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Lymphocytic adenohypophysitis mimicking a pituitary macroadenoma

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Abstract A 24-year-old woman developed headache and rapidly progressive visual disturbances during the last trimester of her first pregnancy. Magnetic resonance tomography (MRI) of the brain documented an intra- and suprasellar mass lesion. For preservation of vision, transsphenoidal microsurgical decompression was performed. Immediately postoperatively, visual acuity improved and hemianopia resolved. Histological examination yielded the diagnosis of primary lymphocytic adenohypophysitis. This is a rare inflammatory pituitary disease. There are no typical clinical, laboratory, or radiological findings that allow precise preoperative diagnosis. Even though this autoimmune disorder is principally steroid-responsive, an improvement of visual disturbances under steroid therapy cannot be predicted. Therefore, surgery is justified not only to establish the diagnosis, but also to restore vision by decompression of the optic nerves and the chiasm.

Key words Lymphocytic adenohypophysitis · Pituitary adenoma · Pituitary surgery

Since the spontaneous pregnancy rate in female pituitary adenoma patients is only 2.4% [16], the possibility of lymphocytic adenohypophysitis must be considered in pregnant women presenting with a syndrome of the optic chiasm or signs of pituitary dysfunction.[15] We demonstrate this diagnostic problem and the results of microsurgical transsphenoidal decompression in the case of a 24-year-old pregnant woman with primary lymphocytic adenohypophysitis.

Case report

Beginning in the 28th week of her first pregnancy, a 24-year-old woman developed headaches, followed by progressive visual loss. Until then, her pregnancy had been without complications. Previous medical history was uneventful, except for a subtotal thyroidectomy 14 years earlier for Graves' disease. Postoperatively, there was no need of further medication for hyperthyroidism, as the patient remained symptom-free.

The first ophthalmologic examination in the 32nd week of gestation documented a reduction in visual acuity to 0.1 in the right eye and 0.7 in the left, and perimetry revealed complete bitemporal hemianopia. MRI showed a large space-occupying lesion in the sella region with suprasellar extension and compression of the optic chiasm (Fig. 1). The posterior pituitary lobe and infundibulum were not involved.

A pituitary macroadenoma seemed to be the most probable diagnosis. However, as paramagnetic contrast-enhancing media could not be applied, differentiation between the lesion and normal pituitary tissue was impossible. Prolactin serum concentration was within normal values for the 32nd week of gestation (60.1 ng/ml), thus excluding a prolactinoma. There were no clinical signs of thyroid dysfunction, endocrine ophthalmopathy, or pituitary insufficiency.

As rapid further deterioration of visual acuity was observed, the indication for surgical decompression of the chiasm was given. Using a transsphenoidal approach, selective microsurgical removal of the lesion was performed. Pre- and perioperative obstetrical examinations, including intraoperative monitoring of the cardiocotogram, were normal. Intra- and postoperative treatment with fenoterol (Partusisten) was carried out to prevent premature labor.

The tissue obtained at transsphenoidal surgery was found macroscopically to be remarkably solid. Histologically, all types of pituitary cells were present in normal physiological proportions.
Fig. 1a, b Preoperative T1-weighted MRI scans show an intra- and suprasellar space-occupying lesion distorting the optic chiasm. a Coronal (TE 20, TR 450); b sagittal (TE 20, TR 560). The neurohypophysis is visible at the lower posterior bottom of the sella. A differentiation between normal pituitary tissue and the lesion in unenhanced MRI scans is impossible, but the use of paramagnetic contrast-enhancing media (Gd-DTPA) was also impossible due to pregnancy with enlargement of chromophobe cells, a normal observation during pregnancy. However, there was considerable lymphocytic inflammation with fibrosis, and lymphocytic adenohypophysitis was diagnosed (Fig. 2).

Postoperatively, rapid and complete restoration of visual acuity and visual field defects was observed. An episode of symptomatic diabetes insipidus subsided spontaneously after 10 days of treatment with antidiuretic hormone (ADH). No signs of pituitary insufficiency were present upon discharge from the hospital. Six weeks later, the patient gave birth to a healthy child. Follow-up MRI scan 5 months postoperatively showed no signs of local recurrence (Fig. 3). For a follow-up period of 2 years, vision remained normal and there were no symptoms of pituitary insufficiency. However, due to recurrence of Graves' disease 18 months postoperatively, thyrostatic medication with carbimazole 10 mg/d was necessary.

Discussion

The incidence of pituitary adenomas is linked to age and increases with each decade, reaching 20% at the age of 80 [1]. In comparison, inflammatory diseases of the hypophysis are the exception. They comprise bacterial and granulomatous inflammations, secondary inflammatory reaction to tumors in the sella or perisellar region, and lymphocytic adenohypophysitis [2, 9, 17].

Lymphocytic adenohypophysitis is a rare, non-neoplastic cause of pituitary enlargement and insufficiency. So far, approximately 70 cases have been described. Its etiology is unknown, but an autoimmune mechanism is suspected [8], as antibodies against pituitary gland tissue are present in some patients [20] and association of the disease with autoimmune disorders such as Hashimoto's thyroiditis is observed [7, 14].

The morphologic alterations begin with enlargement of the hypophysis due to inflammation and proceed to atrophy of the anterior pituitary gland, with destruction of the endocrine tissue and its replacement by fibrosis and subsequent panhypopituitarism [5]. Rapidly progressive visual loss may be the result of suprasellar extension of the inflammatory pituitary swelling and the resulting compression of the optic nerve and chiasm [16, 18]. Without treatment, the disease may progress to pituitary insufficiency and death [6].

However, the features of endocrinological disturbances are not uniform: pituitary insufficiency is the most frequent symptom, but cases of hyperprolactinemia and isolated corticotropin deficiency were also described [4, 11]. As in the present case, the inflammation usually spares the neurohypophysis. In single cases of adenohypophysitis with concomitant central diabetes insipidus, biopptic specimens from the posterior pituitary lobe showed inflammatory alterations similar to those of the anterior pituitary gland [10, 12, 19].

Lymphocytic adenohypophysitis occurs predominantly in women, most often in association with pregnancy or the immediate postpartum period. As pituitary adenomas are infrequent in pregnant women (the spontaneous pregnancy rate in female pituitary adenoma patients is only 2.4% [16]), the possibility of lymphocytic adenohypophysitis must be considered in pregnant women presenting with an optic chiasm syndrome or signs of pituitary dysfunction.

However, clinical differentiation between pituitary adenoma and inflammation is difficult. Due to the more rapid growth of the inflammatory lesion, visual disturbances (i.e., loss of visual acuity and development of bitemporal hemianopia) are more frequent in hypophysitis [16] than in adenoma. The development of headache and other signs of meningeal irritation is caused by distension and distortion of the dura mater and the diaphragma sellae by the growing pituitary lesion [13] and therefore seems to be more often associated with inflammation than with neoplastic growth [9]. Pituitary insufficiency is frequently seen in hypophysitis, but is not a prerequisite [2].

Radiological examinations, especially MRI, do not allow a differentiation between tumor and inflammation, as specific neuroradiological findings cannot be defined for inflammatory lesions of the adenohypophysitis [16]. Honegger and coworkers [9] described thickening of the sphenoid sinus mucosa, enlargement of the pituitary stalk, and a tongue-shaped extension of the lesion along the basal hypothalamus as typical MRI findings in hy-
Fig. 3a, b Native MRI scans 5 months after transsphenoidal resection of the lesion. The hypophysis and contrast-enhanced infundibulum are visible at the bottom of the sella. a T1-weighted coronal view (TE 20/TR 450); b Gadolinium-enhanced sagittal view (TE 20/TR 500) showing optic nerve completely decompressed. There are no signs of recurrent inflammatory disease.

hypophysitis. However, these radiological signs are not pathognomonic.

For example, enlargement of the pituitary stalk is not a sign of adenohypophysitis, but of infundibuloneurohypophysitis, a distinctly different clinical entity with its own characteristic MRI findings [2]. In contrast to lymphocytic adenohypophysitis, necrotizing infundibulohypophysitis also typically affects the pituitary stalk and induces primary central diabetes insipidus [2], and histological examination discloses a distinct pattern of changes with necrosis, fibrosis, and chronic inflammation [2]. In the absence of pathomonic neuroradiological findings, lymphocytic adenohypophysitis remains a histopathological diagnosis.

Our patient presented in the last trimester of her first pregnancy with symptoms typical of a space-occupying pituitary lesion. Her main complaints were headache and a rapid loss of visual acuity. MRI demonstrated an intra- and suprasellar lesion compressing the optic nerve and chiasm that was highly suspect of pituitary macroadenoma. MRI was also necessary to rule out endocrine ophthalmopathy, as Graves’ disease was known from the patient’s former medical history. Since prolactin levels were within normal ranges for the stage of pregnancy, a prolactinoma was improbable. With headache as an unusual symptom of pituitary adenoma [9], hypophysitis was taken into consideration, but there were no signs of complete or partial pituitary insufficiency. A definite diagnosis of hypophysitis on the basis of clinical, laboratory, and radiological findings was impossible.

As visual loss continued during the period of diagnostic tests, we refrained from a diagnostic trial with steroids and proceeded immediately to surgery in order to preserve or restore vision. Immediately after decompressive surgery, considerable amelioration of vision was observed. The diagnosis of lymphocytic adenohypophysitis was established by histological examination of the resected tissue. Postoperatively, an episode of central diabetes insipidus occurred that resolved after 10 days of ADH analogue treatment. Because preoperative MRI had documented an intact neurohypophysis (Fig. 1) and the patient had been asymptomatic in this respect until surgery, we considered this symptom to be related to surgical manipulations and not to a concomitant neurohypophysitis.

After the uncomplicated delivery of a healthy child, the patient remained asymptomatic for signs of recurrent hypophysitis or hypophysseal insufficiency for a clinical and neuroradiological follow-up period of 2 years. This is remarkable, as recovery of pituitary function after surgery for hypophysitis is considered to be unlikely [9]. Lymphocytic hypophysitis is probably an autoimmune disease principally responsive to steroid treatment [18]. Therefore, in cases of suspected autoimmune hypophysitis in pregnancy, a therapeutic trial with steroids is recommended by several authors [3, 6, 15, 20]. However, the success of steroid therapy cannot be predicted, and recurrence of visual disturbances after reduction of the steroid dose has been reported [18]. In cases of rapidly progressive visual loss from compression of the optic pathways, losing time with a therapeutic trial of steroids is not justified. On the contrary, transsphenoidal microsurgical decompression is the method of choice for these patients, as vision dramatically improves immediately after surgery [18]. Only in patients with suspected hypophysitis whose vision is not threatened does a trial of steroids seem to be justified [15].

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References