Case Report

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Clinical aspects of autoimmune hypothalamitis, a variant of autoimmune hypophysitis: Experience from one center

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Abstract

Objective: Autoimmune hypothalamitis (AHT) is a rare inflammatory disorder that involves the hypothalamus. It remains unclear whether autoimmune hypophysitis (AH) and AHT represent different diseases or different aspects of the same disease. Thus, further investigation of AHT is required.

Methods: A retrospective review of medical and pathological records of AHT patients from the Chinese PLA General Hospital were examined from January 1, 2005 to May 1, 2017. Clinical data, treatments, and outcomes were investigated.

Results: Five female patients were identified (median age, 42.6 years). Symptoms included central diabetes insipidus, hypopituitarism, hyperprolactinemia, headache, and hypothalamic syndrome. The following hormonal deficits were noted: follicle-stimulating hormone, luteinizing hormone, adrenocorticotropic hormone, thyroid stimulating hormone, and growth hormone. One patient underwent high-dose methylprednisolone pulse treatment (HDMPT) and azathioprine plus intensity modulated radiation therapy (IMRT), and two patients underwent HDMPT and two rounds of replacement therapy. During follow-up, one patient died because of non-compliance with therapy and the others were in remission or they recovered.

Conclusions: AHT had similar MRI results, pathology, and treatment compared with AH. Thus, it may be a subtype of AH, and AHT patients may also show hypothalamic syndrome.

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Introduction

Hypophysitis is rare, with an annual incidence of about one in nine million.[1] Autoimmune hypophysitis (AH), which is a chronic inflammation that involves the pituitary gland, is the most common histologic variant, with over 390 cases reported.[2] Anatomically, AH can be classified as adenohypophysitis, neurohypophysitis, or infundibulohypophysitis if inflammation is present in the anterior gland, posterior gland, or pituitary stalk, respectively. Involvement of the entire gland is also possible, which is defined as panhypophysitis. If inflammation extends to the hypothalamus, it can be defined as hypothalamitis.[3] It remains unclear whether the AH and autoimmune hypothalamitis (AHT) represent different diseases or different aspects of the same disease. However, based on existing studies, they share the same pathological features, i.e. focal or diffuse infiltration of predominantly lymphocytes that accompany plasma cells, eosinophils, and fibroblasts.[3,4] Moreover, both refer to autoimmune inflammation of the sellar area and are part of a continuous anatomical structure.

AHT typically appears as a predominantly suprasellar mass, which involves the hypothalamus. Patients with AHT may complain of headache and visual disturbance and have diabetes insipidus and hypopituitarism symptoms. These symptoms can be relieved with high-dose methylprednisolone pulse treatment (HDMPT). To the best of our knowledge, only a few cases of AHT have been reported in the literature.[3,5–7] Herein, we report a case series of patients with AHT at a single institution.

Materials and methods

Patients' data were retrieved from electronic medical record database at the Chinese PLA General Hospital. The study was approved by the PLA Institutional Review Board and informed consent was waived because of the retrospective nature of the study. The recruitment period was January 1, 2005 to May 1, 2017.

AHT was either pathologically or clinically diagnosed. Pathological diagnosis of AHT was considered to be positive if lymphocyte-dominated infiltration with plasma cells, neutrophils, and fibrocytes was observed. MRI revealed an isolated hypothalamic mass, which showed mild hypointensity/isointensity in T1-weighted imaging and mild hyperintensity in T2-weighted imaging, the mass was homogeneous and significantly enhanced by contrast, and the posterior pituitary bright spot (PPBS) was absent on T1-weighted images with an intact pituitary and fossa floor, which suggests the presence of AHT. A positive response to HDMPT or a self-healing nature confirmed the diagnosis.

The medical history, laboratory test results, and MRI results from patients were collected and analyzed. An empty sella (ES) suggested a flattened pituitary gland with or without hypopituitarism.

Results

Case 1

In April 2016, a 41-year-old G2, P2 woman who had polyuria for 6 months and amenorrhea for 4 months was admitted to our clinic. Basal endocrine assessments (Table 1) and stimulation tests confirmed the presence of hyperprolactinemia and hypopituitarism, which is characterized by central diabetes insipidus (CDI), central hypogonadism, central hypothyroidism, and decreased growth hormone (GH) and insulin-like growth factor (IGF)-1 levels. A sellar MRI (Figure 1A,a) revealed a mass in the hypothalamus and loss of PPBS, while the visual field was normal. Additionally, the patient had no remarkable medical history, and therefore an etiological diagnosis of AHT was suspected. Replacement therapy with cortisone acetate (10 mg/day) and desmopressin acetate (DDAVP, 150 μg/day) was prescribed. The patient was administrated HDMPT in April (500 mg × 5 days), May (500 mg × 3 days), and July (500 mg on day 1, 250 mg on days 2–4, 500 mg on day 6). Azathioprine (AZP, 100 mg/day) was also administered starting on May 30, 2016.

After treatment, symptoms were relieved and the mass decreased in size (Figure 1B,b). Serum total thyroxine (TT4;

Table 1. Serum level of basal hormones at the onset.

	Case 1	Case 2	Case 3	Case 4	Case 5
Serum osmolality (mosm/L)	312	286	306	300	313
Urinary osmolality (mosm/L)	79	176	143	101	114
TT3 (nmol/L) (1.01–2.95)	2.61	0.76	1.7	3.02	–
TT4 (nmol/L) (55.3–160.9)	54.9	34.8	80.2	64.7	–
FT3 (pmol/L) (2.76–6.3)	4.76	1.71	4.22	4.32	–
FT4 (pmol/L) (10.4–24.3)	7.86	7.14	11.3	7.96	9.86
TSH (mU/L) (0.35–5.5)	2.77	6.14	0.2	1.01	–
TGAb (IU/mL) (<60)	16.1	343.19	189.1	–	–
TPOAb (IU/mL) (<60)	41.5	>1300	<28	–	–
LH (IU/L) (M 1.5–9.3/F 0.5–76.3)	0.21	<0.07	<0.07	<0.07	0.57
FSH (IU/L) (M 1.4–18.1/F 1.5–33.4)	1.62	0.48	1.18	0.22	3.43
T (nmol/L) (M 8.4–28.7/F 0.5–2.6)	0.55	–	<0.35	<0.35	1.28
Estradiol (pmol/L) (M≤353.1/ F 48.2–1532)	85.74	36.7	<43.31	<36.7	45.53
PRL (μg/L) (M 2.1–17.7/ F 2.8–29.2)	45.77	45.80	95.14	127.3	17.5
ACTH (pmol/L)					
8:00 (<10.12 pmol/L)	7.1	<2.2	<1.1	6.03	–
0:00	3.91	<2.2	<1.1	5.46	–
16:00	5.24	<2.2	<1.1	5.04	–
Cortisol (F; nmol/L)					
8:00 (198.7–797.5 nmol/L)	271.95	<25.7	<25.7	164.2	–
0:00 (0–165.7 nmol/L)	<25.7	<25.7	161.77	123.1	–
16:00	106.04	<25.7	297.78	52.9	–
UFC (nmol/24 hours) (98–500)	84.9	<25.7	–	277.3	–
GH (μg/L) (0.06–5.0)	0.24	0.17	<0.05	0.83	–
IGF-1 (ng/dL)	130 (101–267)	(69–200)	130 (101–267)	60.2 (109–284)	(127–424)

Note: TT3, total triiodothyronine; TT4, total tetraiodothyronine; FT3, free triiodothyronine; FT4, free tetraiodothyronine; TSH, thyroid stimulating hormone; TGAb, thyroglobulin autoantibody; TPOAb, thyroid peroxidase autoantibody; LH, luteinizing hormone; FSH, follicle-stimulating hormone; T, testosterone; PRL, prolactin; ACTH, adrenocorticotropic hormone; F, cortisol; UFC, urine free cortisol; GH, growth hormone; IGF-1, insulin-like growth factor-1; -, not available; M, male, F, female.

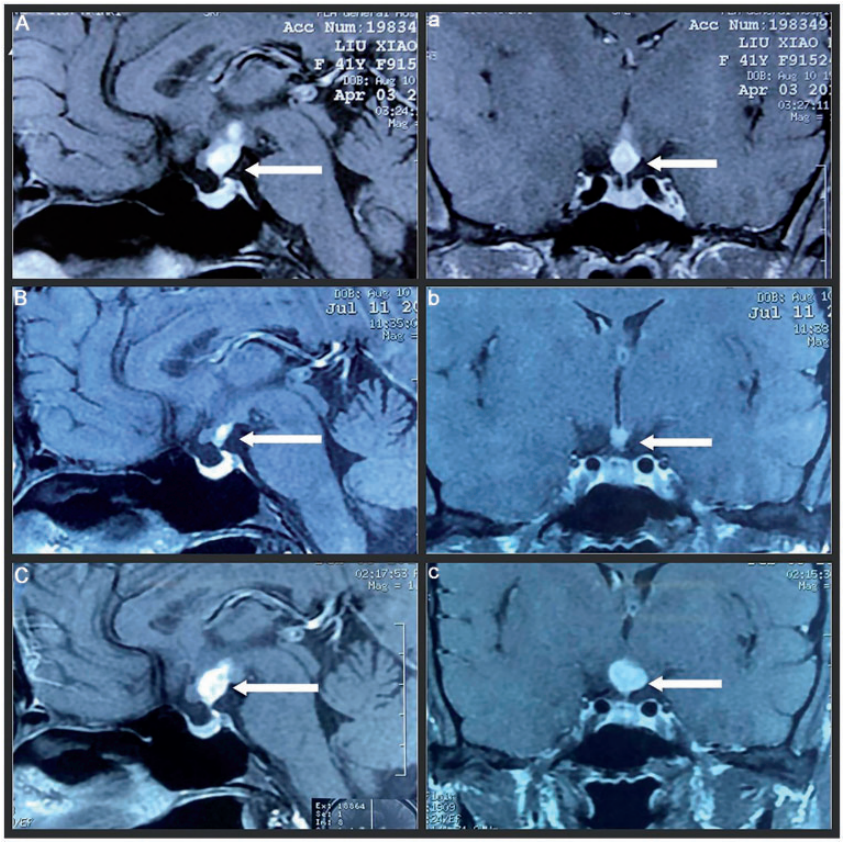

Figure 1. (A,a) A flaky lesion was observed in April 2016. (B,b) The lesion decreased after three rounds of HDMPT therapy in July 2016. (C,c) After cortisol and AZP were gradually withdrawn, the lesion significantly enlarged, and the sella turcica and pineal body are intact.

88.4 nmol/L) and free thyroxine (FT4; 13.61 pmol/L) levels increased to the normal range. However, amenorrhea persisted. Artificial menstrual cycle treatment was rejected by the patient and consequently, prednisone therapy was suspended in August 2016, while AZP was suspended in October 2016.

During the follow-up visit in February 2017, MRI results (Figure 1C,c) indicated the presence of a larger mass. After performing a craniotomy, the lesion appeared to be off-white in color and have a uniform shape. Histological examination revealed diffuse infiltration of inflammatory cells including lymphocytes and histological cells (Figure 2a). Additionally, immunohistochemical staining confirmed the presence of CD20-positive B lymphocytes (Figure 2b) and CD3-positive T lymphocytes (Figure 2c), which were all consistent with a diagnosis of AHT. Thus, considering the patient's poor response to the drug, intensity modulated radiation therapy (IMRT) was scheduled (25 rounds of 45 Gy), which continued until May 4, 2017.

Case 2

A 70-year-old female who had polyuria for 1 year was admitted for the evaluation of

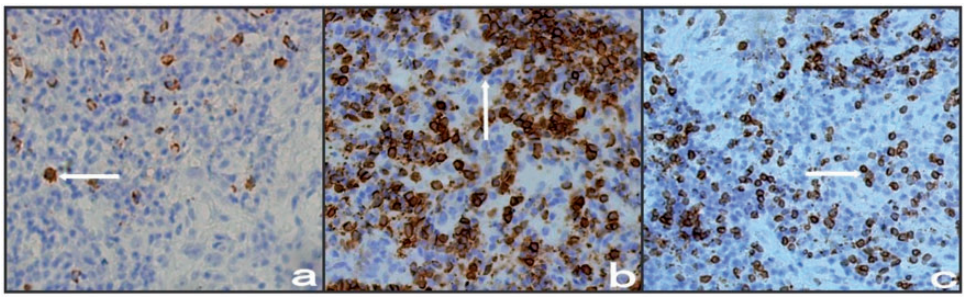

Figure 2. (a) IgG4(+) cells (←) were scattered in the lesion. (b) CD20(+) cells (↑) were largely distributed in the field. (c) CD3(+) cells (→) were distributed in the lesion.

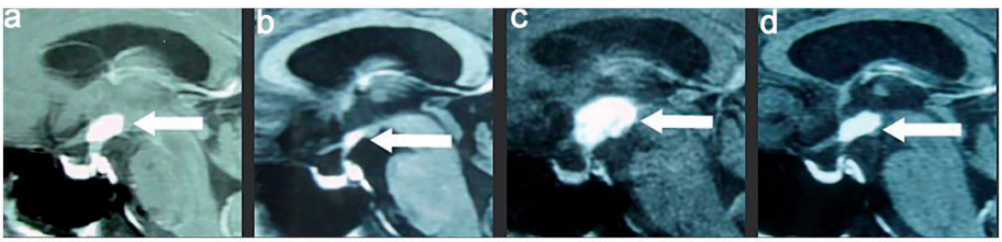

Figure 3. MRI imaging pre- and post-treatment. (a) Initial image taken before treatments. MRI revealed a mass in the hypothalamus. (b) Lesion size decreased post-HDMPT treatment. (c) Recurrence of the mass accrued because of the patient's spontaneous drug discontinuance. (d) Lesion size decreased again following HDMPT and AZP treatment.

polydipsia on March 20, 2006. The patient complained of fatigue, feeling cold, and weight loss, and she had a medical history of hyperthyroidism and osteoarthritis. The physical examination showed mild goiter and no nodules were palpable in the thyroid, while her visual field was normal. Laboratory test results showed an erythrocyte sedimentation rate (ESR) of 32 mm/hour and high sensitivity C reactive protein (hsCRP) of 1.24 mg/dL, and endocrine assessments displayed panhypopituitarism (Table 1). MRI indicated a hypothalamus mass that was enhanced homogeneously and the PPBS was absent (Figure 3a). Therefore, AHT was suspected and glucocorticoids were administrated. The proposed therapy included prednisone (20 mg three times per day × 2 weeks), which was tapered by 5 mg every 2 weeks until withdrawal. DDAVP (100 μg/day) and levothyroxine (100 μg/day) were prescribed once.

Symptoms mentioned above were significantly relieved and hormonal levels all returned to within the normal range. Six months post-treatment, an MRI (Figure 3b) scan showed the mass shrinking into a dotted nidus. The patient took the medicine irregularly and skipped check-ups without the doctor's permission. One year after the initial presentation, the patient's symptoms, including polydipsia, polyuria, and fatigue, worsened, and she was re-admitted to the hospital. MRI revealed that the mass had grown to 20 × 13 mm (Figure 3c). HDMPT in combination with AZP therapy was then administered. The proposal was methylprednisolone at a dose of 200 mg/day for 3 days

intravenously (iv) followed by 100 mg/day for 3 days iv, which was subsequently changed to prednisone at a dose of 15 mg/day in combination with AZP at a dose of 100 mg/day. Three months later, an MRI scan showed lesion shrinkage (Figure 3d). During the next 3 years of follow-up, the patient showed poor compliance with the replacement therapy. In 2008, the patient was diagnosed with diabetes mellitus and subsequently died of hypoglycemia in 2010.

Case 3

A 43-year-old female with no medical history who had amenorrhea for 16 months, polydipsia and polyuria for 14 months was admitted to our clinic on June 20, 2014. She also had headache, fever, lethargy, decreased libido, and weight gain. Endocrinological evaluations indicated CDI, hypogonadotropic hypogonadism, and mild adrenal insufficiency. MRI showed a loss of the PPBS and a hypothalamus lesion with homogenous enhancement (Figure 4A,a). The patient showed no signs of infectious and/or rheumatological diseases. A provisional diagnosis of AHT was made, and replacement therapy was prescribed in the form of prednisolone (5 mg/day), levothyroxine (62.5 μg/day), and DDAVP (200 μg/day).

The patient's symptoms resolved except for amenorrhea. Follow-up MRIs were performed 18 months (Figure 4B,b) and 3 years post-treatment, and the results indicated that the hypothalamic lesion was invisible and the anterior pituitary lobe was progressively flattening (Figure 4C,c). The patient continued to take replacement therapy.

Case 4

A 39-year-old woman was admitted to our department in September 2008, and she had complained for 3 months of polydipsia, polyuria, and amenorrhea followed by debilitation, anorexia, and hair loss. The patient had a history of rheumatoid arthritis. After physical examination, she had triggered lactation. Her pituitary hormonal profile is summarized in Table 1. MRI imaging (Figure 5A-a) showed a nodule-like lesion in the hypothalamus and the PPBS had disappeared. There was no evidence of tumors, Langerhans cell histiocytosis (LCH), or sarcoidosis. She was diagnosed with AHT, which was caused by panhypopituitarism. HDMPT (800 mg × 3 days) was initiated and several days later, symptoms of polydipsia and polyuria improved, while repeated MRIs demonstrated that the lesion size had decreased. Levothyroxine plus DDAVP and the prednisolone tapering scheme were started. The patient still had no menstruation. Nine months later, the replacement dose was stable and MRI results (Figure 5B-b) revealed a further reduction in the lesion size. Eighteen months later, a follow-up MRI of the sellar region (Figure 5C-c) showed that the lesion vanished. There was no improvement in endocrine deficiency.

Case 5

A 20-year-old female with no medical history complained of amenorrhea for 4 months and polydipsia for 3 months on September 27, 2010. She also complained of hair loss, headache, and pyrexia with a maximum body temperature of 38.9°C. Laboratory tests showed hypopituitarism with characteristics of CDI, central hypogonadism, and central hypothyroidism. MRI (Figure 6A,a) demonstrated a hypothalamic lesion, and the PPBS was absent. AHT was highly suspected. Replacement therapy consisting of levothyroxine and DDAVP (150 μg/day) was initiated immediately. Six months later, the patient started menstruation and her cycle became regular again, while MRI revealed mild mass enlargement (Figure 6 B,b). During the 5-year follow-up,

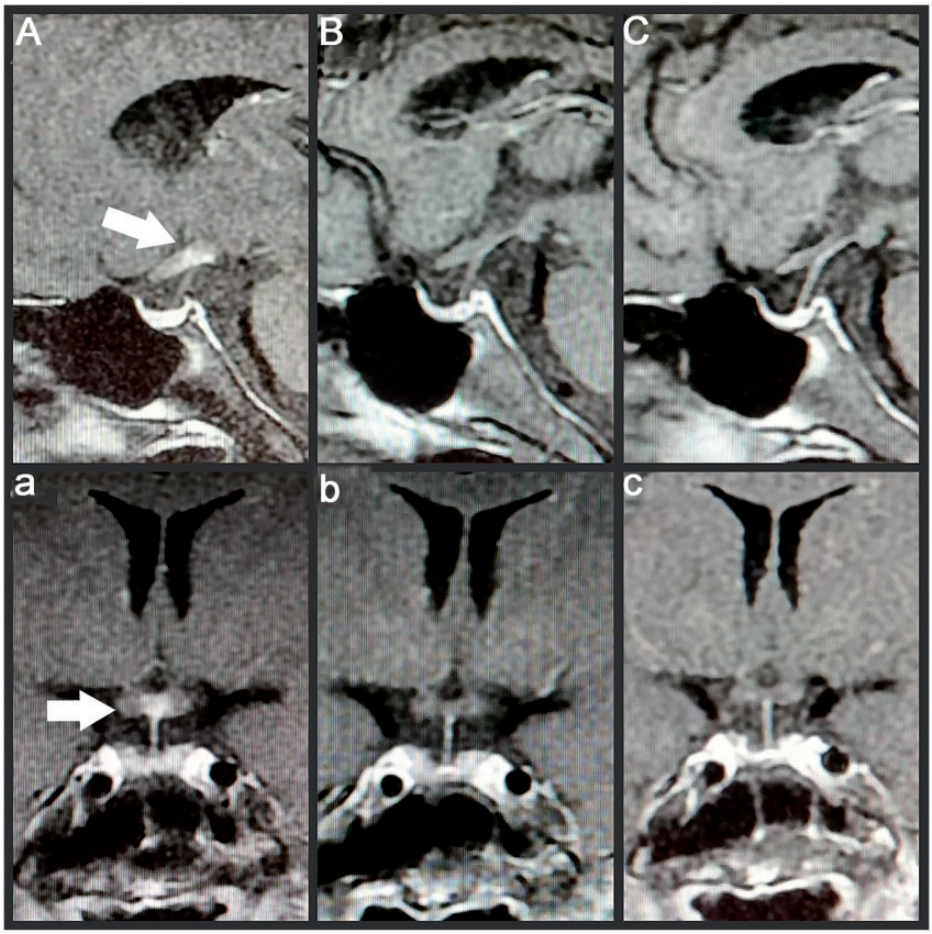

Figure 4. MRI imaging pre- and post-treatment. (A,a) A hypothalamic mass was detected before treatment. The pituitary was slightly flattened and the PPBS was gone. (B,b) An MRI re-scan showed regression of the mass post-therapy. (C,c) No signs of relapse were observed.

the patient took medications irregularly and conceived spontaneously in 2014. She had a full-term caesarean section and gave birth to twins. The most recent MRI scan showed that the lesion was nearly invisible (Figure 6 C,c).

Discussion

Masses identified in the hypothalamus usually appear to be tumors, LCH, or sarcoidosis, while AHT seems to be rarely reported. Biopsy specimens showed inflammatory cell infiltrates, which were mainly composed of lymphocytes, plasma cells, and histiocytes.[5–7] Remarkable improvements in MRI and patients' symptoms were observed after administration of steroid and immunosuppressive therapy with AZP. The hypothalamus is a direct upward extension of the neurohypophysis and infundibulum, and it is closely associated with the pituitary gland in both histology and function. Moreover, AHT is almost identical to hypophysitis in pathology, clinical manifestations, diagnosis, therapeutic scheme, and prognosis (Table 2).[3,5–7]

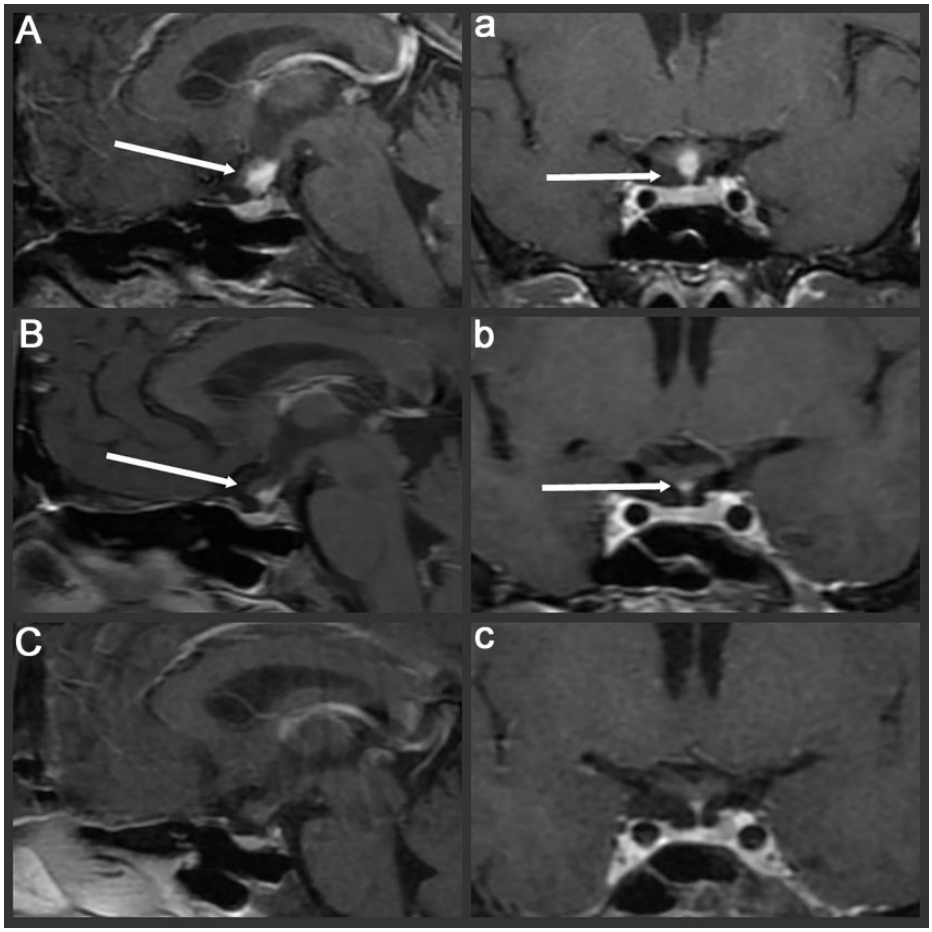

Figure 5. (A,a) A tuberous abnormal signal (10 × 6×7 mm) (→) was detected in the hypothalamic zone with distinct edges that could be enhanced markedly and uniformly at the onset. (B,b) The abnormal high signal intensity area on the contrasted T1-weighted image was decreased after HDMPT treatment. (C,c) At the follow-up after 2 years, no lesion was detected.

Thus, we consider that hypothalamitis is a subtype of hypophysitis.

The series of five patients registered at our center over the last 12 years provide novel insight into the clinical characteristics and therapeutic responses of AHT (Table 2). All five patients were female, two of whom had comorbidity with autoimmune diseases (AID) such as rheumatoid arthritis and Hashimoto thyroiditis. This was consistent with other studies suggesting that hypophysitis[8] predominantly occurs in women with AIDs. The median age at presentation in our series was 42.6 years (20–70 years), which was older compared with patients with hypophysitis, whose mean age was 30–40 years.[9] None of them had any association with late pregnancy or postpartum, which suggested that the association between AHT and pregnancy was far less common compared with hypophysitis. The symptom duration ranged from 3 to 12 months, with an average duration of 8.6 months.

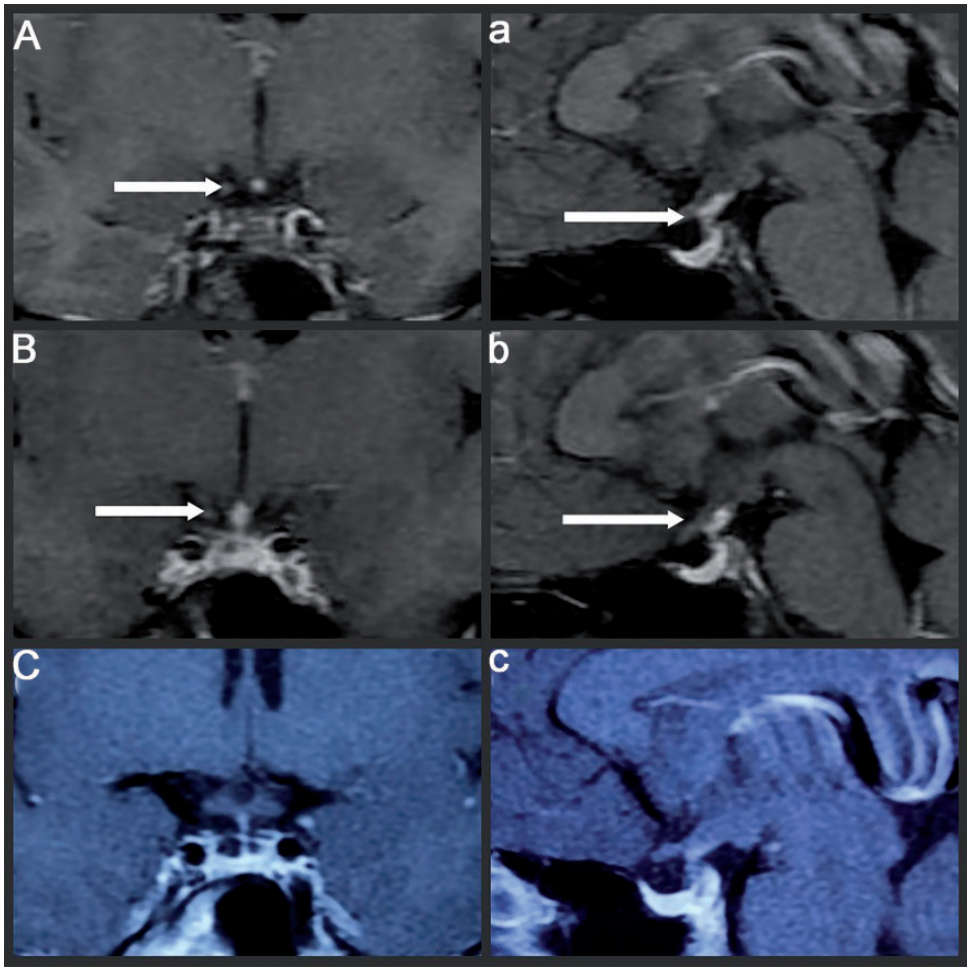

Figure 6. (A,a) September 2010: A homogeneously enhanced mass (5 mm, white arrow) in the hypothalamus. (B,b) March 2011: The mass appeared slightly larger. (C,c) May 2017: The lesion become spontaneously invisible.

In our series, CDI was the most common endocrine symptom (5/5 patients; 100%), which was largely consistent with results of hypophysitis reported by Wang et al.[10] and Park et al.[11] Another common manifestation was hypopituitarism (100%) and the following hormonal deficits were observed: follicle-stimulating hormone-luteinizing hormone (FSH-LH; 5/5 patients, 100%), adrenocorticotropic hormone (ACTH; 3/5 patients, 60%), thyroid-stimulating hormone (TSH; 2/5 patients, 40%), and GH (1/5 patients, 20%). This pattern is no longer in accordance with the typical pattern of "ACTH>TSH>LH/FSH>IGF-1" which, based on previous studies, has diagnostic value.[12] While two patients, each from single-case reports, presented with panhypopituitarism at the onset of illness,[4,6] we suggest that the typical pattern of hormone deficiency may not be present in all the subtypes and populations. This speculation should be verified in larger cohorts.

Table 2. An overview of the cases from our institution and the literature.

Case	Sex	Age (y)	Symptom	Hypopituitarism	CDI	MRI	Rreatment	Replacement	Outcome
1	F	42	Polydipsia, amenorrhea	Y	Y	Suprasellar mass and uniform enhanced, loss of PPBS	HDMPT IMRT	Y	Relapse
2[5]	F	70	Polyuria, fatigue	Y	Y	Hypothalamus mass enhanced homogeneously, loss of PPBS	Mild dose of prednisone HDMPT combination with azathioprine therapy	Y	Relapse died
3	F	43	Amenorrhea, polydipsia and polyuria	Y	Y	Hypothalamus mass enhanced homogeneously, loss of PPBS	N	Y	Remission spontaneously without recovery of pituitary function
4	F	39	Polydipsia, polyuria and amenorrhea	Y	Y	Nodule-like lesion in hypothalamus, loss of PPBS	HDMPT	Y	Remission without recovery of pituitary function
5	F	20	Fever, headache, amenorrhea, polydipsia	Y	Y	Hypothalamus mass enhanced homogeneously, loss of PPBS	N	Y	Remission spontaneously with recovery of pituitary function
Zhang S[6]	M	20	Polyphagia, polyuria, polydipsia, deterioration of memory, and personality change	Y	Y	Hypothalamic mass, loss of PPBS	Mild dose of prednisone combination with azathioprine therapy	Y	Remission without recovery of pituitary function
Bertulli L[7]	F	67		Y	Y	A lesion involving the hypothalamus, the optic chiasm, with dyshomogeneous T1 signal and intense contrast enhancement, loss of PPBS	HDMPT combination with azathioprine therapy	Y	No relapse or worsening of the endocrinological or behavioral symptoms
Bianchi A[3]	F	48	Polyuria, polydipsia, Asthenia, nausea, vomiting	Y	Y	Suprasellar retrochiasmatic lesion, iso-intense in T1-weighted images, hyperintense in T2-weighted images, with homogeneous contrast enhancement, loss of PPBS	Steroid therapy combination with azathioprine		Complete resolution of the suprasellar lesion without recovery of pituitary function

CDI, central diabetes insipidus; IMRT, intensity modulated radiotherapy; HDMPT, high dose methylprednisolone pulse treatment; PPBS, posterior pituitary bright spot; y, years; Y, yes; N, no; M, male; F, female.

The incidence of hyperprolactinemia (80%) in AHT was higher compared with hypophysitis.[10,11] The predominant effect of the hypothalamus on PRL secretion is tonic suppression, which is meditated by regulatory hormones that are synthesized by tuberohyphyseal neurons. Inflammatory infiltration directly causes neuronal dysfunction in the hypothalamic area and reduces inhibitory agents, resulting in hyperprolactinemia. Mass effects such as headaches and stroke were present in 40% of the patients in our series. Neuro-ophthalmic examinations all appeared to be normal in our series. There is a discrepancy between AHT and hypophysitis: headache is the most frequent non-endocrinal abnormality that is found in hypophysitis.[13] Based on existing studies, the pituitary that is infiltrated by inflammatory cells initially enlarges, developing into a sellar mass that extends upward and crushes the optic chiasm and the dura mater, or laterally invades the cavernous sinus. This results in symptoms of severe and often generalized headache and visual disturbances. We assume that mass effects happen more often in a bony structure that is rigid, such as in the sellar region compared with the hypothalamus, but this conclusion should be verified in larger cohort studies.

The hypothalamus regulates many vital processes and functions in the human body, such as ingestion, material metabolism, maintenance of temperature and sleep rhythm, formation of emotions, and behavior. Once abnormalities, mostly tumors, occur in the area, hyperpyrexia, malfunctioning of the endocrine and metabolism system, and psychiatric and behavioral disorders, which are also known as hypothalamic syndrome, emerge. For example, in case 5, the patient once had fever and syncope, but there was no evidence of an infectious agent. Hyperpyrexia could not be relieved by antibiotics or antipyretics until anterior hypopituitarism was rectified.

Morphologically, at presentation, AHT is characterized by a hypothalamic mass with homogenous post-contrast enhancement while the pituitary gland and stalk are of normal size[5,6] or atrophic,[3,7] and loss of the PPBS is very common (5/5, 100%). As the disease progresses or subsides, the lesion enlarges or reduces accordingly, occasionally resulting in an ES.[3,7] Cases of AH with secondary ES have also been reported.[14,15] In our series, we suggested that secondary ES (2/5, 40%) could be the consequence of AHT.

Although the certainty of the AHT diagnosis can only be attained by histological examination, it is not practical to obtain tissue in every case because of the deep location of the lesion in the brain. Previous studies have concluded that surgery is rarely essential for the treatment, and a non-invasive diagnosis can often be made based on clinical manifestations, biochemical profiles, MRI features, and responses to experimental therapy. One patient in our case series was diagnosed pathologically while the other four patients were diagnosed clinically.

The etiology of a hypothalamic mass causing neuroendocrine disorders could be tumors (craniopharyngioma, germinoma, glioma, metastatic tumors, leukemia, or neuroblastoma), inflammatory diseases (meningitis, encephalitis, sarcoidosis, or LCH), or vascular (subarachnoid hemorrhage, aneurysm, or arteriovenous malformation) or structural brain defects. The underlying disease should be determined by analyzing the clinical presentation, radiological features, and hormonal deficiency pattern. Craniopharyngioma mostly affects young populations, and it presents as a cystic, lobular, and ring enhancement suprasellar mass on MRI, with eggshell calcification on CT. A germ cell tumor (GCT), which is often exclusively found in male adolescents, develops from the interbrain, mostly from the pineal and hypothalamic regions; this bifocal illness presents mostly

as GCT. Characteristically, α-fetoprotein and β-human chorionic gonadotropin levels in cerebrospinal fluid are elevated in patients with GCTs. Gliomas, which originate from the optic apparatus or hypothalamus, can be quite large, cystic-solid, or solid with multi-microcysts, and they usually cause visual disturbances first and lack hypothalamic or pituitary dysfunction. The lesions are often hypointense on T1-weighted and hyperintense on T2-weighted on MR images, which can be markedly enhanced. A solitary hypothalamic metastasis, which may cause panhypopituitarism, is an exceedingly rare complication of malignancy,[16] while metastatic pituitary tumors are also rare, most being breast and lung metastases.

Symptoms of diabetes insipidus and visual disturbances are the most common clinical presentations. Based on the literature, patients with metastasis are older compared with those with hypophysitis. LCH is seen in all age groups but is most common in children. It can manifest as an intracranial mass lesion that is usually in the hypothalamic pituitary area or the pineal gland.[17] If potential extracranial lesions, such as bony, cutaneous, pulmonary, and lymph nodes, are detected, a definite diagnosis can be established using histopathology. However, in the absence of extracranial lesions and of the CD1a-positive and s100-positive cells in cerebrospinal fluid (CSF), a biopsy of the hypothalamic mass should be considered.[18] Signs of an infectious process including fever, chills, and leukocytosis strongly indicate a central nerve system infection. MRI and CT scans are of high value for their diagnosis of vascular and structural deformities.

A good response to glucocorticoids combined with immunosuppressors can be a primary way to differentiate between AHT and lesions of other origins. Therefore, HDMPT is an optimal choice for patients who are highly suspected of having AHT. It saves time in the acute phase of the disease by significantly relieving symptoms, eliminating surgery, and confirming the tentative diagnosis. Immunosuppressants such as AZP, have been reported to relieve symptoms in patients who show recurrence and who are resistant to glucocorticoids.[19] However, histological diagnosis is not mandatory unless there are multiple relapses. In case 1 in our series, the disease recurred after months of effective control. At our center, the positive effects have been seen for patients treated with radiotherapy, which was consistent with previously reported studies.[8,20] Thus, we consider radiotherapy to be a viable treatment option for patients whose treatment has included failed surgical or medical management.

Because it is an autoimmune disease, AHT may relapse or regress, leading to a morphologically flattened and functionally impaired pituitary gland. Alternatively, AHT may be self-limited with chronic partial or complete hypopituitarism, or it may spontaneously disappear with recovery of pituitary function, which happens in only a few cases. Long-term follow-up is necessary for patients with AHT. At our center, patients are advised to have their endocrine evaluation yearly and a pituitary MRI every other year to regulate substitute doses.

Abbreviations

AH, autoimmune hypophysitis
AHT, autoimmune hypothalamitis
HDMPT, high-dose methylprednisolone pulse treatment
IMRT, intensity modulated radiation therapy
CDI, central diabetes insipidus
MRI, magnetic resonance imaging
ESR, erythrocyte sedimentation rate
hsCRP, high sensitivity C reactive protein.

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Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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