

# Autoimmune hypophysitis may eventually become empty sella

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## Abstract

Autoimmune hypophysitis (AH) is commonly believed to be a rare chronic inflammatory condition of the pituitary gland. In clinical practice, however, the disease is often seen indeed. It typically presents with hypopituitarism and pituitary mass found by MRI. We report here unusual presentations of two females with AH followed by empty sella syndrome. The two females, aged at 64 and 57-years-old, presented with anterior pituitary dysfunction, diplopia and diabetes insipidus. By MRI the two patients shared the common characteristics with diffuse homogeneous contrast enhancement of the gland and increased stalk thickness. After a long period treatment with glucocorticoids, empty sella was eventually detected by MRI.

## INTRODUCTION

Autoimmune hypophysitis (AH) is a rare chronic inflammatory condition which typically presents with hypopituitarism and a pituitary mass. The disease is found six times higher in females than males, typically presenting during pregnancy or postpartum (57%) (Howlett *et al.* 2010). Clinically, headache and visual disturbance are common. Hypopituitarism of anterior lobe shows the deficiency in adrenocorticotropin (ACTH), thyrotropin (TSH), gonadotrophins (GnRH) and coexistence of hyperprolactinemia occasionally, while posterior dysfunction reveals central diabetes insipidus. Diagnosis of AH is pathological, but the studies by MRI, are also very useful for clinical diagnosis. In 85–95% of autoimmune hypophysitis cases, by MRI it shows a symmetrically enlarged pituitary gland and administration of gadolinium homogeneously enhances the gland. The pitu-

itary displays a relative low signal on T1-weighted images and a relatively high signal on T2-weighted images (Molitch & Gillam 2007). The two cases we are presenting here are representative examples for the natural course of AH in which empty sella was the final outcome (Karaca *et al.* 2009).

## PATIENTS AND METHODS

### Case 1

A 64-years-old female presented with a history of nausea, vomiting and diplopia for three months. She was hospitalized and diagnosed as “hypopituitarism”, because basal pituitary function evaluation showed adrenocorticotropin, thyrotropin and gonadotropin insufficiency (Table 1). Her urine output, urine osmolality and serum osmolality were normal. At the same time, pituitary enlargement and homogeneous enhancement were revealed by MRI (Figures 1a,1b). We found

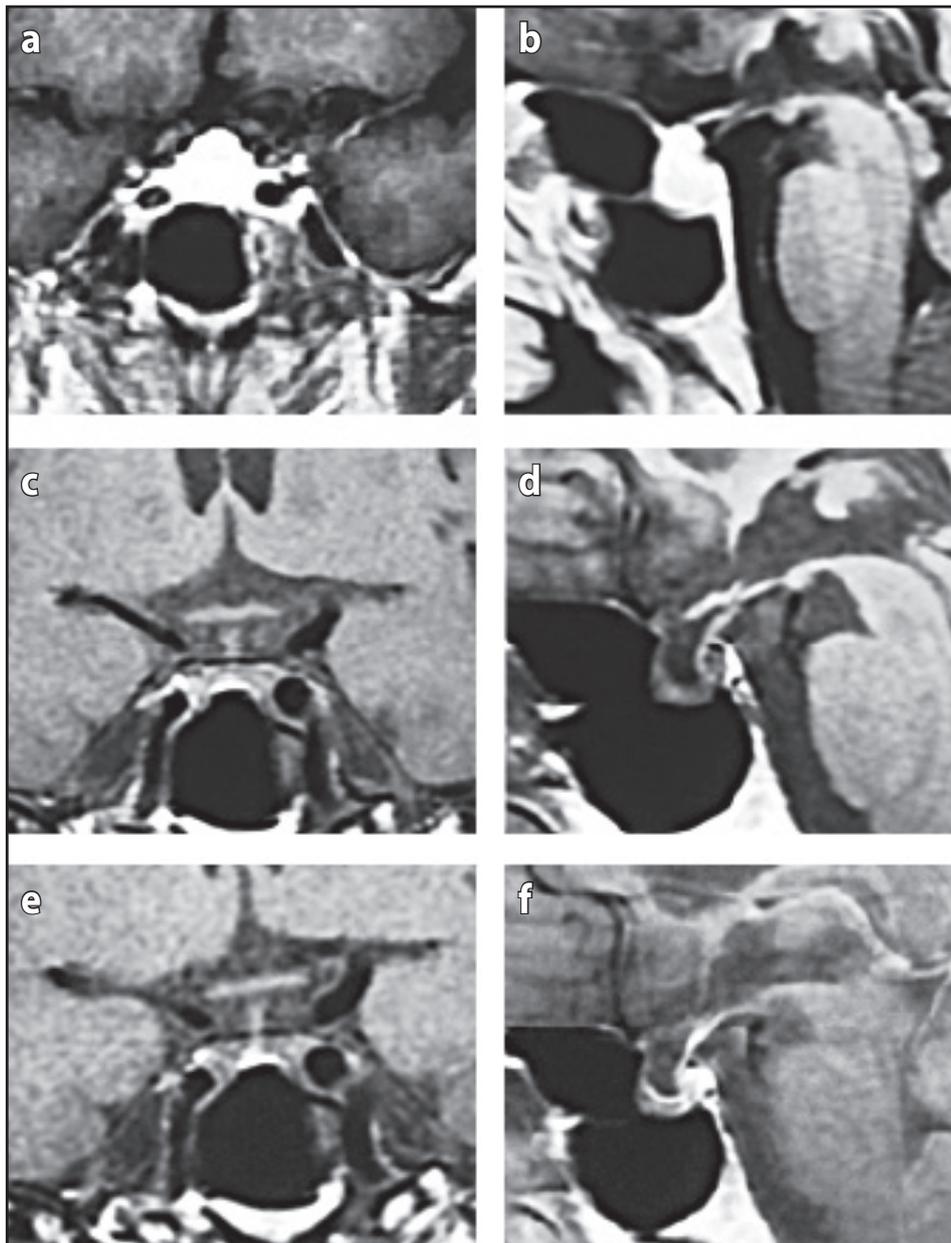
that there were no tumor cells but many white blood cells in the cerebrospinal fluid on lumbar puncture.

Methylprednisolone 120 mg was initiated intravenously per day for six days and the dose was then reduced to 40 mg per day. Ten days later, her nausea, vomiting disappeared completely. She continued the treatment of methylprednisolone 40 mg intravenously per day, and was treated with levothyroxine replacement therapy. The pituitary MRI revealed that an intrasellar herniation of the suprasellar cistern with empty sella turcica was described 30 days later (Figures 1c, 1d). Methylprednisolone treatment for 45 days, diplopia was better than before and endocrine re-evaluation

revealed normal serum TSH, FT4 and PRL but serum FSH and serum LH were still at a low level (Table 1), and the pituitary MRI re-evaluation showed empty sella and no recurrence of the sellar mass (Figures 1e, 1f).

#### Case 2

A 57-years-old female presented with polyuria and polydipsia, and she was hospitalized. The initial laboratory studies showed hypogonadotropic hypogonadism with basal LH, FSH lower than the normal reference values of postmenopausal women. PRL in the serum was elevated than the normal level, and the levels of ACTH, cortisol, TSH and FT4 were normal (Table 1).

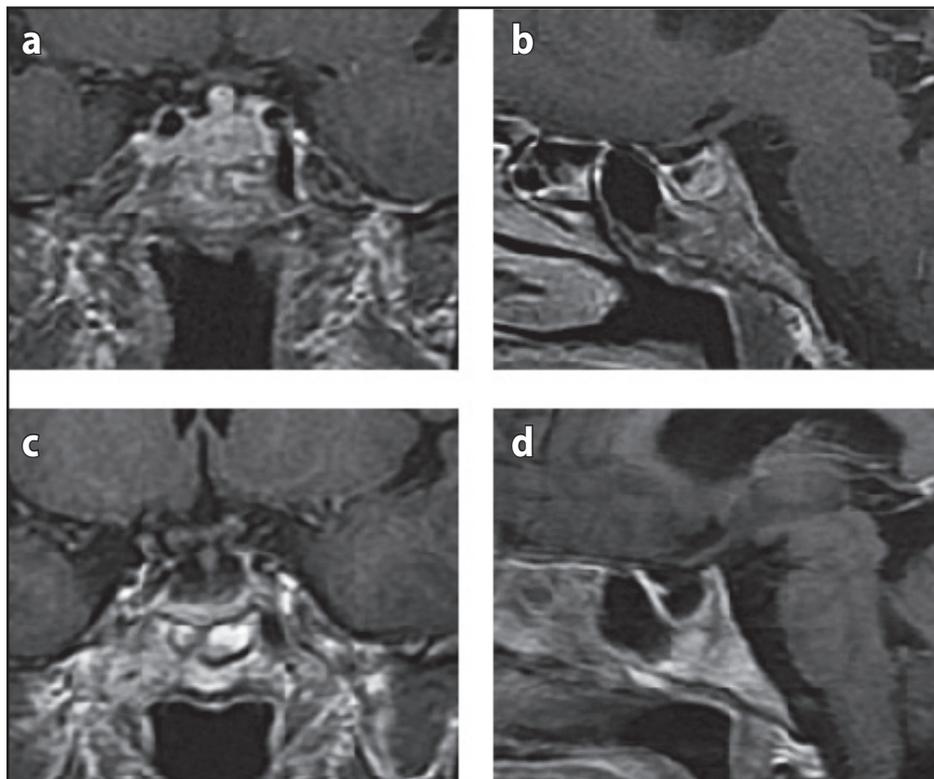


**Fig. 1** a and b. Pituitary enlargement and homogeneous enhancement were revealed by MRI on the first admission. c and d: After treatment with glucocorticoids of 30 days, empty sella was observed on MRI. e and f: After treatment with glucocorticoids of 45 days, empty sella was observed on MRI (case 1).

**Tab. 1.** Serum level of basal hormones.

		Case 1		Case 2	
		On admission	45 days after treatment	On admission	30 days after treatment
ACTH	(0–46 pg/ml)	5.76	---	14.2	---
Cortisol	(5–25 µg/dl)	1.8	---	19.1	---
TSH	(0.3–5.0 mU/L)	0.083	2.184	1.90	---
FT3	(3.5–6.5 pmol/L)	1.97	2.28	3.8	---
FT4	(11.5–23.5 pmol/L)	7.74	12.09	13.98	---
FSH	(2.5–10.2 IU/L)	1.08	1.90	4.2	4.25
LH	(1.9–2.5 IU/L)	0.007	0.25	0.2	0.23
PRL	(2.8–29.2 ng/ml)	4.91	8.64	19.66	46.62
GH	(0.06–5 µg/L)	<0.05	---	<0.05	---
ESR	(0–20 mm/h)	28	12	36	23
ANA	(<1: 80)	1:100	negative	1:100	negative
Serum Na	(135–155 mmol/L)	138	143	150	145
Serum K	(3.5–5.5 mmol/L)	4.55	4.62	4.0	4.2

Note: ACTH: adrenocorticotrophic hormone ; TSH: thyroid stimulating hormone ; FT3: free triiodothyronine ; FT4: free tetraiodothyronine ; FSH: follicle-stimulating hormone; LH: luteinizing hormone; PRL: prolactin ; GH: growth hormone; ESR: erythrocyte sedimentation rate; ANA: autoantibody to nuclear antigen; Na: sodium; K: potassium ; ---: not available.



**Fig. 2** **a** and **b**. Pituitary enlargement and homogeneous enhancement were revealed by MRI on the first admission. **c** and **d**: After treatment with glucocorticoids of 2 years , empty sella was observed on MRI (case 2).

Her water intake and urine output a day were 8L, and urine osmolality was 178 mOsm/kg and serum osmolality was 368 mOsm/kg. Water balance was normalized when vasopressin was given, suggesting it was central diabetes insipidus. Diffuse thickening of the pituitary stalk was shown by MRI while enhanced contrast enhancement of the gland and loss of neurohypophyseal “bright spot” were also detected as well (Figures 2a, 2b).

Methylprednisolone 40–80 mg was given intravenously per day. After the treatment with methylprednisolone for 23 days, the symptoms of polyuria and polydipsia was improved for her water intake and urine output a day were 4L, and urine osmolality was 339 mOsm/kg and serum osmolality was 315 mOsm/kg. Then the patient was given tablets of methylprednisolone 4–24 mg per day and the pituitary MRI revealed an appearance of empty sella two years later (Figures 2c, 2d).

## DISCUSSION

AH is a rare but increasingly recognized disorder that typically presents as a mass in the sella turcica showed by MRI. Females are believed much more easily affected than males. The disease is usually associated with pregnancy or postpartum period (Rumana *et al.* 2010). The clinical presentation of AH is variable and comprises hypopituitarism, diabetes insipidus, sellar compression, and hyperprolactinemia. Here, we describe two cases of postmenopausal women with AH and the two patients presented with anterior pituitary dysfunction, diplopia and diabetes insipidus on the first admission. In our case report, we make many endocrinological examinations, but we have no results of stimulatory test (i.e. insulin tolerance test, TRH test, and LHRH test) and anti-pituitary antibody. Those results are extremely important and we should make those tests in the future research. In case 1, the lumbar puncture is to definite the reason of seriously nausea and vomiting in the beginning, and many white blood cells was found in the cerebrospinal fluid suggesting that it was a inflammatory disease.

It has been reported that studies by MRI are useful for the differential diagnosis of AH from pituitary adenoma. Marked and homogeneous contrast enhancement of the pituitary gland is the major characteristic of AH, while pituitary adenoma often show moderate enhancement (Yamagami *et al.* 2003). But unusual findings include heterogeneous and ring-enhancing may also be revealed in pituitary MRI in AH (Howlett *et al.* 2010). In AH there is the loss of T1 high signal in the neurohypophysis, and if the posterior section of pituitary is not impaired we may see the hyperintensity of neurohypophysis (Caturegli *et al.* 2005). In the present cases, the gender, clinical presentation, laboratory findings and the imaging studies have all suggested AH.

Glucocorticoids can be effective for treating AH, both as antiinflammatory agents to reduce the size of the pituitary mass or the thickened stalk, and as replacement of defective adrenal function. In our

patients, methylprednisolone was given to reduce the size of the pituitary and to improve the clinical symptoms. International research advocate that glucocorticoid pulse is the first choice of treatment for AH, and the dose of prednison 20–40 mg/d and methylprednisolone 120 mg/d, but the specific dose is still controversial (Mirocha *et al.* 2009). Lu *et al.* (2009) reported one case of AH was treated with methylprednisolone 800 mg/d pulse and gradually reduce, and have got good effects. From our experience, methylprednisolone 40 mg/d was given intravenously for one month and the pituitary MRI re-evaluation showed marked reduction of pituitary, then the patient was given tablets of methylprednisolone 4–24 mg/d.

Empty sella may be the final outcome of LH. Empty sella associated with AH was first reported by Unluhizarci (2001). Matta reported an interesting case of a recurrent AH mimicking aseptic meningitis followed for about 9 years who developed partial empty sella (Matta *et al.* 2001). Zuleyha reported another interesting case with AH who developed empty sella over a 13-year period (Karaca *et al.* 2009). Lupi *et al.* (2011) reported that the progression in a mouse model of autoimmune hypophysitis developed empty sella. In our report, we found that AH eventually became empty sella after glucocorticoids therapy for 30 days in case 1 and for 2 years in case 2. It is important that we should closely monitor pituitary MRI in the first month of the treatment after diagnosis in future studies.

In conclusion, the present cases are representative examples for the natural course of AH in which empty sella was the final outcome. Conversely, in patients with empty sella, it is important to suspect AH and to have retrospective studies of the disease progression.

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

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