**Skull base**

**Lymphocytic Infundibulo-Neurohypophysitis with Hypothalamic and Optic Pathway Involvement: Report of a Case and Review of the Literature**

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**BACKGROUND**

Lymphocytic adenohypophysitis and lymphocytic infundibulo-neurohypophysitis are rare auto-immune mediated diseases of the anterior and posterior pituitary, respectively. The former usually manifests as insufficiency of anterior pituitary hormone secretion, associated in many patients with disturbances of vision. The latter presents as diabetes insipidus of central origin.

They present most commonly in pregnant or postpartum females. There have been infrequent reports in females with no association with pregnancy, and in males.

**CASE DESCRIPTION**

We present a nulliparous female with central diabetes insipidus, pan-hypopituitarism, and severely impaired vision. Magnetic resonance imaging demonstrated a large mass involving the hypothalamus, infundibulum, optic nerves, chiasm, and tracts. At operation, the optic pathways were found to be grossly involved in the inflammatory mass. Histological examination of a biopsy demonstrated a nonspecific, mixed inflammatory infiltrate, composed predominantly of lymphocytes and plasma cells. She responded dramatically to treatment with dexamethasone, with disappearance of the mass on serial imaging studies and improvement in vision. In addition, she received hormone replacement therapy.

**CONCLUSION**

We present a case of lymphocytic infundibulo-neurohypophysitis unique in the degree of optic pathway inflammatory involvement, with a documented response to steroids. © 2002 by Elsevier Science Inc.

**KEY WORDS**

Lymphocytic infundibulo-neurohypophysitis, optic chiasm, nerves, tract.

Increased awareness of chronic inflammatory lesions involving the pituitary gland and neighboring structures, and the availability of magnetic resonance imaging (MRI), have led to a growing number of reports of these conditions in the literature [15].

Though lymphocytic adenohypophysitis and infundibulo-neurohypophysitis are the commonest of these conditions [15], they remain relatively uncommon and poorly understood. Their importance lies in the possible association with serious complications such as panhypopituitarism, central diabetes insipidus, and visual impairment which, if unrecognized or treated too cautiously, can lead to significant morbidity and mortality.

**Case Report**

A 23-year-old, nulliparous female clerk presented with a 4-year history of amenorrhoea, a 4-month history of polyuria and polydipsia, and sudden loss of vision in the left eye 2 months before referral to our unit.

She denied any history of inexplicable fatigue, heat or cold intolerance, recent unexplained changes in body weight or size of clothing, or disturbances in libido. A diagnosis of hypothyroidism was made by the family practitioner and levothyroxine sodium was prescribed 2 months before referral to our unit.
During the course of endocrine investigations an MRI scan of the brain was conducted, leading to the referral.

She was of slender build, normotensive and apyr-axial. She lacked axillary and pubic hair. The remainder of the general examination was unremarkable. She was alert and correctly oriented, with intact speech, memory, and higher functions.

The left pupil was dilated and unreactive to direct light, but reacted normally consensually. There was severe optic atrophy, with vision restricted to counting of fingers at 50 cm. The right pupil was of normal size and reacted to direct light, with no consensual reaction. There was marked optic atrophy, with visual acuity of 6/60, and a macular sparing temporal field loss. The remainder of the neurological examination was normal.

Laboratory investigations revealed a hypernatremia of 156 mmol/lt, and the serum hormone assay results were as illustrated in Table 1.

The MRI scan showed a 20 × 40 × 40 mm strongly enhancing mass involving the hypothalamus, optic nerves, chiasm, and tracts as well as the infundibulum. The adenohypophysis was not involved, and the usual enhancement of the posterior pituitary was preserved (Figure 1).

Initial treatment consisted of cortisone and des-
mopressin nasal drops, with levothyroxine sodium re-introduced once the serum cortisol level had been corrected. In addition, she was placed on a contraceptive pill (Demulen®, Searle) by our endocrinologists.

Once her metabolic and endocrine parameters were satisfactory, a right pterional craniotomy was performed. A firm mass, pinkish grey in color with gross enlargement of the distal optic nerves, chiasm, and proximal tracts, was encountered. A biopsy was taken from the inferior part of the expanded chiasm. Histological examination revealed extensive inflammation with lymphocyte and plasma cell infiltrate. Occasional neutrophils and foci of haemorrhage were present. There were no features of granuloma or neoplasia.

Owing to concern about the accuracy of the biopsy, associated with worsening of the radiological picture (Figure 2), the procedure was repeated after 2 months. Once again, the histology showed inflammatory infiltration with lymphocytes and plasma cells. Treatment with dexamethasone was begun and hormone replacement therapy continued.

Over the next 4 months, there was a dramatic reduction in size (Figure 3) and, finally, disappearance of the mass (Figure 4), with improvement in the vision of her right eye to an acuity of 6/18, though with persistence of the macular sparing temporal field loss. The vision in the left eye remained unchanged. This improvement persisted after the dexamethasone was gradually withdrawn.

She remains on cortisone, levothyroxine sodium, and desmopressin nasal drops, and is followed by the Endocrine as well as Neurosurgical outpatient departments.

**DISCUSSION**

Lymphocytic adenohypophysitis and lymphocytic infundibulo-neurohypophysitis are two distinct conditions [19]. Both are believed to be autoimmune diseases [16], and are regarded as part of the spectrum of autoimmune diseases such as autoimmune thyroiditis [7], pernicious anaemia [10], organ specific antibodies including anti-pituitary an-
tibodies [13], anti-mitochondrial [2], anti-parietal [14], and antinuclear antibodies [8].

They occur predominantly in females in pregnancy or the postpartum period. Six cases in males have been reported [12], as have thirteen in females unrelated to pregnancy [3,6,18,19,20]. Lymphocytic adenohypophysitis usually presents as a large mass with visual impairment and hormonal disturbances, while lymphocytic infundibulo-neurohypophysitis presents as a small mass with no visual impairment [9,18].

The histological features of these lesions are characterized by lymphocytic infiltration, destruction of the normal organoid pattern, and replacement by fibrosis [15,19].

Lymphocytic adenohypophysitis may cause hypopituitarism and visual impairment. Diabetes insipidus is uncommon, the neurohypophysis reported to being normal in most cases [4,15].

By contrast, lymphocytic infundibulo-neurohypophysitis, is known to be a cause of central diabetes insipidus [18], with inflammation restricted to the neurohypophysis and infundibulum [9], the adenohypophysis usually being spared on MRI imaging and histological examination [11]. The natural course is progression from inflammatory enlargement of the pituitary stalk or posterior pituitary gland to fibrosis and atrophy of these structures. No cases of spontaneous recovery have been reported [19].

Necrosis is not a feature of lymphocytic hypophysitis, but has been reported in two cases of lymphocytic infundibulo-hypophysitis. These have been labeled as necrotizing infundibulo-hypophysitis [1]. Compared to the majority of reported cases, our patient appears to differ in certain respects. There was no association with pregnancy [3,6,20]. She presented with both pan hypopituitarism and diabetes of central origin. In this regard she differs from the commonly described clinical picture in which partial or complete hypopituitarism accompanies lymphocytic adenohypophysitis, while lymphocytic infundibulo-hypophysitis is associated with central diabetes insipidus [15]. In addition, a large mass was present with profound visual impairment, as opposed to the usual small mass...
without visual impairment described as being typical findings in lymphocytic infundibulo-neurohypophysitis [9,18]. The visual impairment appears to have been because of direct inflammatory involvement of the optic nerves, chiasm and tracts rather than compression of these structures. Visual impairment in this condition has hitherto been regarded as being because of compression of the optic pathways by the inflammatory mass [4,15]. As far as we are aware, actual direct involvement of the optic pathways noted on neuroimaging and confirmed at operation has not been described before.

Biopsy or chiasmal decompression in the presence of impaired vision, accompanied by appropriate pre- and postoperative hormone replacement, is usually advised [5]. It has been recommended, though, that at least for some cases—especially those related to pregnancy, with consistent clinical findings, supportive laboratory results, and non-responsiveness to bromocriptine—where appropriate, a presumptive, noninvasive diagnosis may be made and corticosteroid therapy instituted along with appropriate hormone replacement, provided there is no visual compromise necessitating decompression [4,15]. This patient responded very well to a course of dexamethasone, suggesting that steroid treatment was effective in the treatment of lymphocytic infundibulo-neurohypophysitis as it is in the more common lymphocytic adenohypophysitis [19].

REFERENCES


COMMENTARY

Lymphocytic adenohypophysitis is a rare idiopathic lymphocytic inflammatory condition confined to the pituitary gland (lymphocytic hypophysitis). The process can involve the pituitary-hypothalamic axis. It occurs predominantly in women, usually during pregnancy or postpartum [1,2,5]. The pituitary gland is infiltrated with lymphocytes and plasma cells, with scattered eosinophils and histiocytes [4]. In most cases, the lymphocytes are mostly CD4 cells [4], and there is evidence of panhypopituitarism. Diabetes insipidus can be caused by lymphocytic infundibuloneurohypophysitis. In most cases of lymphocytic hypophysitis, there is evidence of hypopituitarism. Amenorrhea is the most common initial symptom [4,5]. In
some women the disorder first becomes evident during pregnancy [5]. CT and MR imaging often show marked uniform contrast enhancement of an enlarged pituitary gland, resembling a macroadenoma [5]. There may be only enlargement of the infundibulum or infundibulo-hypothalamic axis. Imura et al [4] have reported 17 patients with idiopathic diabetes insipidus. In all patients, the normal hyperintense signal of the neurohypophysitis on T1-weighted images was not seen. In addition, 9 of 17 patients had thickening of the pituitary stalk, enlargement and enhancement of the neurohypophysis, or both on MR imaging. Imura et al called this entity “lymphocytic infundibuloneurohypophysitis.” The natural course of the disease suggested a self-limited process. They concluded that lymphocytic infundibuloneurohypophysitis is a common cause of what was previously considered to be idiopathic (autoimmune) diabetes insipidus. Antibodies against magnicellular neurons of the hypothalamus have been detected in some patients with secondary diabetes insipidus, leading to speculation that it is an autoimmune disorder [4,5]. They also stated that this entity is probably not a variant of lymphocytic hypophysitis. It is, however, possible that the two entities are related, with one affecting the anterior pituitary and the other having the posterior as the principal site of inflammation. Other causes of a thickened infundibulum and hypothalamus associated with contrast enhancement on CT and MRI include sarcoidosis, tuberculosis, lymphoma, Langerhans cell histiocytosis, intracranial plasma cell granuloma, germinoma, granular cell tumor (granular myoblastoma), and metastasis.

Ouma et al report an excellent case of a lymphocytic infundibuloneurohypophysitis with hypothalamic and optic pathway involvement. It is important to realize that the CT and MRI appearance of sarcoidosis, Langerhans histiocytosis, and lymphoma may be identical to lymphocytic adeno-
opophysitis with involvement of the hypothalamus and optic pathways as well. It is also important to remember that occasionally meningiomas may contain plasma cell and lymphocytic components [3] that may cause a diagnostic problem.

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REFERENCES

Lymphocytic adenohypophysitis and lymphocytic infundibuloneurohypophysitis, although rare entities, are usually evaluated and treated by the endocrinologists. These entities are even less commonly seen by the neurosurgeon—as in this case, when the clinical problem has been progressive loss of vision and the diagnosis is in question (i.e., tumor versus inflammatory etiology).

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The policy of being too cautious is the greatest risk of all.

—Jawaharlal Nehru