduced pituitary lesions (Fig. 2). Because secondary diabetes occurred in this patient, multiple subcutaneous injections of insulin were given, and glycemic control was satisfactory. The patient experienced polydipsia, polyuria, cold intolerance, hypohidrosis, and drowsiness. MRI performed in May 2008 showed abnormal oval signals in the hypothalamus with much greater homogeneous enhancement than observed in October 2006. No relapse was observed. Recurrent hypophysitis was considered, and methylprednisolone (200 mg/d) was given for 3 days followed by 100 mg/day for 3 days. Prednisone (15 mg/d) plus azathioprine (100 mg/d) were given for a total of 16 weeks. Levothyroxine, prednisone, and desmopressin acetate replacement therapy was continued. Symptoms were significantly relieved, and repeat MRI showed significantly reduced hypothalamic lesions (Fig. 2); the recurrence-free follow-up period was 6 months. MRI showed no further relapse of disease after treatment at 10 months. Permanent hypopituitarism was present in this patient.

Case 3

A 32-year-old married female was admitted to our hospital on July 20, 2006 due to polydipsia, polyuria and menstrual disorders with headache and dizziness for the past 8 months. Physical examination revealed slightly dry skin over the entire body. High-sensitivity C-reactive protein was 1.7 mg/dL; blood and urine osmolality were 288 mOsm/L and 180 mOsm/L, respectively. Endocrine hormone levels are shown in Table 1. MRI revealed "tongue-like" changes; an intrasellar mass with ring-like enhancement and diffuse and enhanced thickening of the pituitary stalk, which was shifted towards the left side. This was similar to a case reported by Honegger *et al.* [8]. The absence of high signals in the posterior pituitary was also noted (Fig. 3). Autoimmune hypophysitis was diagnosed, and the patient received HDMPT treatment. Cranial MRI showed a thinner pituitary stalk and smaller pituitary 30 days post-treatment. Prednisone (30 mg/d) was given with gradual reduction of dosage by 5 mg per week after 4 weeks. Polydipsia and polyuria were improved significantly, and menstrual periods became regular. Prednisone dose was reduced to 5 mg/d on November

Fig. 2 Pretreatment and follow-up MRI of Case 2. **A.** Before treatment MRI, showing abnormal, enhanced, and homogeneous signals in the pituitary stalk and hypothalamus. In addition, a tongue-like change above the saddle (hypothalamus), hypothalamicitis, was also observed. **B.** MRI 4 weeks after prednisone therapy. The abnormal signals in pituitary stalk and hypothalamus were significantly reduced. **C.** MRI after relapse. After the treatment was stopped for 16 months, the abnormal signals in hypothalamus were evenly enhanced. **D.** After the 16-week treatment regimen with HDMPT plus azathioprine, the lesion almost disappeared.

Fig. 3 Pretreatment and follow-up MRI of Case 3. **A.** Before treatment MRI, showing an enlarged pituitary, an intrasellar mass with ring-like enhancement and diffuse and enhanced thickening of the pituitary stalk with homogeneous enhancement. **B.** MRI 4 weeks after prednisone therapy. The lesions in pituitary and pituitary stalk were significantly reduced. **C.** MRI after relapse. The lesion reappeared after the dose of prednisone was reduced. Pituitary and pituitary stalk were enlarged with homogeneously enhanced signals. **D.** After the 16-week treatment regimen with HDMPT plus azathioprine, the lesions in pituitary and pituitary stalk almost disappeared, and the pituitary was reduced in size.

9, 2006, and headache and menstrual irregularity were again observed. Urine osmolality was 522 mosm/L and blood osmolality was 293 mosm/L. Pituitary hormone levels are shown in Table 1. Pituitary functions were within normal ranges at onset and relapse. MRI showed enlarged pituitary and thickening of pituitary stalk with heterogeneous enhancement, thereby relapse was considered (Fig. 3). Prednisone tablets (30 mg/d, reduced by 5 mg after 4 weeks and by 5 mg weekly thereafter), azathioprine (100 mg/d), and desmopressin acetate (0.1 mg/d) were administered. All drugs were withdrawn after 16 weeks. The patient was re-checked in October 2008 and April 2010; her anterior pituitary function was normal, and pituitary lesions were significantly reduced in size (Fig. 3) and stable. In addition, her IGF-1 levels were 178 ng/mL and 159 ng/mL in October 2008 and April 2010, respectively. At that follow-up, the patient was not taking medication, and her menstruation was normal; the recurrence-free follow-up period was 18 months. MRI showed no further relapse of disease after treatment at 36 months.

Discussion

We present clinical and treatment data of three patients with recurrent AH, including a post-menopausal woman with concomitant autoimmune thyroiditis (case 2) and two non-pregnant women (cases 1 and 3). Their clinical manifestations were different: case 1 had headache and diplopia; cases 2 and 3 had diabetes insipidus, and case 2 also had obvious manifestations of anterior pituitary dysfunction. All cases have the typical MRI manifestations of autoimmune hypophysitis [5]. All three patients were treated with glucocorticoids combined with azathioprine, relieving symptoms as early as one day after initiating therapy. Repeat MRI during follow-up revealed significant reduction of lesions and at last follow-up for each patient, 48, 10 and 36 months and the recurrence-free follow-up period was 36, 6, and 18 months for cases 1, 2 and 3, respectively. MRI showed no further recurrence of disease.

AH is an autoimmune endocrine disease involving lymphocytic infiltration and inflammation of the pituitary. Recent reviews indicate that AH occurs primarily in young women during pregnancy or postpartum [2, 4], but it also occurs in postmenopausal women [1], non-pregnant women [9], and men [10, 11, 12]. In the present study, all three cases were female, one of which was postmenopausal. AH has also been

associated with other autoimmune diseases such as Hashimoto's thyroiditis, Addison's disease, Crohn's disease, Wegener's granulomatosis and dacryadenitis [2, 11, 13]. Concomitant autoimmune thyroiditis was observed in case 2.

Since AH occurs only rarely, research is lacking and knowledge of its clinical features or long-term prognosis is insufficient; pathophysiology is largely unknown [3]. AH does not have specific clinical manifestations and, as cases are reviewed, clinical features have become increasingly complex; onset is typically hidden, and clinical manifestations depend on the extent and severity of inflammation [1-3, 7]. It may manifest as symptoms of anterior pituitary dysfunction, including cold intolerance, fatigue, and drowsiness, and may also manifest as diabetes insipidus. If the pituitary enlarges and grows towards the suprasellar region and compresses the optic chiasm, symptoms such as headache, abnormal visual acuity and abnormal visual field may result [4]. The cavernous sinus is sometimes involved, and signs and symptoms of cranial nerve palsy can be present [13]. As an autoimmune disease, the natural course of AH varies. It can relieve spontaneously and recur after effective treatment. Impaired pituitary function can return to normal or decline progressively [14].

Diagnosis of autoimmune hypophysitis is challenging as it is difficult to differentiate from pituitary adenoma, other sellar masses (e.g., germ cell tumors), and other inflammatory diseases (e.g., granuloma) [5]. However, germ cell tumors are usually unresponsive to hormone therapy, and granulomatous and infiltrative diseases, such as sarcoidosis and histiocytosis, generally present more insidiously; therefore, they can be excluded by examining the patient history [5]. A presumptive diagnosis can be made based upon clinical and laboratory findings and MRI; however, a definitive diagnosis requires pathological analysis. In the present study, the first case was diagnosed based upon pathological findings; lymphocyte infiltration was observed in the pituitary using tissue obtained during resection. Diagnoses of cases 2 and 3 were based upon response to treatment. As previously reported, diagnosis of lymphocytic hypophysitis can be confirmed upon spontaneous remission or response to corticosteroid treatment in patients with suspected autoimmune hypophysitis [2, 3, 5, 7]. In the absence of a serum marker, response to treatment as a diagnostic marker avoids more invasive diagnostic procedures (i.e., biopsy with pathologi-

cal examination). The initial diagnosis of AH can be given based on clinical manifestations and imaging findings, and the fact that corticosteroid treatment is effective can serve as the main basis for an AH diagnosis [5, 7].

Only several reports of treatment of recurrent AH are found in the literature [4, 13, 15, 16, 17]. Among these cases, four were young women (aged 26 to 38 years) [4, 13, 15, 17] and one case was a post-menopausal woman (age 53 years) [16]. Recurrence was diagnosed between 12 and 72 months after surgery. Sinha *et al.* [4] report relapse occurring in a 26-year-old woman during her second pregnancy with spontaneous recovery after delivery. Remission was achieved in the remaining four patients after the second surgery [16], moderate-dose corticosteroid treatment [13, 17] and HDMPT [15]. The time of relapse, however, cannot be generalized with limited reports, and no standard treatment protocol is recommended for recurrent AH. Among our patients, relapse occurred twice in case 1, first at four months postoperatively and again 14 months after HDMPT. In case 2, relapse occurred 16 months after discontinuing moderate-dose prednisone treatment, and relapse occurred in case 3 during dose reduction after effective HDMPT. Close follow-up is essential in recurrent AH, but time or likelihood of relapse cannot be predicted.

Corticosteroid treatment has been an inconsistently effective non-surgical treatment for AH [13], and relapse is possible even in patients receiving surgical treatment [15]. Some investigators advise avoiding surgery because the natural course of AH may be self-limiting [3, 11]. Kristof *et al.* introduced HDMPT as treatment for lymphocytic hypophysitis, advocating it as a high-dose, short-term way to administer methylprednisone while minimizing unwanted side effects of chronic corticosteroid therapy [7]. Therapeutic results in nine patients with AH included improved clinical, endocrine, and MRI findings. Another case of AH with gross visual disturbance was successfully treated with HDMPT using a protocol similar to Kristof *et al.*, dramatically reducing visual symptoms on the day after treatment began [18].

Azathioprine-6 also is used for treating AH with inconsistent results. For example, Lecube *et al.* reported the first successful treatment of AH with azathioprine after corticosteroids failed, and no clinical or radiological evidence of AH remained 18 months after treatment [12]. In addition, Papanastasiou *et al.* reported

the successful treatment of primary hypophysitis with azathioprine in two female patients both of which suffered serious side effects from the initial glucocorticoid treatment [19]. However, after an initial transient improvement with methylprednisolone pulse therapy, a 3-month treatment with azathioprine in a male patient with lymphocytic hypophysitis did not restore pituitary function or reduce the pituitary mass [20]. The extensive fibrosis within the pituitary gland as well as the short period of azathioprine treatment may account for the lack of response in the latter case. Although no further relapse has been observed upon azathioprine treatment in the patients reported in this study, we cannot conclude that it prevents relapse. Spontaneous remission of pituitary swelling can occur. Therefore, follow-up is crucial in these patients to rapidly detect relapse and expedite treatment.

Azathioprine, an anti-metabolic agent with immunosuppressive activity, is widely used in immunosuppressive therapy for organ transplant patients and in autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus and autoimmune hemolytic anemia. Because positive results have been obtained using azathioprine for other autoimmune diseases and considering the above reports of HDMPT and azathioprine, we adopted a treatment protocol with combined glucocorticoids and azathioprine for treatment of recurrent AH, achieving favorable outcomes. Patients' symptoms were relieved after initial HDMPT, and MRI showed significant reduction in lesion size during follow-up. Normal pituitary function resumed in two patients, and MRI showed no further recurrence of disease in any patient at last follow-up (Table 2). In addition, adverse events associated with azathioprine use, including bone marrow suppression, neutropenia, aplastic anemia, acute pancreatitis, toxic hepatitis, hair loss, mouth ulcers, peritoneal and retinal hemorrhage, pulmonary edema, loss of appetite, nausea, and liver damage, were not observed, which is similar to Lecube *et al.* [12] and Papanastasiou *et al.* [19].

In conclusion, our results suggest that glucocorticoids combined with azathioprine constitute effective treatment for recurrent AH. We emphasize the importance of long-term follow-up of AH, including endocrine and radiologic studies. Our data may provide useful information for diagnosis and treatment of recurrent AH. Further investigation with a larger cohort and long-term follow-up is needed to determine whether our treatment method may prevent AH recurrence.

Table 2 Summary of three patients with recurrent AH

	Case 1	Case 2	Case 3
Age	22	70	32
Course of disease (month)	6	12	8
Clinical manifestations	Headache and diplopia	Polydipsia and polyuria accompanied by fatigue and drowsiness	Polydipsia and polyuria accompanied by menstrual disorder
MRI manifestations	Abnormal signals in suprasellar cistern, lesions were enhanced significantly, pushing the optic chiasm upward and wrapping the bilateral internal carotid arteries, the infundibular stem was not shown clearly	Abnormal signals in the infundibular stem and hypothalamus with homogenous enhancement, high signals in the posterior pituitary disappeared	Pituitary was increased in size, infundibular stem was thickened significantly and shifted towards the left side, high signals of the posterior pituitary disappeared.
Protocol of the first treatment	Surgery	Moderate-dose prednisone	HDMPT
Time of relapse	First relapse occurred 4 months after surgery; second relapse occurred 14 months after drug withdrawal	Sixteen months after withdrawal of glucocorticoids	During dose reduction process of glucocorticoids
Treatment after relapse	HDMPT+ azathioprine	HDMPT+ azathioprine	Low-dose steroids+ azathioprine
Duration of treatment after relapse	16 weeks	16 weeks	16 weeks
Treatment during follow-up	None	L-thyroxine 100ug/day Desmopressin acetate 0.1mg/day Prednisone 7.5mg/day	None
Duration of follow-up	48 months	10 months	36 months
Outcome	Normal pituitary function	Anterior pituitary dysfunction; diabetes insipidus	Normal pituitary function

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