Lympohocytic hypophysitis complicated by post-partum haemorrhage

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SUMMARY. We report the anaesthetic management of a primiparous patient presenting in late pregnancy with rapidly progressive bitemporal hemianopia due to a pituitary mass caused by autoimmune hypophysitis. Caesarean section was complicated by post-partum haemorrhage. Anaesthesia is discussed together with a review of the literature on lymphocytic hypophysitis.

CASE REPORT

A 23-year-old primiparous patient was referred to our unit at 36 weeks gestation with a 4-week history of deteriorating vision. This had initially presented as decreased field of vision for which she had consulted her optician. Formal visual field testing demonstrated bitemporal upper quadrantic hemianopia but no change in visual acuity. Computerized tomography (CT) and magnetic resonance imaging (MRI) scans at her local hospital showed an enlarged pituitary gland impinging on the optic chiasm but no erosion of the pituitary fossa.

She was transferred to our unit for neurosurgical advice following a rapid deterioration of her visual symptoms. On admission, a range of investigations (full blood count, urea and electrolytes, chest X-ray and ECG) were all normal and she weighed 68 kg. She underwent a series of endocrinological blood tests which showed plasma prolactin of 2410 mU/l (compatible with late third trimester), free T4 8.9 pmol/l (compatible with late third trimester), TSH less than 0.03 mu/l, cortisol 238 nmol/l, FSH and LH both less than 0.2 U/l and both compatible with late pregnancy. Visual field testing showed bitemporal full quadrantic hemianopia and visual acuity had deteriorated. Fundoscopy performed by neurologists and neurosurgeons did not indicate signs of raised intracranial pressure and the patient had no headache; together these were taken to mean that intracranial pressure was not elevated. Fetal growth was normal.

After consultation between neurosurgeons, endocrinologists, ophthalmologists and obstetricians, it was felt that the differential diagnosis was that of pituitary tumour (of which the most likely was a macroprolactinoma) or lymphocytic hypophysitis. Delivery of the baby by caesarean section was recommended by the neurosurgeons. Intravenous hydrocortisone 100 mg 6 hourly was started.

After discussion with the patient about the choices of anaesthesia available to her, a combined spinal-epidural technique (CSE) was chosen. The patient was given 150 mg ranitidine orally on the ward and 30 ml 0.3M sodium citrate in the anaesthetic room. A 16 gauge intravenous cannula was inserted under local anaesthesia and 500 ml of Hartmann’s solution and 10 mg metoclopramide were given. The initial blood pressure was 130/75 mmHg. A CSE was performed at the L3/4 interspace with the patient in the left lateral position on the operating table. A volume of 2 ml of a mixture containing 0.5% heavy bupivacaine with 10 µg/ml fentanyl was given intrathecally; she was immediately turned supine with an inflatable wedge under the right buttock and a sensory block to blunted pinprick sensation at T4 was obtained within 3 min. No anaesthetic or test dose was given via the epidural catheter. Cardiovascular signs were stable during this period. The patient was taken into the operating theatre where the monitoring was reattached and oxygen given by Hudson mask at 3 l/min.

Initial surgery and anaesthesia were uneventful. A live female infant was delivered after 10 min of surgery and following delivery 5 units of Syntometrine was given by slow intravenous injection. The procedure was then complicated by brisk haemorrhage
from aberrant uterine venous sinusoids over the lower uterine segment. Surgical control of the bleeding was achieved after about 6 min and the blood loss was estimated from the measurement of blood in the suction bottle and weighing of swabs and blood clots; an allowance was made for the likely volume of liquor lost at delivery. Immediate blood loss in the first 6 min was estimated at 2500 ml with a further 1500 ml before transfer from the operating theatre. Fluid resuscitation, administered by a rapid infuser, consisted of a total of 6 units of blood (two of emergency uncrossmatched O Rhesus negative blood), 2000 ml colloid and 2000 ml crystalloid. Oxygen, which had been removed at delivery of the baby, was reinstituted. A further five units of Syntometrine was given by slow intravenous injection and an infusion of 10 U/h Syntocinon started. The blood pressure never fell below 90/50 mmHg and the heart rate was never greater than 120 beats per minute. The patient remained conscious throughout the operation, but vomited within 3 min of each dose of Syntometrine. During peritoneal closure, the patient complained of some uncomfortable traction pains in the abdomen and 5 ml of 0.25% plain bupivacaine with 5 μg/ml fentanyl was given via the epidural catheter.

Postoperatively, the patient was transferred to a high dependency bed on the delivery unit. Standard fluid management was given and further fluid resuscitation was not needed to maintain acceptable urine output, blood pressure and heart rate. The epidural catheter was found to have been dislodged and so analgesia was provided via a patient controlled analgesia pump containing morphine (1 mg/ml) and cyclizine (2 mg/ml). Postoperative recovery was otherwise normal. On the first postoperative day, the haemoglobin was 12.8 g/dl and the coagulation profile, which had shown a prothrombin time of 19.5 sec (normal 12.5 to 14.5 sec) and a partial thromboplastin time of 35.2 sec (normal 24 to 32 sec) in the immediate postoperative period, returned to within normal limits with no further therapy. The patient reported that her vision had improved such that she was once again able to read a magazine. Forty-eight hours after delivery the visual acuity and fields had returned to normal in the left eye and by 4 days post-partum she was left with a small defect in the upper temporal quadrant of the right eye only. A repeat MRI scan showed a 50% regression of the pituitary enlargement with no chiasmal compression, an increase in the signal intensity of the pituitary gland and no radiological evidence of haemorrhage or infarction.

The patient was allowed home on the eleventh postoperative day with a supply of prednisolone to be tailed off within the 10 following days, with outpatient follow up by the endocrinologists.

DISCUSSION

Enlargement of the pituitary gland occurs normally during pregnancy as a consequence of hyperplasia of the prolactin producing lactotrophs. This causes a 10-fold increase in prolactin concentration during pregnancy but the increase in size of the gland does not usually cause symptoms related to intracranial mass or pressure effects. Pathological pituitary tumours, in contrast, often cause mass effects, together with hormone imbalance which can be difficult to interpret during pregnancy. It is rare for a pituitary tumour to cause raised intracranial pressure, although it may do so by compression of the third ventricle and subsequent hydrocephalus; very occasionally it may enlarge into the middle and anterior cranial fossae to form a space occupying lesion. Our patient had no clinical or radiological features of raised intracranial pressure.

The differential diagnosis in this patient was between a pituitary tumour and lymphocytic hypophysitis. The onset of visual impairment had been followed by a rapid deterioration in visual fields. Initial radiological investigation showed that although the pituitary gland was enlarged there was no erosion of the pituitary fossa indicating rapid glandular enlargement. The hormonal profile also showed values entirely consistent with third trimester pregnancy and did not support the diagnosis of a secreting endocrine tumour. This distinction is extremely important since it has significant prognostic importance and guides management of the mother. Lymphocytic hypophysitis may be expected to improve following delivery of the baby, and if there had been no improvement following delivery an urgent surgical decompression of the pituitary may have been indicated; hence the decision to deliver her urgently by cesarean section was taken for both diagnostic and therapeutic reasons.

The definitive diagnosis of lymphocytic hypophysitis requires a tissue biopsy, but increasingly, the diagnosis is made on clinical grounds, radiological imaging and hormonal levels in the blood. The condition was first described in a 22-year-old woman who died from cardiovascular collapse 8 h after appendicectomy. She had had an uneventful pregnancy and delivery 14 months before, but had suffered from post-partum secondary amenorrhoea. Post-mortem examination showed lymphocytic infiltration of the pituitary and thyroid glands, for which an autoimmune mechanism was postulated. Since then, about 100 cases of the condition have been described. Nearly 85% of cases are female, with a mean age at presentation of 30 years compared with 40 years in males. Two-thirds of reported cases have been associated with pregnancy,
with 50% of these presenting in the second or third trimester and the other 50% in the first 6 months post partum. Lymphocytic hypophysitis is suspected to have an autoimmune origin, with extensive infiltration of the anterior lobe of the pituitary gland by lymphocytes, plasma cells and occasionally eosinophils. Destruction of the normal architecture may result, at one extreme, in a diffusely enlarged gland with areas of morphologically normal tissue, or at the other, in an atrophic, fibrotic gland. In pregnancy, the aetiology is likely to be autoimmune given that anti-pituitary antibodies have been detected in women with the condition\[1,13\] and that antibodies have been shown to react with hyperplastic lactotrophs.\[14\] There is an association with other autoimmune conditions, notably thyroiditis.\[4,12,13\] Radiological findings are not diagnostic although some features have been described which may be found in lymphocytic hypophysitis.\[10\]

In pregnancy, the condition may present at any stage ante- or post-partum. Clinical features may be due to mass effects, hyperprolactinaemia or anterior pituitary insufficiency.\[10\] Mass effects result in headache and visual disturbances in 60% of cases and are the most common presentation in pregnancy. This case is typical of the enlarged pituitary compressing the optic chiasm, and the rapid deterioration in visual fields dictated the need for urgent intervention.\[15\] Diplopia may occur in 6% of cases as a result of extension of the inflammatory mass into the cavernous sinus.\[10\]

Hyperprolactinaemia occurs in 40% of patients with the condition. Although prolactin hypersecretion is a normal feature of pregnancy, it does not entirely account for the prolactin excess seen in lymphocytic hypophysitis. Of nearly 20 cases reported previously, several were males and more than half the females were not pregnant or were not breast feeding at the time of diagnosis.\[10\]

Partial or complete hypopituitarism is noted in 65% of patients, with the loss of adenohypophyseal cells probably due to a targeted autoimmune attack. In 20% of patients, diabetes insipidus is found due to neurohypophyseal involvement and 20% of patients have evidence of other autoimmune conditions, most commonly primary hypothyroidism resulting from chronic lymphocytic thyroiditis. The natural history of the condition is variable, ranging from spontaneous resolution of the mass and complete recovery of pituitary function\[9,12,16\] to death.\[13\] Active treatment is therefore indicated in all patients. This may vary from conservative management with hormone replacement therapy if pituitary insufficiency is diagnosed, glucocorticoids to reduce inflammation of the pituitary temporarily (although their use in this context has not been studied closely), bromocriptine to suppress pituitary function and regular assessments of pituitary size by both clinical (formal visual field testing) and radiological (CT or MRI) methods. In the absence of critical pituitary enlargement, these may be all that is required in the anticipation of regression of the condition. However, if such critical pituitary enlargement occurs, urgent neurosurgical debulking may be needed for both diagnostic and therapeutic purposes.\[15\]

Glucocorticoids were administered in our patient in order to reduce inflammation of the pituitary and to prevent pituitary apoplexy during the perioperative period. From the anaesthetic viewpoint, the most significant feature of this patient's preoperative condition was that intracranial pressure was not raised; this would have been a contraindication to the use of central neuraxial anaesthesia. A regional anaesthetic technique is widely accepted as being safer for the mother, allows her to communicate any changes in neurological condition and, after a full discussion of the potential risks and benefits of both types of anaesthesia, it was also the patient's choice. The two potential disadvantages of regional anaesthesia were felt to be hypotension (which could reduce an already compromised blood flow to the pituitary), and post-dural puncture headache (which could have been difficult to interpret in the presence of an enlarged pituitary). However, hypotension following regional anaesthesia may be avoided quite readily by fluid preloading, positioning and prophylactic or early use of vasopressors, while the development of headache postoperatively would have been an indication for further CT or MRI scan. It was felt that there was no indication for the use of general anaesthesia in this patient.

Postoperatively, her anaesthetic recovery was unremarkable and she required no specific fluid or resuscitative therapy. Unfortunately, the epidural catheter was dislodged postoperatively and could not be used for analgesia; this would have been a good route of administration in this patient. The choice of a morphine/cyclizine patient-controlled analgesia pump, which is a standard regimen in our unit, was questioned by the neurosurgeons who felt that the drowsiness which it caused interfered with their interpretation of her clinical condition. However, her visual fields improved rapidly and by 4 days post partum had returned almost to normal. Such recovery from lymphocytic hypophysitis has been documented before\[9,12,15,16\] and the rapidity of the resolution helped to confirm the initial diagnosis, since a prolactinoma would not have been expected to resolve without surgical intervention.

Unfortunately, the procedure was complicated by haemorrhage from aberrant venous sinusoids running across the lower uterine segment, making it impossible to deliver the baby without cutting the vessels.
Although the blood loss was corrected rapidly, the patient is still at significant risk of developing Sheehan's syndrome. This syndrome, first described in 1937, refers to the development of pituitary necrosis within a few hours of delivery. Classically, this has been attributed to obstetric haemorrhage leading to hypotension, arteriolar spasm and ischaemia of the anterior lobe of the pituitary, with the assumption that the normally hyperplastic gland of pregnancy is more vulnerable to a reduction in blood supply. It may present acutely, with persistent hypotension, tachycardia, hypoglycaemia and failure to lactate, or may present months or even years later with failure of lactation, amenorrhoea, cold intolerance and fatigue. The diagnosis is often made in the absence of documented hypotension and it is likely that these cases represent undiagnosed lymphocytic hypophysitis. Our patient had an abnormally enlarged pituitary gland in which the vascular supply may well have been compromised. She, therefore, had two risk factors for developing the syndrome but did not develop the acute form. She had elected to bottle feed her baby and so the clinical sign of failure of lactation was not available. The post-partum MRI scan did not show signs of infarction but this is an insensitive test.

In the three months after discharge from hospital she had a low plasma prolactin level (800 mU/l), low free T4 (11 pmol/l which fell to 7 pmol/l), poor cortisol and growth hormone responses to an insulin stress test and failed to lactate, all of which indicated depressed pituitary function. She continued to take long-term steroid and thyroid replacement therapy. However, after three months, she had a spontaneous menstrual period and a further MRI scan showed that the pituitary gland had remained the same size as in the post-operative scan, which may indicate return of pituitary function. She was, therefore, due for long-term follow-up in the endocrinology clinic, both to monitor the resolution of signs as lymphocytic hypophysitis improves and to monitor any future development of hormonal imbalance which might signal a late presentation of Sheehan's syndrome.

REFERENCES