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CASE REPORT

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Autoimmune Hypophysitis Presenting as Solid-Cystic Mass Managed Conservatively

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Summary

Background: Autoimmune hypophysitis (AH) is a rare inflammatory condition of the pituitary gland and usually affects women of childbearing age. It commonly leads to pituitary dysfunction. Moreover, pituitary enlargement may lead to compressive symptoms, which necessitates urgent surgical decompression. Resection of the pituitary gland causes iatrogenic hypopituitarism which requires lifelong hormonal supplementation. With an increasing number of suspected cases of pituitary diseases, there has been a paradigm shift in the management by conservative measures, especially, when surgery is not urgently needed.

Case Report: We report a case of AH in a premenopausal woman presenting with headache. MRI revealed a solid-cystic mass involving the anterior lobe of the pituitary gland. The infundibulum was also thickened and enhancing; however, it was still in the midline. Ancillary MRI findings and hormonal profile were favouring the diagnosis of AH over pituitary neoplasm. The patient was managed conservatively with high doses of glucocorticoids, which resulted in prompt resolution of the lesion. During subsequent follow-up over 6 years, there was no recurrence and partial restoration of the pituitary function was seen. This case is interesting due to an unusual MRI appearance of AH, presenting as a solid-cystic mass. Moreover, disease resolution with conservative treatment strengthens the approach to limit surgery to those patients with compressive symptoms or uncertain diagnosis.

Conclusions: AH should be included in the differential diagnosis of solid-cystic pituitary masses along with clinical correlation, which includes early involvement of ACTH and TSH and a relatively rapid development of hypopituitarism. In uncertain cases or with lack of compressive symptoms, a trial of steroids is worthwhile.

MeSH Keywords: Autoimmune Diseases • Pituitary Diseases • Pituitary Gland, Anterior

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Background

AH is a rare inflammatory condition of the pituitary gland which usually presents with compressive symptoms or hormonal dysfunction secondary to hypopituitarism. Although any sellar mass may lead to pituitary dysfunction, the pattern of hormonal involvement may herald a suspicion of AH on clinical grounds. The usual MRI appearance of AH involves pituitary enlargement with solid homogeneous enhancement. Rarely, there may be cystic degeneration, hence, making AH indistinguishable from neoplasms. Despite being a non-neoplastic condition, surgical management is essential to relieve compressive symptoms. Furthermore, confirmatory diagnosis is established by histopathology of the resected specimen. However, a major disadvantage of surgery is the subsequent development of iatrogenic hypopituitarism which necessitates lifelong hormonal supplementation. Because of that, physicians currently prefer an initial trial of conservative management in cases provisionally diagnosed as AH on the basis of characteristic clinical and radiological findings. This approach is particularly indicated in individuals with non-emergency clinical manifestations. [1,2].

Case Report

A 50-year-old premenopausal, multiparous woman with pre-existing diabetes mellitus presented with insidiously progressing, persistent headache for 2 months. She also complained of fatigue, cold intolerance, facial puffiness, galactorrhoea and oligomenorrhoea. No significant past history of infection, systemic illness or any visual abnormality was present. Chest X-ray, abdominal ultrasound and digital perimetry were normal.

CECT of the head performed as part of a routine evaluation for headache, revealed an incidental sellar mass. For further evaluation and delineation of its extent, MRI was performed (Figure 1A–1D). It showed circumscribed enlargement of the anterior lobe of the pituitary gland, especially involving its right lateral lobe. It was predominantly hypointense on T1WI and of heterogeneous signal intensity on T2WI. On postcontrast scans, there was intense peripheral enhancement. However, lack of central enhancement led to a mixed solid-cystic appearance. Pituitary stalk was also thickened and intensely enhancing. It was compressing the chiasma, but there was no stalk deviation. Posterior pituitary bright spot was absent. There was no cavernous sinus invasion, encasement of the internal carotid or extracranial extension (Figure 2A, 2B). The floor of the sella turcica was intact, as evidenced on CT.

Endocrinal evaluation revealed marginal hyperprolactinemia and panhypopituitarism with reduction in FT4, gonadotropin and cortisol production. Serum TSH *was within the lowest quartile of normal limits*. Serum LH was undetectable which was abnormal in a postmenopausal women (Table 1). No clinical or biochemical evidence of diabetes insipidus was present. These findings were suggestive of exclusive involvement of the anterior lobe of the pituitary gland.

In summary, the clinicoradiological findings included:

i) Characteristic pattern of pituitary dysfunction with early loss of adrenocorticotrophic hormone and thyroid-stimulating hormone;
ii) Relatively rapid development of hypopituitarism;
iii) Characteristic MRI features such as near-symmetric enlargement of the pituitary gland, thickened but non-displaced stalk with strong contrast enhancement.

Considering the subacute presentation, pattern of endocrine involvement and radiological features, a diagnosis of autoimmune hypophysitis was most probable. A pituitary

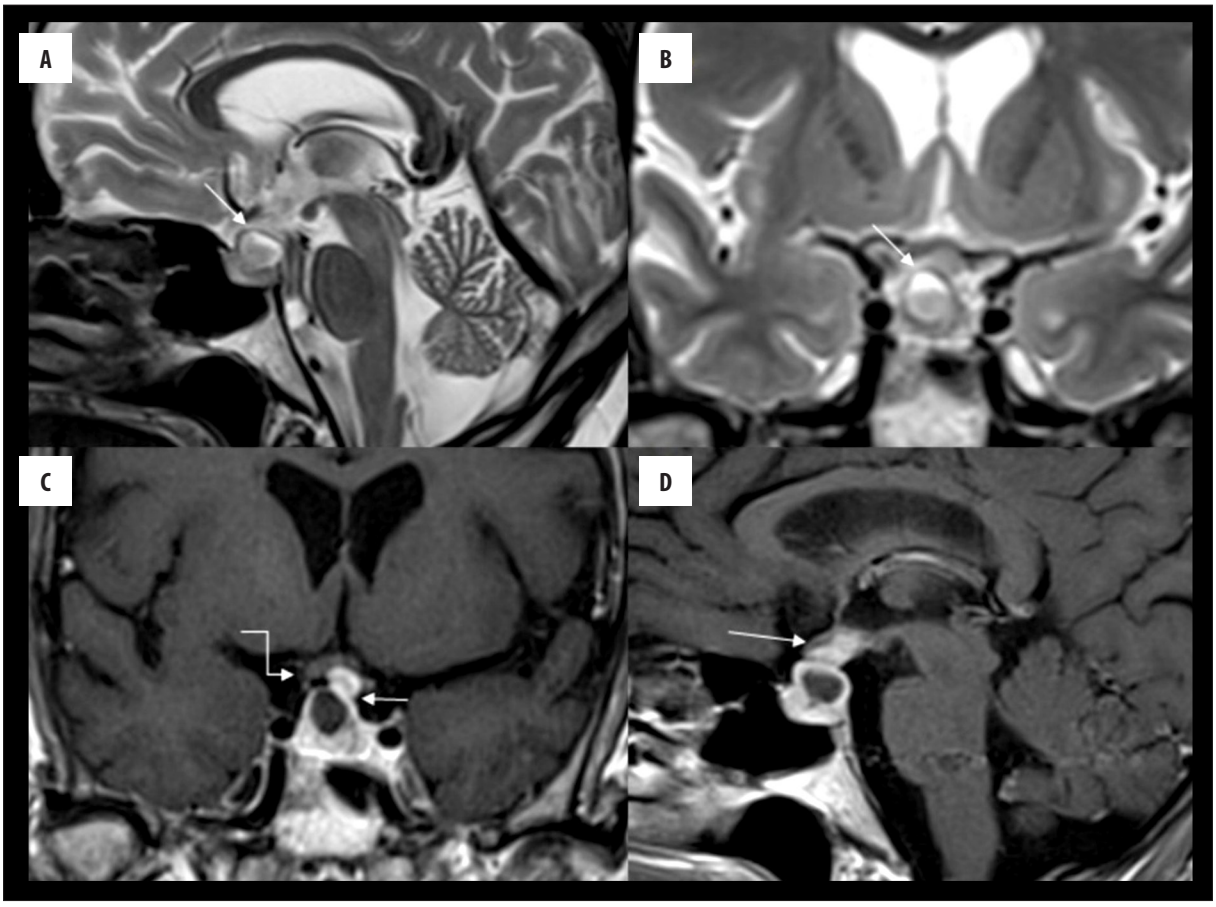

Figure 1. (**A, B**) T2W sagittal and coronal images (**A, B**) showed a well-defined, heterogeneously hypointense enlargement (7.8×7.9 mm) of the anterior pituitary lobe (arrow). (**C, D**) Postcontrast coronal and sagittal images (**C, D**) showing intense, peripheral enhancement of the pituitary gland; however, the centre of the lesion was non-enhancing resulting in solid-cystic appearance. The pituitary stalk was also thickened and intensely enhancing (arrow in **D**); nonetheless, it was maintained in the midline. There was indentation on the optic chiasma (curved arrow in **C**); although there were no visual complaints.

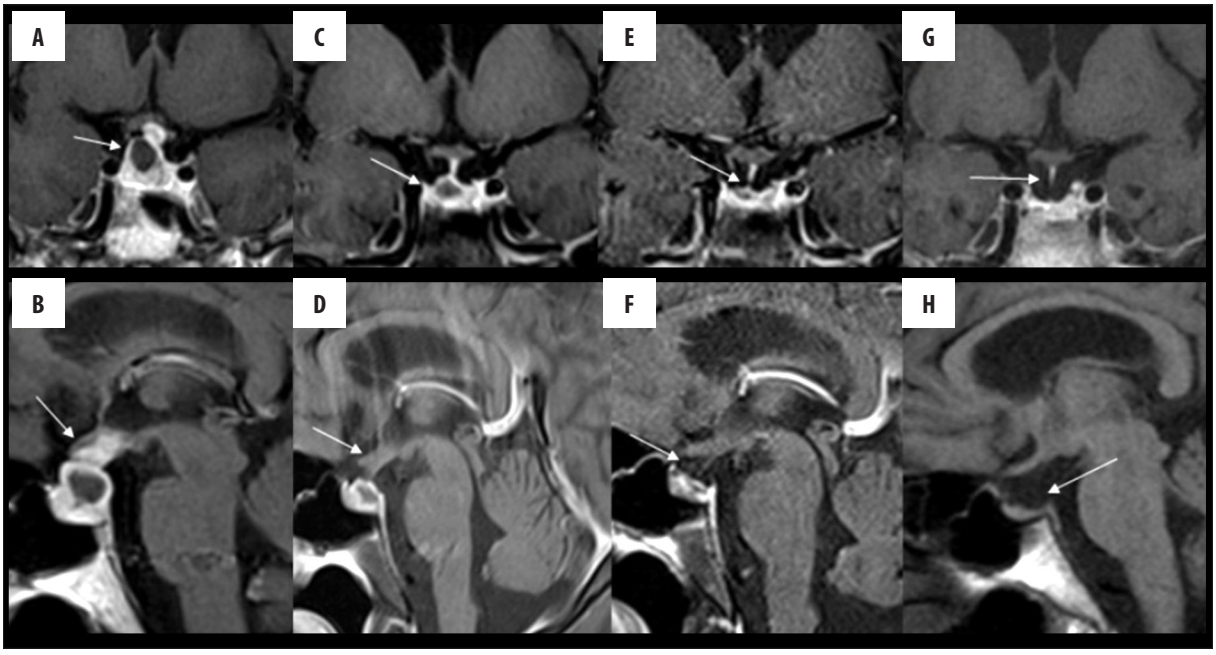

Figure 2. Serial MRI scans of the sella over 6 years, postcontrast (except **G** and **H**) coronal (top row) and sagittal images (bottom row) for comparative analysis. At initial presentation (**A, B**), the anterior lobe of the pituitary gland was enlarged with a solid-cystic appearance (arrow in **A**). Pituitary stalk was also thickened (arrow in **B**). At 4 weeks (**C, D**), a significant reduction in the size of the lesion (arrow in **C**) and thickness of the pituitary stalk are seen (arrow in **D**). (**E, F**) At 10 weeks, a near-complete disappearance of the mass with persistence of a tiny cystic remnant is seen (arrow in **E**). The height of the pituitary gland was also decreased with a flattened upper margin (arrow in **F**), unusual for a multipara. (**G, H**) At 6 years, a partial empty sella, thinned pituitary stalk (arrow in **G, H**) and absence of lesion were noted.

Table 1. Endocrinal profile at presentation.

Hormonal level	Value	Reference range
a) Prolactin	55.64 ng/mL	2.74–19.64 ng/mL
b) FT4	0.63 ng/dL	0.7–1.8 ng/dL
c) S.TSH	1.19 µIU/mL	0.3–5.5 µIU/ml
d) Serum cortisol	1.58 µg/dL	5–25 µg/dL
e) Serum LH	Undetectable	11.3–39.8 IU/L

FT4 – free thyroxine; S.TSH – serum Thyroid-Stimulating Hormone.

macroadenoma was the next differential consideration due to certain atypical MRI findings such as cystic degeneration. However, pituitary macroadenomas (benign or malignant) usually cause deviation of the pituitary stalk and bone destruction, which was not present in this case. As the patient was stable without any manifestations requiring urgent neurosurgical intervention, a decision on initial conservative management was made on the basis of the presumptive diagnosis of AH. Immunosuppressive doses of oral glucocorticoids were given initially for 10 weeks. Furthermore, initiation and up-titration of thyroxin replacement was done.

After 4 weeks, there was a remarkable clinical improvement and significant reduction in the overall size of the mass on MRI (Figure 2C, 2D). The cystic component had also significantly regressed. After 10 weeks, follow-up MRI (Figure 2E, 2F) revealed near-complete resolution of the lesion with persistence of only a small cystic remnant. In the following months, thyroxin and glucocorticoid supplementations were continued (Table 2). After 11 months, glucocorticoid supplementation was withdrawn. During the subsequent follow-up over 6 years, thyroxin supplementation was continued. There were no new complaints. Serum cortisol levels remained within the normal range. However, serum gonadotropin levels had been persistently low since the onset, signifying lack of recovery of gonadotropin secretion. A recent MRI scan, performed after 6 years, revealed a partially empty sella with complete disappearance of the pituitary lesion (Figure 2G, 2H).

Discussion

Inflammatory lesions of the pituitary gland, also referred to as hypophysitis, are broadly categorized aetiologically into 4 subtypes – purulent, granulomatous,

Table 2. Endocrine tests at 10 weeks follow up.

Serum LH ≤0.001 IU/L(expected >20 IU/L)
Serum FT4=2.29 (0.8–1.9) ng/dL
Serum Cortisol=ND
Serum GH=ND
Serum prolactin=47.3(2.5–17) ng/mL
Tests for DI negative

LH – luteinizing hormone; FT4 – free thyroxine; GH – growth hormone; DI – diabetes insipidus; ND – not detectable.

lymphocytic or secondary to an associated pathological process. Autoimmune hypophysitis (AH) or lymphocytic hypophysitis is an extremely rare entity. It usually affects women of childbearing age, during pregnancy or in the immediate post-partum period, which strongly suggests an autoimmune basis. Uncommonly, it may occur in post-menopausal women and in men. Anatomically, based on pituitary lobe involvement, it may be further classified into: adenohypophysitis, infundibulo-neurohypophysitis or panhypophysitis; the former being the most common [1–5].

Clinically, AH is usually subacute in onset and manifests with a relatively rapidly developing panhypopituitarism with an early involvement of ACTH and TSH secretion. Confirmatory diagnosis of AH is essentially established on histopathology of the resected specimen, in which lymphocyte and plasma cell infiltration is seen. Organ-specific antibodies may be present in some cases [1,4]. With an ever increasing role of MRI in the evaluation of sellar/suprasellar lesions, AH may be suspected non-invasively by the presence of certain features in a pituitary lesion. It characteristically causes symmetric enlargement of the anterior lobe of the pituitary gland, which usually shows intense homogeneous enhancement, comparable to the cavernous sinus. The infundibulum may be thickened; however, due to the symmetric enlargement of pituitary gland, there is no stalk deviation. Uncommonly, there may be central necrosis, which appears cystic due to lack of enhancement. Differential considerations of AH include pituitary macroadenoma from which it can be distinguished by considering collective clinico-radiological findings (Table 3). Hormonal profile and especially the pattern of involvement of pituitary hormones may help arrive at the diagnosis in certain cases. Solid-cystic sellar masses on imaging, as in our case, may resemble pituitary macroadenomas in which cystic degeneration is fairly common. However, deviation of the pituitary stalk is usually present in macroadenomas due to asymmetrical involvement. Furthermore, there is no thickening of the stalk, in contrast to our case [5–8].

Due to the pituitary enlargement and its consequent mass effect, AH requires urgent neurosurgical intervention. Surgery is also indicated in certain indeterminate cases which are indistinguishable from pituitary neoplasms (commonly macroadenoma). Following surgery, compressive symptoms are relieved; however, endocrinological dysfunction persists, resulting in iatrogenic hypopituitarism requiring lifelong hormonal supplementation. Hence, nowadays a trial of conservative management with steroids is worthwhile, especially. in the absence of compressive symptoms [1,2].

In our case, a significant reduction in the size of the mass within 4 weeks of glucocorticoid treatment initiation might have resulted from suppression of inflammatory activity. This case also highlights the possibility of recovery of hormone production after complete insufficiency during the active inflammatory phase. Long-term studies have documented that while 73% of patients required replacement of

Table 3. Comparative analysis of MRI findings and pattern of pituitary hormone in autoimmune hypophysitis and pituitary macroadenoma [6–8].

Feature	Autoimmune hypophysitis	Pituitary macroadenoma
MRI findings		
a) Asymmetric mass	Rare	+
a) Pre contrast homogeneous signal	+ (Uncommonly heterogeneous if cystic degeneration)	–
c) Intact sellar floor (accurately assessed on CT)	+	–
d) Suprasellar extension	+	+
e) Stalk thickening	+	-
f) Stalk displacement	-	+
g) Homogeneous enhancement	+	_
h) Loss of hyperintensity of posterior pituitary bright spot	+/–	–
i) Endocrinal dysfunction	Relatively rapid development of hypopituitarism Early involvement of ACTH and TSH	Early involvement of growth hormone followed by gonadotrophins

at least one hormone. However, in approximately 16% of cases no hormonal supplementation was required [9–11].

No long-term data on the benefits of surgical treatment over medical management are available. Moreover, only short-term follow-up of surgical cases is available in the literature; however, it suggests recovery in the majority of cases. Nonetheless, few reports suggest recurrence with iatrogenic hypopituitarism in a significant proportion of cases, in in particular ,diabetes mellitus. For the reasons mentioned above, most authors prefer a conservative approach whenever feasible. Nonetheless, the precondition for conservative management is a non-invasive diagnosis of AH, which requires clinicians to be acquainted with its clinical and imaging features. [9,10]

Conclusions

AH is rare but increasingly recognized. It should be considered in the differential diagnosis of any non-secreting pituitary mass, especially in women. In the absence of surgical emergency (for e.g. impending vision loss), medical management, medical management, i.e. monitoring the patient's endocrine status combined with sequential MRI imaging, is preferable. However, this approach precludes a definitive pathologic diagnosis. If symptoms persist or worsen, or if the patient does not tolerate high doses of glucocorticoids, transsphenoidal surgery should be performed.

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