SHORT REPORT

Lymphocytic hypophysitis: can open exploration of the sella be avoided?

AVINASH PRASAD,1 VIJAY S. MADAN,1 PRAHALAD K. SETHI,2 MANJU L. PRASAD,3 TARVINDER B. S. BU XI,4 & CHANDRA K. KANWAR,3

Departments of 1Neurosurgery, 2Neurology, 3Pathology and 4Radiology, Sir Ganga Ram Hospital, New Delhi, India.

Abstract
A case of lymphocytic hypophysitis (LYHY) in a menopausal woman is presented. A review of the literature suggests that conservative treatment may be tried in suspected cases of LYHY, if the vision of the patient is not threatened. A transphenoidal stereotactic biopsy of the mass may be performed if the patient fails to improve or deteriorates, thus avoiding open exploration of the sella in selected cases.

Key words Autoimmune disease, hypopituitarism, lymphocytic hypophysitis, pituitary tumour.

Introduction
To date, 10 cases of lymphocytic hypophysitis (LYHY) have been diagnosed at autopsy and 21 cases, including the present case, have been operated upon.1 An additional two cases have been described in the Japanese literature.2,3 Zeller et al.4 and Ikeda and Okudaira5 have reported two suspected cases of LYHY successfully treated with hormone replacement alone. Lack of a tissue diagnosis has deterred clinicians from favouring a conservative approach. With increased awareness, improved diagnostic facilities and safer operative techniques a definite increase in the incidence of various types of sellar lesions, including LYHY, has been noted. The aim of this study was to review the surgically proved cases of LYHY to identify the best form of management.

Case report
A 44-year-old hypertensive lady was admitted for evaluation of continuous moderate to severe headache for 2 years, amenorrhea for one year and impaired vision for one month. There was no other symptom of endocrine dysfunction. The visual acuity was 6/12 in both eyes. There was bitemporal hemianopsia. The optic fundi showed temporal pallor. Routine haematological and biochemical investigations revealed no abnormality except an erythrocytic sedimentation rate of 85 mm/h. Endocrine evaluation was done using standard radioimmunoassay kits. Serum T3 was 57 μg/dl (normal 70–200), T4 was 0.4 μg/dl (normal 5.5–13.5) and TSH was 4.4 μU/ml (normal 0–6.0). Morning and evening plasma cortisol levels were 0.20 μg/dl (normal 4–26) and 0.05 μg/dl (normal 2–14) respectively.
FSH was 2.2 mIU/ml and LH was 0.2 mIU/ml. Serum PRL was 1.1 ng/ml (normal 0–20) and GH was 0.4 ng/ml (normal 0–7). Dynamic pituitary function tests were not performed. The IgG level was 1086 mg/dl (normal 712–1550), IgA was 281 mg/dl (normal 120–220) and IgM was 165 mg/dl (normal 65–170). Rheumatoid and antinuclear factors were negative. Antibodies to pancreatic islet cell, parietal cell, smooth muscle, thyroid microsomal and thyroid antigens were negative. Radiographs of the skull revealed an enlarged sella turcica. A computed tomographic (CT) Scan showed a well-circumscribed sellar and suprasellar contrast enhancing mass (Fig. 1). A diagnosis of endocrinologically inactive pituitary adenoma was made.

A right frontotemporal craniotomy was performed and a greyish-white, firm mass was seen arising from the pituitary fossa, compressing the optic chiasma. The pituitary capsule was dense and firmly adherent to the underlying mass. The mass could be partially removed with sharp dissection. The frozen section biopsy specimen could not rule out a pituitary adenoma. Histopathological sections of the anterior pituitary gland showed extensive infiltration by chronic inflammatory cells, predominantly lymphocytes. A small number of plasma cells and some lymphoid follicles without germinal centres were also identified (Fig. 2). Special stains for bacteria, fungi and acid-fast bacilli were negative.

Deparaffinized tissue sections were studied with the avidin-biotin complex technique using rabbit antihuman TSH (B subunit), LH (B subunit), GH and ACTH antisera. The presence of immunoreactive GH and TSH was noted. Staining with LH and ACTH antisera was negative.

One week after the operation, the patient's visual field became completely normal and headache disappeared. She was discharged on prednisone and thyroxine. Pituitary function tests were carried out one year after surgery. Serum T3, T4 and TSH were noted to be 191 µg/dl, 6.20 µg/dl and 0.05 µg/ml, respectively. Morning and evening cortisol levels were 0.20 and 0.10 µg/dl, respectively. Another CT scan at this time revealed a small enhancing mass in the sella (Fig. 3). At about 2 years post-operative follow-up, the patient is asymptomatic and requires only prednisone replacement.

Discussion

LYHY is a rare autoimmune disease leading to a diffuse lymphocytic non-granulomatous infiltration of the adenohypophysis. This dis-
order occurs mainly in females in temporal relation to pregnancy and presents with symptoms of hypopituitarism⁶,⁷ and a contrast enhancing sellar mass with variable extensions. Notwithstanding the subtle clinical and endocrinologic differences between a pituitary adenoma and LYHY, the diagnosis in the majority of cases of hypopituitarism with an enhancing sellar mass remains an enigma.¹ The differential diagnosis includes non-functioning pituitary adenoma, granulomatous hypophysitis, sarcoid granuloma, tuberculosis and LYHY. Magnetic resonance imaging studies, in a limited number of such cases, has not been found to be useful. Anti-pituitary antibodies have been observed in only two of the five cases in which it has been studied. The significance of these antibodies is not very clear since they have also been found in normal post-partum women.⁸,⁹ Thus at the present time, in spite of a strong clinical suspicion, a tissue diagnosis becomes indispensable in selected cases where conservative treatment fails.

The criteria for diagnosis of a clinically highly probable case of LYHY should include:

1. gestational or post-partum hypopituitarism, especially after a delivery uncomplicated by excessive haemorrhage or hypotension; and
2. presence or absence of a contrast enhancing sellar mass (the sellar mass has been found to be contrast enhancing in all 14 LYHY cases, including the present one, in which a enhancing CT was done).

In the above clinical setting, if a patient suffers from headache or minor visual symptoms, he/she should be given supportive treatment and observed closely without surgical

**Hypopituitarism with Sellar Mass**

(Without associated Hyperfunction)

- **Gross Visual Impairment**
  - **Yes**
    - Subtotal Decompression
  - **No**
    - Conservative
      - No Improvement/ Deterioration
        - Transsphenoidal Stereotactic Biopsy
          - Improves
          - Follow-up

*Fig. 4. Management paradigm for a case of hypopituitarism without any evidence of hyperfunction.*
intervention. In cases of acromegaly, serious visual impairment and severe hyperprolactinaemia the conservative treatment is contraindicated. Radiological and endocrinological progress of the patient should be observed carefully. A trans-sphenoidal stereotactic biopsy may be performed if the patient fails to improve or deteriorates neurologically or radiologically. The subsequent management should depend on the tissue diagnosis. In cases of pituitary adenoma, a second stage radical or total decompression of the mass may be performed. In 10 out of 21 operated cases of LYHY the visual symptoms were absent or minimal and thus an open exploration of the sella was, in our opinion, unwarranted. A tissue diagnosis could have been achieved by a trans-sphenoidal stereotactic biopsy avoiding the inherent risks of an open exploration of the sella. When the vision is threatened, a subtotal decompression is desirable.\textsuperscript{6,10} A total decompression, in fact, may lead to an irreversible worsening of the pre-existing hypopituitarism.\textsuperscript{6,10} The management paradigm shown in Fig. 4 may avoid this complication in a selected group of patients with granulomatous hypophysitis, tuberculosis, sarcoid granuloma and LYHY. The present case emphasizes the inability of ancillary tests to confirm the diagnosis, and that the tumour appears to resolve with time, but the endocrine function rarely returns.

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References

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