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(CASE REPORT)

# Autoimmune hypophysitis? A presumptive diagnosis arising from incidentally discovered central hypothyroidism

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## Abstract

Inflammatory lesions of the hypothalamo-pituitary axis are rare, accounting for 0.38% of pituitary abnormalities. Among these, autoimmune hypophysitis is a key etiology to recognize. It requires early initiation of hormone replacement therapy and corticosteroids to preserve vital prognosis and reverse neuro-ophthalmological and/or pituitary symptoms.

We report the case of a chronic hemodialysis patient, candidate for a kidney transplant, in whom the pre-transplant biological assessment revealed central hypothyroidism, a sign that led us towards the presumptive diagnosis of primary hypophysitis.

Through this case, we aim to highlight the diagnostic challenges posed by this condition due to its nonspecific clinical and radiological signs, and the risk of misdiagnosis due to biased clinical management.

**Keywords:** Autoimmune hypophysitis; Central hypothyroidism; Pituitary MRI; Corticosteroid therapy

## 1. Introduction

Hypophysitis is a rare condition characterized by chronic inflammation of the pituitary gland, with complex and poorly understood pathogenesis. The first histologically confirmed case was reported in 1980. Since then, approximately 400 cases have been reported, predominantly lymphocytic and granulomatous forms [1].

The natural history of primary hypophysitis remains unclear and its treatment controversial. Conservative management with close monitoring is often proposed due to the often benign and transient evolution of the disease [2]. Clinical symptoms are nonspecific, with headaches and visual field defects being frequent. MRI remains the gold standard imaging modality despite the lack of radiological specificity [3].

## 2. Case Report

We report a 41-year-old male, chronic smoker, first hospitalized in 2011 at the age of 29 for severe helmet headaches and a sudden decrease in visual acuity. During hospitalization, he was diagnosed with hypertension and end-stage chronic kidney disease of undetermined glomerular origin, showing endo- and exocapillary proliferation.

The patient was therefore placed on corticosteroid therapy, an antihypertensive treatment with the use of hemodialysis sessions.

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Currently, our patient is admitted for a pre-transplant assessment, during which central hypothyroidism was confirmed by a TSH level of 0.47 µIU/ml, at the lower limit of normal (normal values: 0.27–4.2 µIU/ml), and a sharply decreased free thyroxine (FT4) level of 0.55 ng/dL (normal values: 0.7–1.48 ng/dL), which was checked several times.

Clinically, he was asthenic with no other significant signs. A full pituitary hormonal panel revealed no other hormonal deficits. Prolactin was 19 ng/mL (3.46–19.4 ng/mL), cortisol at 7.2 µg/dL (3.7–19.4 µg/dL), testosterone 3.2 ng/mL (1.27–10.2 ng/mL), and LH 8.53 mIU/mL (0.5–12 mIU/mL). Immunologically, our patient underwent a limited workup (search for anti-nuclear antibodies, cytoplasmic antineutrophils, antiglomerular basement membrane antibodies, antiphospholipids, rheumatoid factor) with rheumatoid factor positivity.

Pituitary MRI revealed vascular demyelinating lesions of the supratentorial white matter. A thyroid ultrasound showed colloid cysts in the left lobe. Levothyroxine therapy was initiated with good biological response.

**Table 1** Results of biological assessments

| Analysis | Result | Reference values |
|---|---|---|
| TSH | 0.47 µIU/ml | 0.27–4.2 µIU/ml |
| FT4 | 0.55 ng/dL | 0.7–1.48 ng/dL |
| Prolactin | 19 ng/mL | 3.46–19.4 ng/mL |
| cortisol | 7.2 µg/dL | 3.7–19.4 µg/dL |
| testosterone | 3.2 ng/mL | 1.27–10.2 ng/mL |
| LH | 8.53 mIU/mL | 0.5–12 mIU/mL |

## 3. Discussion

Primary hypophysitis was traditionally described in the postpartum period. However, literature now increasingly reports cases in men, prepubescent girls, nulliparous and postmenopausal women [4,5,6,7,8]. The pathogenesis is mostly autoimmune [9,10], and associations with other autoimmune diseases such as thyroiditis [11], systemic lupus erythematosus [12], and primary biliary cirrhosis [13,14] have been observed. However, the autoimmune nature may not always be evident [15].

Clinical signs are nonspecific. Headaches and visual field disturbances are often the most prominent, while oculomotor disturbances are rare [16,17]. These evocative signs were present in our patient during his initial hospitalization in 2011, when he presented with severe headaches and sudden decline in visual acuity.

Inflammation of the anterior pituitary is the most frequently reported form in literature, and clinical signs of anterior hypopituitarism may lead to diagnosis. These signs are mainly due to deficiencies in the corticotropic and thyrotropic axes, followed by the gonadotropic and somatotropic axes [18,19].

In the case of our patient, the current laboratory work-up showed isolated involvement to the thyroid axis, with borderline levels of TSH and collapsed levels of free T4 (FT4).

Depending on the affected axes, signs of adrenal insufficiency may include weight loss, profound asthenia, and hypotension due to cortisol deficiency from ACTH impairment. Complete or dissociated hypopituitarism with axillopubic depilation, lethargy, loss of libido, amenorrhea and erectile dysfunction in the context of androgen deficiency have also been reported [20]. Thyrotropic insufficiency may be revealed by psychomotor slowing, hypersomnia or asthenia, the main symptom found in our patient, or other signs of hypothyroidism. Similarly, episodes of hypoglycemia may occur following combined somatotropic and corticotropic deficiencies. When the neurohypophysis is involved, diabetes insipidus is the most common presentation [20].

Regardless the mode of onset, the gold standard morphological examination is magnetic resonance imaging (MRI) of the hypothalamic-pituitary region, with coronal and sagittal slices before and after gadolinium injection.

It shows abnormalities in nearly 90% of cases [21]. During the active phase of the disease, the most common neuroradiological appearance is a symmetrical pseudotumoral lesion, homogenous and iso-intense on T1-weighted

imaging [21–22]. However, this appearance is not specific and may also and may as well correspond to a pituitary adenoma. The triangular shape of suprasellar extension, although inconstant, is strongly suggestive of hypophysitis. On T2-weighted sequences, these masses are often homogeneously hyperintense [21].

In our case, this crucial imaging was not performed during the patient's earlier hospitalization, despite evident signs. Currently, hypothalamic-pituitary MRI has enabled us to rule out a tumoral process as the main differential diagnosis for inflammatory hypophysitis.

Due to the lack of consistency in case descriptions and follow-up in the literature, it is difficult to outline a clear natural history of hypophysitis. According to published cases, disease progression seems highly variable, making individual prognosis unpredictable. In the absence of treatment, pseudotumoral lesions may spontaneously regress or lead to pituitary atrophy, evidenced by an empty sella turcica on MRI. According to some, this evolution is favoured by corticosteroid therapy [21,22]. One prospective study of nine patients with hypophysitis showed that methylprednisolone improved pituitary function in four patients and MRI findings in seven [3].

Thus, our patient may have presented with typical lesions of the disease that went, our patient could have presented the lesions typical of the disease but which were not diagnosed in time given to non-performance of early imaging;

Moreover, corticosteroid therapy and the possible spontaneous resolution of inflammatory lesions may explain the current negative MRI findings.

On the hormonal level, full recovery of all deficiencies is uncommon (reported in less than 15% of cases) [20,21], and hormonal deficits often persist.

In all cases, anterior and posterior pituitary deficiencies should be investigated and treated. In the event of visual disturbances, treatment with high-dose corticosteroids or neurosurgical decompression may be considered. Surgery should be reserved for cases with unfavorable progression, worsening visual impairment, or persistent headaches despite analgesic therapy.

Although histological confirmation of hypophysitis requires biopsy or surgery, the diagnosis is often made retrospectively. A presumptive diagnosis can be made based on clinical, biological, radiological, and therapeutic context [20,21,3].

In summary, our patient’s diagnosis of probable primary hypophysitis was supported by multiple arguments:

To summarize, our patient's case is particular; the diagnosis of probable primary hypophysitis was based on a combination of factors:

As part of the pre-transplant assessment, our patient underwent laboratory tests that demonstrated central hypothyroidism, with a TSH level of 0.47 µIU/ml and an Ft4 of 0.55 ng/dl. This pattern of central involvement led to a hypophysiogram to assess the other pituitary axes; the results were normal. This concluded that there was isolated involvement of the thyroid axis. As part of the etiological assessment, a hypothalamic-pituitary MRI proved crucial, and returned no abnormalities other than supratentorial demyelination of vascular origin.

Thus, the absence of radiological findings suggesting tumor expansion suggests primary hypophysitis. Returning to the clinical signs described in the literature, intense headaches resistant to analgesic treatment and a sudden decline in visual acuity were present in our patient during his first admission in 2011.

At this time, the discovery of high blood pressure has been linked to the headaches experienced and likely confused the diagnosis, especially since ocular involvement has not been investigated.

As with any hospitalization, our patient underwent a standard workup that demonstrated end-stage chronic renal failure. A renal biopsy was the test of choice to determine the underlying cause, and this concluded with chronic glomerulopathy with endo- and exo-capillary proliferation. The patient was therefore placed on corticosteroid therapy for 6 months and on antihypertensive treatment with the use of dialysis sessions. By analyzing the patient's clinical and previous therapeutic context, as well as the current biological and radiological context, and by comparing it with data from the literature; It is likely that radiological images of hypophysitis are resolved following the initiation of corticosteroid therapy or following spontaneous regression of the lesions.

While the autoimmune context is widely described in the literature, it may be lacking in some cases, as published in a series in which two patients had primary hypophysitis without confirmation of the autoimmune character in them [15]. As for our patient, the immunological assessment demonstrated positivity for rheumatoid factor.

Our patient was therefore put on levothyrox. A follow-up assessment evaluated thyroid function, showing normal TSH and FT4.

## 4. Conclusion

This study aims to shed light on this rare, often overlooked or possibly misunderstood pathology, and to highlight the importance of imaging and biology in this context. Laboratory testing of various pituitary axis hormones plays a key role in establishing the diagnosis of inflammatory hypophysitis, and in this case, it should have been decisive if performed at the time of suggestive clinical signs. We emphasize the importance of cortisol and TSH testing first, in the presence of typical signs that cannot be attributed to another central origin, given that the damage primarily affects the corticotropic and thyroid axes. The laboratory results will help guide the diagnosis and optimize excessive investigations in the presence of intense headaches associated with visual disturbances.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors declare no conflicts of interest.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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