Lymphocytic hypophysitis
Case report

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Lymphocytic hypophysitis is a very unusual disease typically observed in the peripartum period but found also in non-pregnant women or in men. We report the case of a 50-year-old woman with a five-year history of erithema nodosus for which was treated with variable doses of steroids. One year before admission the patient began to complain of headache, amenorrhea and rapidly progressive hypopituitarism. Magnetic resonance imaging showed an expanding sellar mass with homogeneous contrast enhancement while lacking the hyperintense signal of posterior lobe. The MRI findings and the history of autoimmune disease raised the suspicion of hypophysitis. The growth of the lesion and its unresponsiveness to the prolonged steroid therapy made surgery, which is both diagnostic and therapeutic, mandatory. The pathogenesis, diagnosis and management of this unusual clinical condition are discussed.


Key words: Adrenal cortex hormones therapeutic use - Lymphocytic hypophysitis - Magnetic resonance imaging - Pituitary gland surgery.

Lymphocytic hypophysitis is a rare chronic inflammatory disease of the pituitary gland mainly affecting the adenohypophysis. In the literature nearly 100 cases have been reported since the first description of the entity in 1962.\textsuperscript{1-3} Typically observed during the peripartum period it may be found also in non-pregnant or postmenopausal women \textsuperscript{4-6} and in men.\textsuperscript{7-9}

The lesion is frequently associated with autoimmune disorders thus suggesting a common etiology.\textsuperscript{3}

Lymphocytic hypophysitis generally presents with hypopituitarism and/or visual disturbances as any pituitary lesions. However the clinical features and the natural history of the disease are variable thus making both the diagnosis intriguing and the management controversial.

We report the case of a woman affected by erithema nodosus who developed the disease in the menopausal period. The past medical history of the patient and the MR examination were suggestive of an inflammatory disease. The progression of hypopituitarism and its unresponsiveness to the steroid treatment prompted us to undertake the surgical option.

The pathogenesis, MRI features and the management of this rare clinical condition are discussed.

Case report

A 50-year-old female was referred to our department for evaluation of a possible pituitary tumor. In her past medical history, at the age of 44, she was diagnosed to have an erithema nodosus.

At that time the laboratory investigations disclosed an anti-DNA antibody level of 60 U/ml (normal: <30 U/ml). Since then the patient was given methylprednisolone in cycles of variable doses achieving a good disease control.

At the age of 49 she became amenorrheic and began to complain of headache while the endocrinological examinations revealed a thyroid hormone deficiency of pituitary origin requiring an oral replacement therapy (0.1 mg daily).
Fig. 1.—Coronal CT scan after contrast administration shows a homogeneously enhanced mass lesion in the pituitary fossa.

Fig. 2, 3.—Sagittal T1-weighted MRI shows a iso-intense 15 mm pituitary lesion which lacks the usual bright spot signal of the neurohypophysis. After gadolinium administration the lesion presents a homogeneous contrast enhancement.

Over the last year she has assumed alternatively 40 mg daily of methylprednisolone for 1 month and 8 mg daily for three months.

Fig. 4.—Photomicrograph of the surgical specimen showing fibrous and edematous alteration of the normal adenohypophyseal architecture with diffuse lymphocytic infiltration (H&E, x250).

On admission both the general and the neurological examinations were unremarkable.

The laboratory investigations showed a global hypopituitarism (apart from thyroid) and a prolactin level of 45 ng/ml (normal range 5-25 ng/ml). The patient was thus given also cortisone (25 mg daily). A CT scan showed a pituitary lesion with suprasellar extension intensely enhancing after contrast administration (Fig. 1).

MRI disclosed a 15 mm sellar lesion which was isointense on T1-weighted images while lacking the usually observed hyperintense signal of the posterior pituitary lobe (Fig. 2). The lesion showed an intense and homogeneous contrast enhancement after gadolinium administration (Fig. 3).

Though not excluding the diagnosis of hypophysitis, the progression of hypopituitarism and the unresponsiveness to the five-year long steroid therapy for the autoimmune disease prompted us to perform surgery.

The sella was filled with an avascular, yellowish fibrous tissue poorly demarcated from the normal gland. Most of the abnormal tissue was removed a portion of the anterior pituitary being left intact.

The pathologica examination showed diffuse infiltration of lymphocytes mostly of type T and plasma cells, fibrosis and edema (Fig. 4).

In the postoperative period the patient did well while developing a permanent diabetes insipidus controlled by the administration of DDAVP (0.025 twice daily).

At a one-year follow-up examination both the global hypopituitarism and the diabetes insipidus were unchanged thus requiring permanent hormonal replacement therapy.

MRI performed one and three years after surgery do not show any residual or recurring inflammatory tissue.
Discussion and conclusions

Lymphocytic hypophysitis usually presents as a pituitary mass causing hypopituitarism and/or visual disturbances. Since their rarity and the lack of a firm diagnostic pattern these lesions are generally regarded as NF pituitary adenomas. In the presence of a pituitary mass the features suggesting the diagnosis of lymphocytic hypophysitis are its occurrence in the peripartum period and its frequent coexistence with autoimmune disorders due to a probably common etiology.

In fact a review of previously published reports shows that nearly 20% of patients affected by lymphocytic hypophysitis present with a history of autoimmune disorders. Among them the most common disorder seems to be primary hypothyroidism secondary to chronic lymphocytic thyroiditis. Other diseases include adrenalitis and pernicious anaemia.

Evidence for an autoimmune etiology derives also from the frequent identification in the affected patients of organ-specific antibodies including antipituitary, antimitochondrial, antiparietal and antinuclear.

Neuroimaging studies do not show diagnostically patognomonic features. CT scan may only reveal aspecific signs of an expanding sellar mass.

MRI is the more accurate diagnostic tool though not many cases have been studied by this examination. An analysis of such cases shows however that there are no conclusive diagnostic criteria to differentiate between hypophysitis and pituitary adenomas.

The lesions are generally isointense on T1-weighted images while showing a quite homogeneous enhancement after contrast administration. Despite some lack of agreement most of the authors think the loss of the hyperintense bright spot signal of the neurohypophysis and the thickening of the pituitary stalk are the other MR features suggesting the presence of hypophysitis.

Also our case presents many of these features thus supporting the previous observations of most of authors.

The diagnosis is only made histologically. All the affected pituitaries reveal a typical polyclonal inflammatory infiltrate with a mixed T and B cell population. The differential diagnosis should include tuberculosis, sarcoidosis and giant cell granulomas. Sheehan's syndrome can easily be excluded if there is no history of complicated delivery but it may occur that some patients presumed to harbour this syndrome have lymphocytic hypophysitis.

Mc Keel found ultrastructural similarities between lymphocytic and granulomatous hypophysitis suggesting they may represent different phases of the same autoimmune process.

The natural history of lymphocytic hypophysitis is variable and no predictive factors regarding its course have been identified. Progressive permanent hypopituitarism tend to occur in most cases. Spontaneous resolution of the disease with partial or total recovery of the pituitary function has also been described implying that some hypopituitarism is due to a compression rather than to a cellular destruction.

On the other hand cases showing long term enlargement of the pituitary gland or recurrence of the disease have been reported.

When the presence of hypophysitis is suspected conservative care with steroids is recommended as first treatment modality in the absence of gross visual disturbances.

The efficacy of steroids is however uncertain as also our case well illustrates. This may due to the fact that steroids are effective only in the early inflammatory stage of the disease. When the pituitary tissue is destroyed and replaced by fibrosis it becomes unresponsive to steroids. In the
absence of a presumptive diagnosis surgery which is both diagnostic and therapeutic is to be recommended.

In conclusion though very rare lymphocytic hypophysitis should be considered in the differential diagnosis of pituitary lesions especially in females in the peripartum period and in those patients with a coexisting autoimmune disease. The diagnosis can be established only by a pathological examination but in certain circumstances the knowledge of this entity will allow to undertake a possible successful trial of conservative therapy.

References


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Comments

Lymphocytic hypophysitis is a very rare pathologic condition which presents dur-
ing pregnancy or shortly after delivery with symptoms of pituitary insufficiency.

The lesion can be recognized by MRI: it shows contrast enhancement but cannot be easily differentiated from a pituitary adenoma.

Histologically the main feature is the occurrence of lymphocytes and occasional plasma cells and histiocytes. The case presented in the article is a good example of such pathology, presenting a non-pregnant woman and preceded by an autoimmune disease. The last remark seems to confirm the hypothesis of an autoimmune origin of the disease, as suggested by many observations, both cellular and humoral, supported also by the presence in some cases of antibodies to pituitary tissue.

The presentation of a case of hypophysetis is very important for different reasons. First of all it stimulates clinicians to consider this pathology in the differential diagnosis of pituitary tumors. The disease, as demonstrated by the presented case, has usually a good outcome and it is conceivable that, once clinically recognized, it may be treated without surgical intervention. One hundred cases have been reported since the first description in 1962, but it is likely that the lesion may be more frequent.

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