Case report

A 33 year old woman in her second pregnancy developed frontal headaches at 29 weeks of gestation. Her pregnancy had previously been uneventful. Her first pregnancy had ended in a spontaneous miscarriage at eight weeks of gestation. She had no past history of migraine and was otherwise asymptomatic. There was no family history of autoimmune disease. Her blood pressure was normal and there was no proteinuria.

In the 33rd week of pregnancy, her headaches became persistent, more severe on awakening and were accompanied by vomiting. We recommended computed tomography or magnetic resonance imaging of the brain but she declined investigation because of the perceived radiation risk. Her pregnancy progressed uneventfully until term, when following the development of an abnormal cardiotocogram, she was delivered by caesarean section under epidural anaesthesia. There was no evidence of placental abruption. The weight of her infant was 2.9 kg. Her blood pressure was again normal and she had no symptoms or signs of pre-eclampsia. Her headaches persisted after delivery and were associated with visual blurring and failure to lactate. Computed tomography of the brain with contrast was performed three weeks postpartum and showed a uniformly enhancing pituitary mass with suprasellar extension (Fig. 1). Formal visual field perimetry was normal. Endocrine assays on her blood three weeks after her delivery revealed: free thyroxine 9 pmol/L (normal range 11–25 pmol/L); thyroid stimulating hormone 1.6 mu/L (0.35–5.0 mu/L); prolactin <50 mu/L (100–420 mu/L); 9:00 am cortisol <30 nmol/L ( >400 nmol/L); growth hormone 10.7 mu/L (9.5–45 mu/L); insulin-like growth factor-1 36.6 nmol/L (9.5–45 nmol/L); follicle stimulating hormone 4.2 u/L; luteinising hormone 1.3 u/L.

The reduced concentrations of free thyroxine, prolactin and cortisol suggested partial hypopituitarism related to the pituitary mass. A diagnosis of lymphocytic hypophysitis was made on the basis of the typical peripartum presentation, the pituitary mass and the endocrine investigations suggesting partial hypopituitarism. Treatment was started with hydrocortisone 10 mg at 0800 and 1500 h and thyroxine 150 mcg daily. Her headaches completely resolved over the next three days. Regular menstruation resumed two months after her delivery but she failed to lactate. Four months postpartum, magnetic resonance imaging showed complete resolution of the pituitary mass (Fig. 2). At 12 months, thyroxine was withdrawn and her thyroid function remained normal. At 14 months, following omission of the morning dose of hydrocortisone, cortisol and prolactin levels remained undetectable, indicating residual deficiency of ACTH and prolactin production. There was no serologic evidence of autoimmune disease. Two years after her delivery, physiological steroid replacement therapy is maintained and long term follow up in the endocrine clinic is planned. The woman and her partner have not yet tried for a further pregnancy and are using barrier contraception.
They have been advised that there is no contraindication to a future pregnancy.

Discussion

Lymphocytic hypophysitis was first described by Goudie and Pinkerton in 1962. One hundred and fifty-two cases have been reported and there is a marked female predilection, with 129 cases described in women of which 55% were related to pregnancy. It is thought to be an autoimmune disease, with humoral and cell mediated components resulting in destruction of the pituitary gland. The autoimmune process is generally confined to the anterior pituitary and leads to hypopituitarism and a pituitary mass. Histologic examination of the gland shows infiltration with lymphocytes and plasma cells, parenchymal destruction and fibrosis. Other autoimmune conditions such as thyroiditis, atrophic gastritis, systemic lupus erythematosus, adrenalitis and type-1 diabetes mellitus have been reported in up to 30% of cases. Anti-pituitary antibodies have not however been found consistently.

The natural history of lymphocytic hypophysitis varies, from spontaneous resolution, reported in 15 patients, to progressive hypopituitarism. Death due to adrenal insufficiency was reported in 18 cases in earlier series.

Endocrine deficiency was described in 136 of the 152 cases reported, ACTH deficiency in 82 cases, thyroid stimulating hormone deficiency in 62 cases, gonadotrophin deficiency in 59 cases and prolactin deficiency in 50 cases. Hyperprolactinaemia can also occur due to compression of the pituitary stalk by the mass. Although the disease is more commonly associated with failure of the anterior pituitary, involvement of the posterior pituitary with diabetes insipidus has been reported in 20 patients.

There are many causes of headache in pregnancy, including tension headaches, migraine and pre-eclampsia. Lymphocytic hypophysitis should be considered in the differential diagnosis in women with no evidence of pre-eclampsia who complain of headache of recent onset associated with visual impairment. Bitemporal hemianopia, which progresses over a few days, suggests an expanding pituitary mass. Amenorrhea and failure of lactation raise the possibility of pituitary insufficiency. Other symptoms of hypopituitarism including fatigue, lethargy, nausea and vomiting may be attributed to normal pregnancy.

The main diagnostic problem in a woman who has a pituitary mass or hypopituitarism during pregnancy or immediately after delivery is a pituitary tumour. With modern obstetric care, Sheehan’s syndrome is very rare and is usually a consequence of catastrophic obstetric haemorrhage. Serologic investigations should include the endocrine assays mentioned previously, with estimations of plasma glucose, urea and electrolytes. In women with polyuria and polydipsia, diabetes insipidus should be considered. Magnetic resonance imaging or computed tomography with contrast will generally reveal a homogeneously enhancing pituitary mass with suprasellar extension.

The treatment of lymphocytic hypophysitis is controversial. Spontaneous resolution and progression to pan-hypopituitarism and a fatal outcome have been described. A definitive diagnosis can be made only by biopsy. Previous investigators have supported biopsy of the pituitary mass and, in some cases, total hypophysectomy in order to obtain the correct diagnosis. Current medical opinion, however, suggests that in the typical clinical setting of the peripartum period and the characteristic endocrine deficits described in our case, biopsy may be avoided. In the absence of visual failure, pituitary replacement therapy with repeated visual field and radiologic assessment may be all that is required. High doses of corticosteroids have been used in some patients to ameliorate visual impairment, but their use has not been vigorously evaluated. Indications for surgery include progressive visual failure and uncertain diagnosis. Gonadotrophin failure has been reported in over 30% of women and hormone replacement therapy is required to induce withdrawal bleeding and to treat the short and long term effects of hypo-oestrogenism. Spontaneous conception has been reported in 10 women following lymphocytic hypophysitis in previous pregnancies. Of these, eight had no evidence of recurrent disease on computed tomography.
performed after delivery; and in two women computed tomography was not performed. Histologic diagnosis was made in seven women; five were treated with surgery and hormone replacement and two were treated conservatively with glucocorticoid and thyroxine replacement. Due to the variable natural history of lymphocytic hypophysitis, an accurate assessment of the risk of recurrent disease cannot be made. The two women who were treated conservatively had successful pregnancies and did not have recurrent disease\(^3,12\). Successful induction of ovulation with human menopausal gonadotrophin and human chorionic gonadotrophin has been reported in one woman with lymphocytic hypophysitis following resection of a pituitary mass with suprasellar extension\(^13\). She conceived in her fifth cycle of treatment and was delivered by caesarean section in the 38th week of pregnancy. Lactation began on the third postpartum day.

References


Accepted 17 July 2002