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Primary Hypophysitis Mimicking Gonadotroph Adenoma in a Patient with Central Diabetes Insipidus: A Diagnostic Pitfall

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Abstract :

Introduction: Primary hypophysitis is a rare inflammatory disorder that may mimic pituitary adenoma both clinically and radiologically, making etiological diagnosis challenging. We report a case illustrating this diagnostic pitfall.

Case Presentation: A 43-year-old woman presented with a 5-month history of severe polyuria–polydipsia, retro-orbital headaches, recent amenorrhea, and weight loss. Biological evaluation confirmed diabetes insipidus. Pituitary MRI showed an 11-mm intrasellar lesion with homogeneous enhancement and cavernous sinus extension, initially suggestive of macroadenoma, while hormonal findings raised suspicion of a gonadotroph adenoma. However, the remainder of the pituitary and etiological work-up was unremarkable. The absence of the posterior pituitary T1 bright spot and the rapid response to desmopressin confirmed CDI. Serial MRI follow-up demonstrated complete regression of the lesion, strongly supporting primary hypophysitis rather than gonadotroph adenoma. Persistent CDI and subsequent evolution toward a menopausal gonadotroph profile further supported the diagnosis.

Conclusion: This case highlights the importance of integrating endocrine, radiological, and longitudinal follow-up data to avoid unnecessary pituitary surgery.

Keywords: Primary hypophysitis, Central diabetes insipidus, Pituitary adenoma mimic, Gonadotroph adenoma, Polyuria–polydipsia syndrome, Pituitary MRI, Spontaneous regression.

1. Introduction:

Hypophysitis is an uncommon inflammatory disease of the pituitary gland that may involve the anterior pituitary, posterior pituitary, and occasionally the hypothalamus [1]. Anatomically it has been classified into adenohypophysitis, infundibulo-neurohypophysitis and panhypophysitis and etiologically into primary and secondary forms [1]. Hypophysitis is a rare disease, but its recognition has increased in recent years, due to improved MRI characterization and to the increased awareness of its diverse clinical and pathological spectrum [1].

Its diagnosis remains particularly challenging as hypophysitis may clinically and radiologically mimic pituitary adenoma [2]. It is important to distinguish these entities, as management differs significantly: pituitary adenomas are often surgically treated, whereas hypophysitis can be managed conservatively with hormone replacement, glucocorticoids, or in selected cases, simple radiological surveillance [1]. In this context, central diabetes insipidus represents a particularly important warning sign, as it is uncommon in pituitary adenomas and should instead raise suspicion for inflammatory or infiltrative processes involving the posterior pituitary and stalk [2].

We report here an unusual case of central diabetes insipidus associated with an initially adenoma-like pituitary lesion, first suspected to be a gonadotroph adenoma, in whom spontaneous radiological regression ultimately supported the diagnosis of presumptive primary hypophysitis.

2. Case Presentation :

A 43 year-old man was hospitalized for etiological assessment of a severe polyuria-polydipsia syndrome that had started abruptly five months biological evaluation confirmed hypotonic polyuria with a markedly low urinary osmolality at 72 mOsm/l. Its association with a borderline high osmolality at 299mOsm/l, and serum sodium at 144 mmol/l was strongly suggestive of diabetes insipidus.

Initial pituitary MRI revealed an intrasellar mass arising from the anterior pituitary, measuring 11 × 10.5x10 mm on sagittal imaging. The lesion was isointense on T1-weighted sequences, of intermediate hyperintensity on T2, and showed homogeneous enhancement after gadolinium administration. It remained below the optic chiasm but extended laterally into the cavernous sinus, more markedly on the right, with apparent contact with the right internal carotid artery. The sellar floor was preserved. The pituitary stalk was described as thin and deviated, and the posterior pituitary bright spot was not visualized (Figure 1). Given the apparent cavernous sinus extension and the absence of the typical stalk enlargement usually expected in hypophysitis, the initial radiological conclusion favored a pituitary macroadenoma rather than hypophysitis, thereby contributing to the initial misclassification. Ophthalmologic assessment, including fundus examination and Goldman visual field testing, was normal.

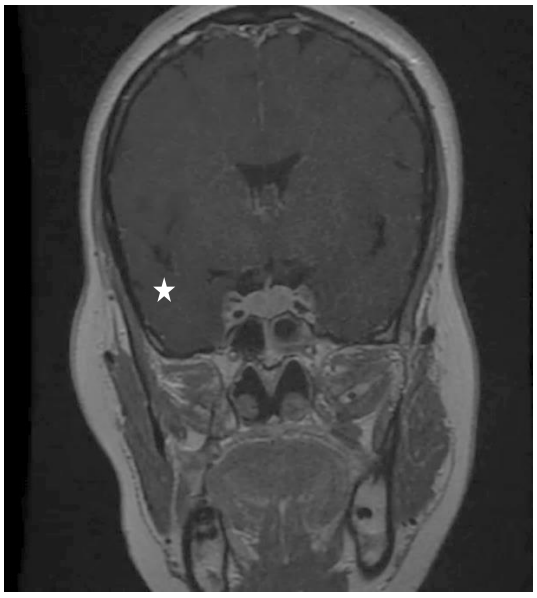
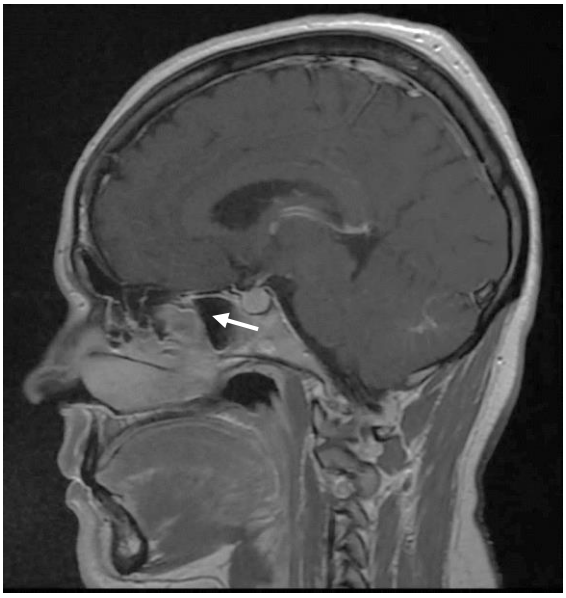
A  B 

Figure 1 : post gadolinium T1-weighted Coronal (A) and sagittal section (B) of MRI images of the patient showing an adenoma-like intrasellar lesion associated with lateral cavernous sinus extension, loss of the posterior pituitary bright spot (arrow) and a thin deviated pituitary stalk (star). (performed at Hassan II University Hospital, Fez, Morocco)

The gonadotropic workup showed inappropriately elevated hormone levels for the early follicular phase, with estradiol at 206 pg/mL, FSH at 28 mIU/mL, and LH at 18.6 mIU/mL, despite the presence of menstrual disturbance The remaining pituitary hormonal evaluation showed no other endocrine abnormalities (table 1). This pattern, together with the MRI appearance, raised the possibility of a gonadotroph adenoma. However, the alpha-subunit of gonadotrophins was not elevated, and pelvic ultrasound showed no signs of ovarian hyperstimulation.

Table 1 : Baseline pituitary hormonal evaluation at the time of initial diagnosis

Hormonal test	Result	Reference range
IGF-1 (ng/ml)	106	71–258 ng/mL (median reference value: 134)
Prolactin (ng/ml)	16.04	5-20 ng/ml
Morning serum cortisol (ug/dl)	17	Preserved morning cortisol secretion
TSH (µIU/mL)	0.46	0.25–5 µIU/mL
Free T4 (pmol/L)	16.23	12–20 pmol/L
Estradiol (pg/mL)	206	Measured during the early follicular phase
FSH (mIU/mL)	28	3.03-8.8 mIU/mL
LH (mIU/mL)	18.6	2.3-6.6 mIU/mL
Alpha-subunit of glycoprotein hormones (IU/L)	0.43	<1 IU/L in premenopausal women

An etiologic work-up was then undertaken to investigate secondary causes of central diabetes insipidus. No clinical, biochemical, or radiological evidence of systemic autoimmune, granulomatous, infiltrative, infectious, or neoplastic disease was identified. (Table 2).

Table 2 : Etiological work-up for secondary causes of central diabetes insipidus

Investigation category	Test	Result
Inflammatory / granulomatous work-up	Erythrocyte sedimentation rate (ESR)	-1 mm at the 1st hour; -3 mm at the 2nd hour
	C-reactive protein (CRP)	0.7 mg/L
	Serum protein electrophoresis	-Mild non-specific hypoalbuminemia
	Angiotensin-converting enzyme (ACE)	30 IU/L
Tuberculosis screening	Chest X-ray	No abnormality detected
	Tuberculin skin test	Negative
	Sputum examination for acid-fast bacilli (3 samples)	Negative
Tumor marker assessment	Alpha-fetoprotein (AFP)	8.10 ng/mL
	β-human chorionic gonadotropin (β-hCG)	<1.2 mIU/mL

Given the high pretest probability of central diabetes insipidus and the risk of dehydration, a formal water deprivation test was not performed, and a therapeutic trial with desmopressin was preferred. This led to rapid symptomatic improvement and strongly supported the diagnosis of central diabetes insipidus.

Clinical follow-up

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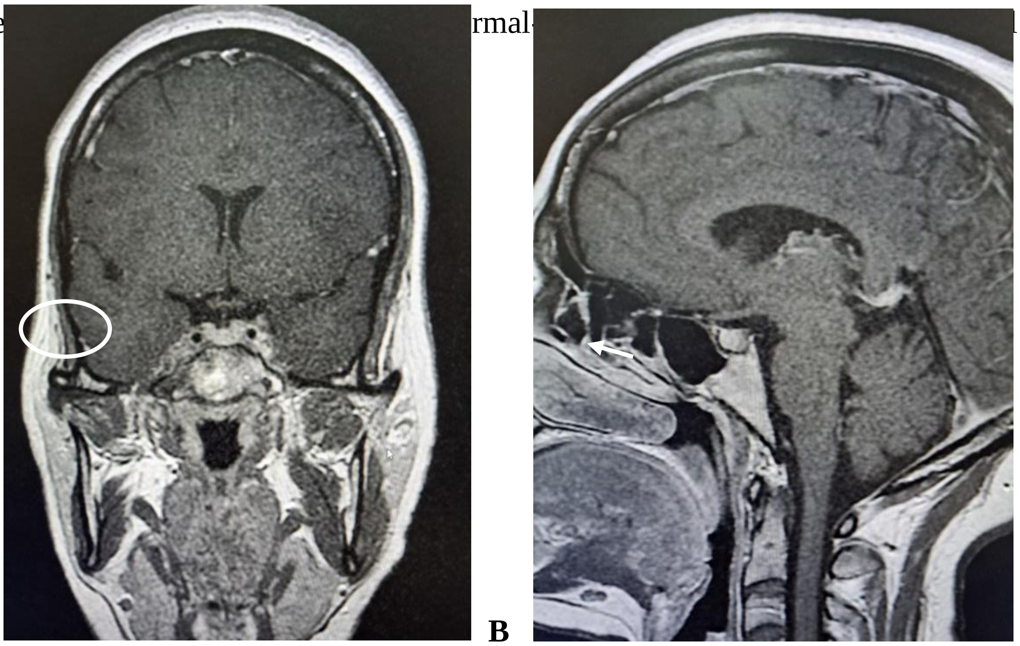

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Figure 2: post gadolinium T1-weighted Coronal (A) and sagittal section (B) of MRI images of the patient (year 1 of the follow up) showing Marked regression in the size of the intrasellar pituitary lesion, regression of the cavernous sinus infiltration (ellipse outline), and persistence of Absence of the posterior pituitary bright spot (arrow). (performed at Hassan II University Hospital, Fez, Morocco)

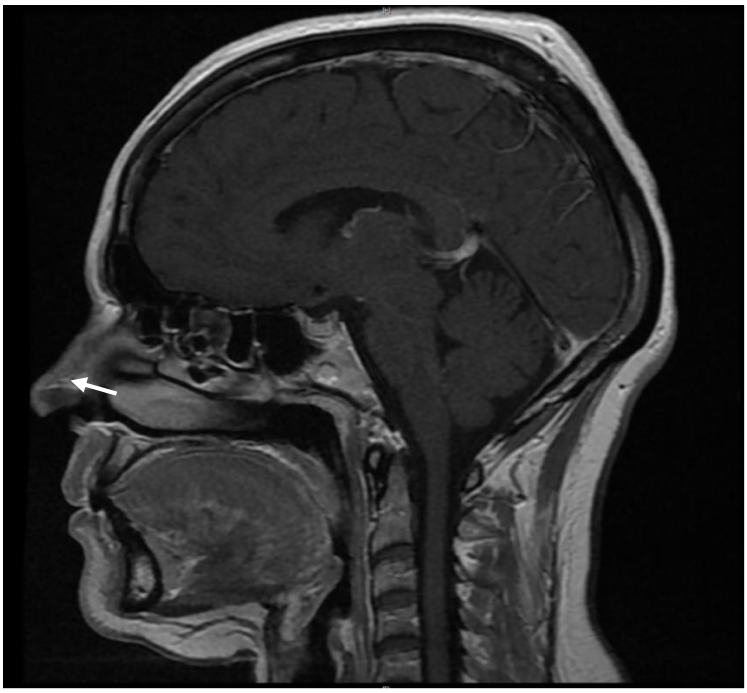

Figure 3: post gadolinium T1-weighted sagittal section of MRI images of the patient (year 2 of the follow up) showing complete regression of the intrasellar pituitary lesion and persistence of Absence of the posterior pituitary bright spot (arrow). (performed at Hassan II University Hospital, Fez, Morocco)

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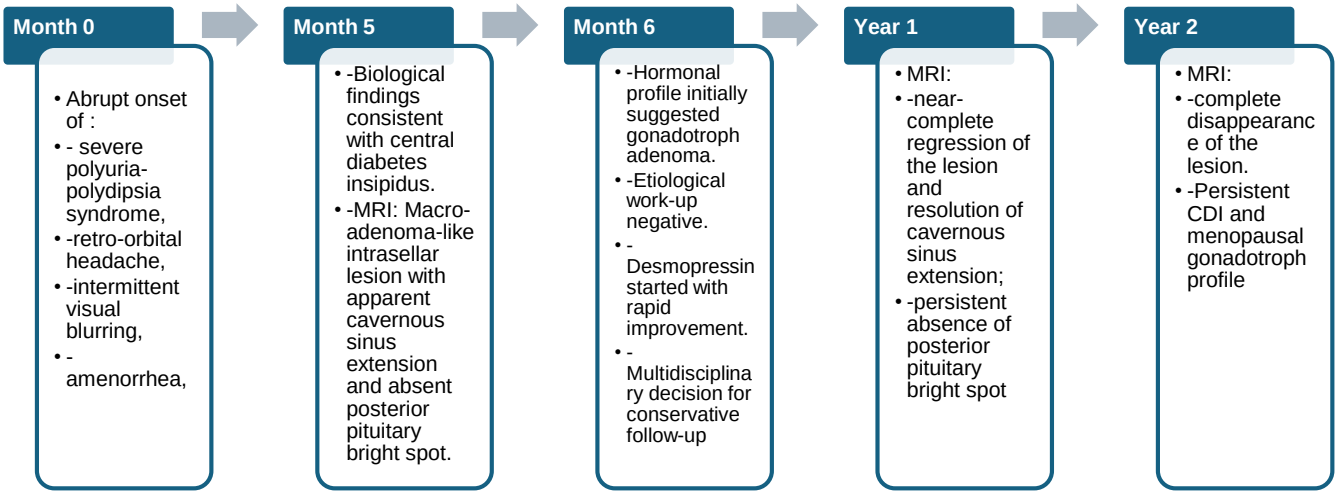

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Diagram showing the clinical course of the patient.

Table 3 : Follow-up endocrine reassessment and CDI etiological work-up

Evaluation category	Test	Result
Endocrine reassessment	Morning serum cortisol (µg/dL)	10.1
	Free T4 (pg/mL)	18.3
	Prolactin (ng/mL)	7.07
	FSH (mIU/mL)	59.36
	LH (mIU/mL)	33.23
	Estradiol (pg/mL)	11
Repeat etiological work-up for central diabetes insipidus	Autoimmune work-up	Unremarkable
	Serum protein electrophoresis	No abnormality
	Angiotensin-converting enzyme (ACE)	3 0
	Tuberculin skin test	Negative
	Sputum examination for acid-fast bacilli (3 samples)	Negative

3. Discussion :

This heterogeneous group of conditions encompasses multiple histological subtypes—including lymphocytic (most frequent), granulomatous, xanthomatous, IgG4- related, necrotizing, and mixed (adenohypophysitis – 65% of cases), the infundibulum and neurohypophysis (infundibulo-neurohypophysitis – 10%), or both compartments simultaneously (panhypophysitis- 25%) [1]. They can

Numerous cases in the literature have described hypophysitis closely mimicking pituitary adenoma, both clinically and radiologically with highly variable presentations (Table 4) [3-6]. Up to 40% of hypophysitis cases are initially misdiagnosed as pituitary macroadenomas [7]. On magnetic resonance imaging, hypophysitis typically manifests as homogeneous sellar enlargement with intense and homogeneous gadolinium enhancement, a thickened but not deviated pituitary stalk and loss of the normal posterior pituitary bright spot on T1-weighted sequences, and variable suprasellar extension [2,8]. These features overlap substantially with those of pituitary macroadenomas, which similarly present as sellar masses with suprasellar extension, however it is more Asymmetric with focal mass effect and heterogenous or delayed enhancement ; also, contrary to hypophysitis, the stalk is typically deviated or compressed but not thickened, and the posterior pituitary bright spot is preserved (unless in case of apoplexy and normally in 20% of healthy subjects [1]. Furthermore, hypophysitis can sometimes present with asymmetric enlargement and cavernous sinus extension, mimicking adenoma, while small adenomas may not deviate the stalk making the final diagnosis even more challenging [2,8]. Importantly, our case displayed precisely

these atypical features, namely asymmetry, apparent cavernous sinus invasion, and the absence of stalk thickening, all of which are usually considered more suggestive of pituitary adenoma than classical hypophysitis and therefore contributed significantly to the initial misdiagnosis.

Case	Age / Sex	Hypophysitis type	Initial diagnosis	Features suggesting adenoma	Clues favoring hypophysitis	Diagnostic confirmation	Management / outcome
Mittal et al. (2012) (3)	15 / F	Lymphocytic	Pituitary macroadenoma	Sellar mass with optic chiasm compression	Diabetes insipidus and stalk thickening	Histopathology after transsphenoidal surgery	Persistent CDI; long-term desmopressin
Chao et al. (2023) (4)	30 / F	Lymphocytic (presumed)	Non-functioning macroadenoma	Enhancing sellar mass with mild chiasmal contact	Clinical and radiological response to glucocorticoids	Therapeutic response and follow-up MRI	Complete radiological resolution
Taieb et al. (2023) (5)	38 / F	Granulomatous (neurosarcoidosis-related)	Pituitary macroadenoma	Sellar–suprasellar mass with homogeneous enhancement	Stalk thickening, diabetes insipidus, systemic granulomatous disease	Biopsy and systemic work-up	Glucocorticoid therapy
Salhi et al. (6)	45 / F	Secondary xanthogranulomatous hypophysitis	Pituitary macroadenoma	Intra/suprasellar mass with visual symptoms	Histology consistent with inflammatory sellar lesion	Histopathology after transsphenoidal surgery	Hormone replacement
Present case	43 / F	Presumptive primary hypophysitis	Gonadotroph adenoma	Adenoma-like sellar lesion, cavernous sinus extension, misleading gonadotroph profile	Central diabetes insipidus, absent posterior pituitary bright spot, spontaneous regression	Longitudinal clinico-radiological evolution	Conservative management; desmopressin; complete radiological resolution

					on serial MRI		

Age ≤ 30 years		
Pituitary volume ≥ 6 cm³		
		→

Feature	Score (if yes)	Our case
Diabetes insipidus	+2	+2
Absence of cavernous sinus invasion	+2	0
Infundibular thickening	+1	0
Absence of visual symptoms	+1	+1
Total score for our patient		**+3 → hypophysitis**

Table 7 : Taieb et al. Scoring system for differentiating hypophysitis from non-functioning pituitary macroadenoma [12]

Feature	Score (if yes)	Our case
Female sex	+3	+3
Presence of headache	-2	-2
Presence of visual disturbances	-2	0
Corticotroph deficiency	+1	0
Pituitary volume < 7 cm³	+0.5	+0,5

A total score ≥ 0,5 suggests hypophysitis with a reported sensitivity of 93.8% and specificity of 87.5%

Loss of posterior pituitary bright spot	+0.5	+0,5
Cavernous sinus invasion	-0.5	-0,5
Pituitary stalk thickening	+4.5	0
Optic pathway compression	-2	0
Total score for our patient		**+1,5 → hypophysitis**

These three scoring systems were analyzed in a comparative review in 2026, which recognized their complementary strengths and their potential usefulness in different clinical settings [13]. Parasellar T2 dark sign has been reported to be a useful radiological clue to differentiate the two conditions, although it may be seen in other chronic inflammatory disorders besides lymphocytic or IgG4-related hypophysitis [14]. However, none of these scores has been prospectively validated, and their diagnostic performance remains uncertain in atypical presentations or in histological subtypes other than lymphocytic hypophysitis [7,11-13]. Retrospective application in our case consistently favored hypophysitis, further supporting their practical value as adjunctive—not diagnostic—tools.

4. Conclusion :

This case depicts the current diagnostic challenge associated with the clinical, hormonal and radiological overlap between hypophysitis and pituitary adenoma. The initial suspicion of gonadotroph macroadenoma was understandable in our patient considering the adenoma-like MRI appearance and the misleading gonadotropic profile. However, the presence of central diabetes insipidus was a major diagnostic clue against a typical pituitary adenoma and should instead raise strong suspicion for inflammatory or infiltrative disease involving the pituitary stalk and posterior lobe.

The longitudinal evolution was the strongest argument in favor of presumptive primary hypophysitis, which showed spontaneous regression and eventual disappearance of the sellar lesion, persistent absence of the posterior pituitary bright spot, and absence of a systemic secondary cause.

Overall, this case illustrates the importance of a comprehensive diagnostic work-up that includes clinical picture, endocrine work-up, detailed assessment of MRI, and serial follow-up. In selected patients without neuro-ophthalmological emergency or progressive mass effect, this strategy may improve the diagnostic accuracy and avoid unnecessary transsphenoidal surgery. Structured scoring systems might help further in the preoperative differentiation, although atypical presentations are still a challenge and need to be carefully assessed on a case-by-case basis.

Disclosure of conflict of interest : The authors declare no conflict of interest.