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A Case Report of Lymphocytic Hypophysitis Related to Pregnancy

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Abstract

A 39-year-old woman consulted in the postpartum period because of agalactia, polyuria, polydipsia, and headache and decreased visual acuity. The initial analysis was compatible with a panhypopituitarism. The magnetic resonance (MRI) showed an expansive sellar and suprasellar lesion of high density in the basal study and enhancement after contrast administration, in contact with the optic chiasm, so urgent surgery was indicated. While waiting for the surgery, intravenous corticosteroids were initiated and the symptoms rapidly resolved. Most of the pituitary axes were recovered, except the diabetes insipidus. The control MRI showed complete resolution of the sellar mass. The surgery was canceled and the diagnosis of lymphocyte hypohpyisitis was made. Lymphocyte hypophysitis is an uncommon disease in which inflammation of the pituitary gland occurs. This results in a permanent or transient hormonal insufficiency. Lymphocyte hypophysitis is a very rare condition that occurs preferentially in women in the peripartum period. Early initiation of high doses of systemic corticosteroids may avoid unnecessary surgery in some cases.

Keywords

Hypophysitis, Pregnancy, Panhypopituitarism, Lymphocytic Hypophysitis

1. Introduction

Lymphocytic hypophysitis is a very rare condition in which an inmune inflammation of the pituitary gland occurs. In general, the lymphocytic hypophysitis is seen in women and is associated with the peri- and postpartum period. It is estimated an incidence of one case per nine million people, but probably, there are not diagnosticated subclinical forms [1]. Initially, the histopathology consists of a monoclonal lypmphocityc infiltrate which

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can leave minimal sequelae or progress to fibrosis. This may result in temporary or permanent hormonal dysfunction. The clinical presentation varies depending on the pituitary segment that is affected and the tumor mass. The therapeutic approach is controversial. There are usually large pituitary tumors, associated with locally compressive symptoms, and often the transesphenoidal surgery is performed. Nevertheless, the conservative medical management is justified in many cases, given the self-limited nature of the inflammatory process. Here we describe the case of a large pituitary mass due to lymphocytic hypophysitis, associated with visual loss, in a patient in the postpartum period with an unexpected improvement after starting systemic corticosteroids.

2. Case Report

A 39-year-old young woman, natural from Algeria, was referred to our hospital because of headache and impaired vision. As personal history, she gave birth 6 months ago, to a live newborn, in the 38th week of gestation.

The patient reported agalactia after the first week of postpartum; one month later she started with polyuria, polydipsia and nocturia; episodes of dizziness, hypotension and amenorrhea. Three months after childbirth, she suffered from an holocraneal tension-type, headache, with partial improvement with conventional analgesia. Finally, she presented decreased visual acuity so she consulted to the emergency unit.

In the emergency department, the fundus opthalmoscopy resulted normal. The campimetric evaluation showed a significant decrease in visual acuity in the left eye (she only saw the movement of the hands) and reduction in the right eye (2 meters away). The patient was hemodynamically stable, blood pressure was 130/72 mmHg, and the rest of the physical examination had no significant findings (**Table 1**). The first blood tests were normal (glucose 85 mg/dL (74 - 110), sodium 137 mmol/L (136 - 146), potassium 3.49 mmol/L (3.4 - 4.5), creatinine 0.50 mg/dL (0.51 - 0.95), hemoglobin 12.8 g/L (11.8 - 14.7), leucocytes 12,890/L (4100 - 9900)). The craneal computed axial tomography (CT) showed an expansive sellar and suprasellar lesion of high density in the basal study and enhancement after contrast administration. The size of the lesion was 18 × 16 mm, and it contacted with the optic chiasm. The image suggested a pituitary adenoma with suprasellar extension or less likely a lymphocyte hypophysitis.

A cranial magnetic resonance (MRI) was performed in order to better characterize the pituitary mass and it confirmed the findings seen on the CT (**Figure 1**).

The hormonal study was compatible with a panhypopituitarism (thyrotropin 0.14 mU/L (0.55 - 4.78), free thyroxine 0.73 ng/dL (0.80 - 1.76), corticotropin < 1.6 pg/mL (4.7 - 48.8), cortisol 0.77 microg/dL (4.2 - 22.4), LH < 0.12 U/L (1.9 - 12.5), FSH 0.6 U/L (2.5 - 10.2), prolactin 25.94 ng/mL (2.8 - 29.2), estradiol 19.33 pg/mL (19.5 - 144.2), progesterone 0.22 ng/mL (3.34 - 25.56), somatotropin 0.18 ng/mL (0 - 8), IGF-1 29.57 ng/mL (78 - 274)). Levothyroxine 25 mcg per day was also initiated. Diuresis of 3000 ml in 12 hours and hypernatremia of 159 mmol/L were recorded. We suspected a insipidus diabetes of central origin, so we initiated desmopressin 10 mgcs every 12 hours oral.

The patient was admitted to the Intensive Care Unit pending surgery and 6 mg of dexamethasone intravenously every 8 hours was started.

Table 1. Physical exam.

Gender	Female
Age	39 years old
Blood pressure	130/72 mmHg
Neurological exam:	
Conscience	Alert
Campimetry	Decrease in visual acucity
Fundus opthalmoscopy	Normal
Sensitivity exam	Normal
Motor exam	Normal
Cardiovascular exam:	Normal

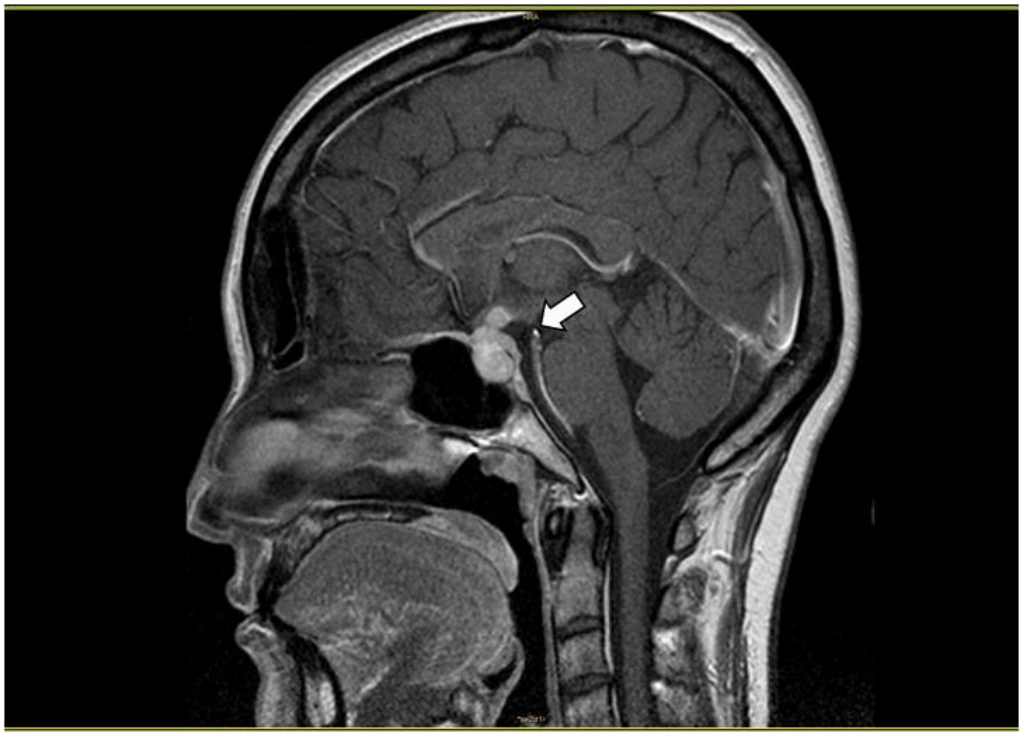

Figure 1. Initial RMI. The first RMI shows an heterogeneous pituitary gland, increased of size, about 18 × 12 × 15 mm of diameter, with globular aspect. After administration of intravenous contrast, an heterogeneous enhancement of the pituitary gland is observed. The pituitary stalk shows an important thickening and lengthening from its insertion to the tuber cinerum, with marked enhancement after administration of contrast. The pituitary stalk has a maximum diameter of 7 mm and compresses the optic chiasm. These features sugest a lymphocytic hypophysitis.

After seven hours of the onset of dexamethasone, the patient had a normalization of the visual acuity, so surgical treatment was postponed and lymphocyte hypophysitis was suspected. In the next 7 days, the patient improved significantly, with a complete recovery of visual acuity and subsequent normalization of the hormonal axes (see **Table 2**), which allowed a progressive reduction of corticosteroid therapy. Moreover levothyroxine was discontinued.

A control pituitary MRI was performed, revealing a total normalization of the size and signal of the infundibular stalk and adenohypophysis, without any evidence of focal lesions (**Figure 2**) after 12 days of treatment. The corticosteroid treatment was withdrawn after five weeks in descending pattern. The insipidus diabetes persisted and the patient maintained a proper water balance with desmopressin.

3. Discussion

Our case highlights the possible relationship between pregnancy and the development of a lymphocyte hypophysitis, and the excellent response of the lymphocyte hypophysitis to steroid treatment. This condition is more common in women than in men and about 55% of cases occur during pregnancy or postpartum [2], especially in the last month of pregnancy or in the first two months postpartum, as happened in our case.

The most frequent presentation form is headache and impaired visual acuity, as described by Gutenberg *et al.* [3]. The average age in their group of patients was 36 years, similar to our case and hormone deficiency was found in 94% of patients.

Upon arrival to the emergency unit, the first suspected diagnosis was pituitary apoplexy, because it is frequent in peripartum period and the symptoms are the same. In our case the MRI and the spectacular response to corticosteroid treatment oriented the diagnostic and helped us avoid an unnecessary surgery.

The first hormone alteration in our patient seemed to be the hypoprolactinaemia, evidenced by the impossibility of breastfeeding. In most of the cases hyperprolactinemia [2] [4] is observed, due the compressive effect.

Table 2. Hormonal evolution after initiation of corticosteroid therapy.

Hormone	Day 1	Day 3	Day 5	Day 10	Normal range
TSH (mU/L)	0.14	4.34	2.86	1.55	0.55 - 4.78
T4 free (ng/dL)	0.73	0.88	1.29	1.29	0.80 - 1.76
ACTH (pg/mL)	<1.6	28.41	13.79		4.77 - 48.8
Cortisol (microg/dL)	0.77	14.58	25.92	12.16	4.22 - 22.4
LH (U/L)	<0.12	2.94	7.75	0.31	1.9 - 12.55
FSH (U/L)	0.6	7.09	15.68	5.63	2.5 - 10.2
Prolactine (ng/mL)	25.94	15.86	28.34	21.65	2.8 - 29.2
Estradiol pg/mL	19.33	<11.8	<11.8	22.59	19.5 - 144.2
Progesterone (ng/mL)	0.22	0.37	0.46	0.36	3.34 - 25.56
GH (ng/mL)	0.18	0.28			0 - 8
IGF-1 (ng/mL)	29.57	94.26			78 - 274

Abbreviations: TSH: thyrotropin; T4 free: free thyroxine; ACTH: corticotrophin; LH: luteinizing hormone; FSH: follicle stimulating hormone; GH: somatotropin; IGF-1: insulin-like growth factor 1.

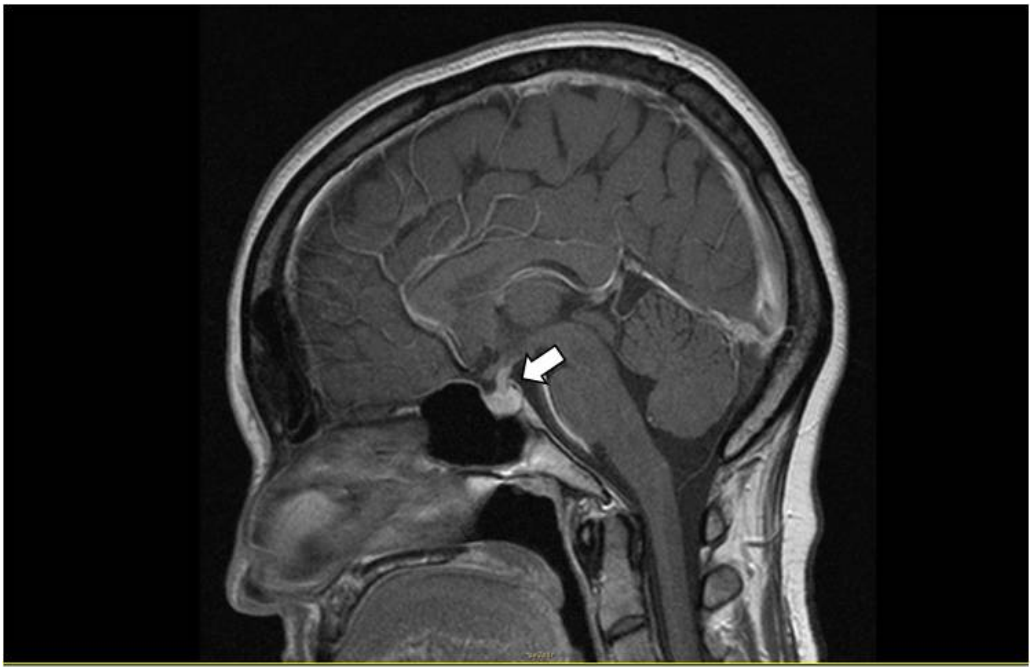

Figure 2. RMI after 12 days of corticosteroids treatment. After 12 days of treatment we can observe normalization of size and signal intensity of the anterior pituitary and the infundibular stalk.

However it is estimated that in up to 11% of cases inhibition of lactation can be found [1]. The following axis affected was the corticotropin, which is characteristic of hypophysitis. In fact, according to the Luppi's revision this is the most frequently axe affected, seen in about a 42% - 65% of all the patients with lymphocytic hypophysitis [4]. Note that this can be a feature to differentiate between a hypophysitis and a pituitary adenoma, in which corticotropin is the last hormone affected (**Table 3**). Insipidus diabetes unmasks in fund ibuloneurohipofisits, which was observed on MRI, probably caused by autoimmune destruction of the neurohypophysis.

The CT scan only showed an expansive lesion at sellar and suprasellar level, unable to differentiate between

Table 3. Differences between hypophysitis and pituitary adenoma. Adapted from (6).

Characteristics	Hypophysitis	Adenoma
Related to pregnancy	Yes	No
First axe afected	Adrenal	Somatotropic
Volume	<6 cm^3	>6 cm^3
Gadolinum enhancement	High	Low
Symmetry	Symmetric	Asymmetric
Posterior pituitary bright	Conserved	Lost
Stalk size	Enlarged	Normal

an adenoma or hypophysitis. However, MRI is the "gold standard" for the study of hypophysitis. The pituitary gland was enlarged and globular with heterogeneous enhancement after intravenous contrast administration. A significant thickening of the pituitary stalk was observed. According to the series of Imber *et al.* radiological changes are found in 90% of patients [5]. The most frequently found radiological sign is the uniform contrast enhancement and the thickening of the pituitary stalk (60% and 66% of patients respectively).

Currently there is no radiological finding with sufficient specificity to distinguish a hypophysitis of a pituitary adenoma. Therefore, it has been proposed a radiological score [6] based on the presence of radiological signs and clinical features (related to pregnancy, volume and symmetry of the pituitary mass, signal strength, homogeneity of the signal after administration of gadolinium, brightness presence of the posterior pituitary gland, the pituitary stalk size and thickness of the mucosa). The sum of this items help to differentiate between a hypophysitis or a pituitary adenoma. The score in our case was −8, which was indicative of hypophysitis.

The inicial reason for starting corticosteroid treatment in our patient was the adrenal insufficiency. The unexpected resolution of headache and visual deficit in less than 12 hours orientated to the diagnostic of lymphocyte hypophysitis. Lupi *et al*. reviewed 40 patients with hypophysitis treated with glucocorticoids [4]. A reduction in the size of the adenohypophysis was found in 87% of patients treated with oral corticosteroids, the function of the adenohypophysis improved in 46% of these patients and the function of the neurohypophysis in 18%. 75% of patients treated with endovenous glucocorticoids had a reduction in the size of the hypophysis, the adenohypophysis function improved in 54% of patients and the neurohypophysis function in 66%. In our patient, all the symptoms improved and so did the majority of the hormone deficiency, except diabetes insipidus. We should emphasize that the pituitary stalk was normalized in the MR.

The amelloriation with glucocorticoid therapy manifest the autoinmune etiology of the hypophysitis, and probably other inmunosupressive drugs could be use in these cases. Glucorticosteroids improve compression symptoms and sustitues the adrenal axis. This treatment must be valorated in patients with lymphocyte hypophysitis and probably surgery could be avoided in many cases.

Although we don't dispose of an anatomic pathological exam for an accurate diagnosis, the clinical features, MRI images and the response to corticosteroids, strongly suggests the diagnostic of a lymphocyte hypophysitis. As mentioned previously, about half of the cases of lymphocytic hypophysitis occurred around pregnancy [7]. Several arguments have been exposed for this. Among them, the most accepted theory is the existence of autoantigens that react with both the placenta and the pituitary gland. In 1998 Decrock demonstrated that up to 70% of patients with biopsy-proven of lymphocyte hypophysitis showed autoantibodies against cytosolic protein 49 kDa [8]. However, this antibody was also found in patients with other autoimmune diseases or pituitary alterations. O'Dwyer found that another antibody, the neuronal specific enolase (NSE), is expressed in both pituitary and placenta cell [7] [8]. It seems that there is a theoretical basis that explains the predilection of the peripartum period for lymphocyte hypophysitis. However more studies are needed to verify this theory.

4. Conclusion

Lymphocyte hypophysitis is a rare disease that occurs preferentially in women in the peripartum period. We should suspect it if we found a patient with a pituitary lesion, compression symptoms and hormone deficiency. In this situation early initiation of high doses of systemic corticosteroids may avoid unnecessary surgery.

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