Ovulation Induction and Cesarean Delivery After Panhpopituitarism Secondary to Lymphocytic Hypophysitis

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Citation

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Abstract

Background: Lymphocytic hypophysitis is an unusual autoimmune disease that causes partial or total hypopituitarism and often is associated with pregnancy. Only four spontaneous pregnancies have been reported after this disease. We report a case of ovulation induction in a woman with this antecedent as well as the course of the subsequent pregnancy and delivery.
Case Report: Ovulation was induced with gonadotropins in a 31-year-old woman with panhypopituitarism secondary to lymphocytic hypophysitis, achieving an uncomplicated single intrauterine pregnancy. A term healthy infant was delivered by cesarean section under epidural anaesthesia. Puerperal evolution was normal.
Conclusions: Ovulation induction response was similar to that in panhypopituitarism of any other cause. Lymphocytic hypophysitis antecedent did not adversely affect pregnancy outcome nor was pregnancy-related disease observed. Epidural anaesthesia was effective for cesarean delivery in this case.

INTRODUCTION

Lymphocytic hypophysitis (LH) is a rare pituitary gland inflammatory disease of suspected autoimmune etiology. Only about 100 cases LH have been reported since 1962. Most of the cases occur in young women, during pregnancy or the first postpartum year. Clinically, there are manifestations of a hypophyseal mass, often requiring surgery. Varying degrees of hypopituitarism can be seen often associated with other autoimmune diseases.

We report the case of a woman with panhypopituita-rism secondary to LH in whom a successful ovulation induction was followed by an uneventful pregnancy of a healthy infant delivered by cesarean section on the 38th week.

As far as we know, only four additional such cases have been published with pre-existing LH. [1 2 3 4] We were unable to find any report on the ovulation induction and anaesthetic management for cesarean delivery in patients with this disease.

CASE REPORT

A 31 year-old woman consulted for infertility treatment. Five years before, she suffered of LH, unrelated to pregnancy, and developed a sellar mass, and panhypopituitarism associated to Hashimoto thyroiditis. A trans-sphenoidal hypophysectomy was performed to relieve compressive symptoms. The remaining pituitary dysfunction required permanent replacement therapy.

The pathologic examination of the sellar mass revealed abundant lymphocytic infiltrate (B cells and numerous T lymphocytes with predominance of CD4 cells over CD8 cells). These findings were diagnostic for LH.

When first evaluated in our Reproductive Medicine Unit, the patient was being treated with hydrocortisone (30 mg daily), L-thyroxine (100 µg daily), desmopressin (5 µg daily) and ethinyl estradiol with L-norgestrel (30 and 150 µg daily). Physical examination, routine serum biochemistry and complete blood count were normal. Endocrinological evaluation showed undetectable pituitary hormones (ACTH, GH, FSH, LH and TSH) with a slightly elevated PRL level (57 µg/mL). Magnetic resonance imaging of the pituitary gland showed an empty sella with some remnants of hypophyseal tissue. Hysterosalpingography revealed a

normal uterine cavity and patent fallopian tubes. The seminogram of her partner showed mild oligospermia with about 20 million motile spermatozoa in the total ejaculate. Neverthless, postcoital test (Sims-Huhner test) was rich, and intrauterine insemination was not considered.

Ovulation induction was initiated with hMG and hCG. Micronized progesterone (300 mg b.i.d.) was used for luteal phase support. Therapy was successful, a single uterine pregnancy being obtained in the fifth cycle. There were no significant side effects. Progesterone was given up to the twelfth week, maintaining the previous replacement treatment. The doses of L-thyroxine and desmopressin had to be slightly increased to keep hormonal normality (125 µg daily and 7.5 µg daily respectively).

The patient was seen for prenatal care every 3 weeks until the 34th week and then every 2 weeks until delivery. Serologic antenatal screening for infections was performed according to our protocol. Other laboratory examinations (complete blood count, serum biochemistry, free-thyroxine, blood osmolarity and urinalysis) were repeted every 4-6 weeks. Ultrasound examination was performed at 10, 18, 28, 33, and 38 weeks. Nonstress test was first scheduled at 32th week gestation and then every 2 weeks.

On the 38th week, an ultrasound scan showed mild oligohydramnios. The stress test was negative. Labor was induced, after cervical ripening with prostaglandin E2 gel, with amniotomy and intravenous oxytocin.

An epidural catheter was inserted for analgesia with a continuous perfusion of 0.0625% bupivacaine and 2 µg/ml fentanyl, after a bolus of 8 ml. 0.125% bupivacaine and 1 ml fentanyl. An excellent analgesia was obtained. Three hours later, cesarean section was decided because of protracted active- phase dilatation. Dextrose in saline solution with 100 mg hydrocortisone was I.V. infused. Epidural anesthesia was carried out with 2% lidocaine and 1:400.000 epinephrine. Surgery was uneventful. A healthy female infant weighing 2490 g was delivered. Puerperal clinical course was normal. Lactation began on the third postpartum day and breastfeeding was maintained for 3 moths. L-thyroxine and desmopressin were reduced to progestational levels in the first postpartum week. Magnetic resonance imaging of the sella turcica at the third postpartum month showed no change. Nine months after delivery the patient remains symptom-free.

DISCUSSION

LH is an uncommon disorder with a striking female predilection of approximately 8.5:1 and is related to pregnancy in about 70% of affected women. The cause is unknown, but the finding of anti-pituitary antibodies in some patients and its association to other autoimmune diseases, mainly thyroiditis, suggests an immune origin. In our patient, the beginning of the picture outside pregnancy or puerperium may suggest a similar, but distinct, reported entity: infundibuloneurohypophysitis, [5] although it seldom involves the adenohypophysis.

No case of ovulation induction in women with previous LH has been reported, to our knowledge. Our approach was to manage the patient as a case of panhypopituitarism. Several authors advise the addition of GH to classical treatment with hMG/hCG in “poor responders” or GH-deficient patients, [6] but this is controversial. In our case, classical hMG/hCG treatment was used. An ovulation being obtained in almost all cycles and pregnancy in the fifth one. We did not need co-treatment with GH, in spite of using normal amounts of hMG.

The natural history of LH, as well as the influence of further pregnancies on it, is unclear. There is a close association between pregnancy and the initial occurence of this disease, so the possibility of LH relapse during subsequent pregnancy was a matter of concern to us. In our patient, in spite of the previous hypophysectomy, we suspected the presence of some residual pituitary tissue, leading to the possibility of a relapse along her pregnancy. The later lactogenesis demonstrated prolactin secretion. No relapse or gestational problems occurred neither in our patient nor in any of four previously reported similar cases (table 1). [1] [2] [3] [4]

Figure 1

Table 1: Summary of pregnancies after lymphocytic hypophysitis

References	Basal hormonal status	Pregnancy course	Pregnancy outcome
Brandes et al. [1]	Hypopituitarism without gonadotropin deficiency	Not specified	Healthy infant at term
Jensen et al. [2]	Isolated ACTH deficiency	Uneventful	Delivery at term
McCutcheon et al. [3]	Normal	Not specified	Healthy infant at term
Trur et al. [4]	Hypopituitarism without gonadotropin deficiency	Uneventful	Healthy infant at term. Vaginal delivery.

The course of the pregnancy was normal, as could be expected, because replacement therapy with close monitoring was provided. [7] Termination of pregnancy was decided on the 38th week, because of mild oligohydramnios

and the convenience of scheduling labor for adequate management of steroid replacement. Cesarean section was indicated because of strict obstetrical reasons.

Anesthesiologic management of these patients with panhypopituitarism have to consider maternal and newborn factors. Epidural analgesia provides the best control of pain along labor, has potential physiological advantages, and offers flexibility to meet the needs of varied obstetric procedures (spontaneous vaginal or forceps delivery, cesarean section). [8] In our case, the avoidance of the adrenergic stimuli of general anesthesia was a further advantage.

Continuous perfusion of 0.0625% bupivacaine in addition to fentanyl epidural has been shown to improve onset and quality of analgesia during labor induced with oxytocin, without evident side effects for mother and newborn. [9] 2% Lidocaine in cesarean section brings about a considerable reduction in motor capacity. With the addition to epinephrine its effect is prolonged, serum concentrations are lowered and increase motor block. An opioid, fentanyl 50-75 mg or sulfentanil 10-20 mg may be added. In our case, it was not use because the cesarean was performed by a failed to induce labor, in which an epidural solution containing opioids has been used.

Labor induction with high doses of oxytocin (often hundreds of units) [10] entailed a risk of water intoxication because of the combined effect of desmopressin. A strict fluid balance, avoiding water generating solutions, was necessary, dextrose in saline being the choice. Fluid needs were calculated as diuresis, plus blood lost, plus 1000 mL daily. [11]

Corticosteroid supplementation should be increased for any patient being treated for chronic hypoadrenocorticism who undergoes a surgical procedure. The degree of perioperative stress (minor versus mayor surgery) determines the dose and duration of therapy. Symptoms and signs such as weakness, fever, confusion, nausea and vomiting, diarrhea, hypotension, hyperkaliemia and possibly metabolic acidosis at any time during operation would inmediately alert us to the possibility of an adrenal crisis. Recommendations for perioperative steroid supplementation vary from author to author. For minor surgery IV hydrocortisone 25 mg preoperatively and 50 mg intraoperatively is frequently recommended to supplement their daily prescription. For major surgery hydrocortisone 25 mg preoperatively and 100 mg intraoperatively or dexamethasone 0.75 mg preoperatively and 3 mg intraoperatively are common prescriptions. [12] In our case, we used IV hydrocortisone 100 mg, six-hourly and when the patient's condition stabilizes, the steroid dose was reduced and oral treatment was reassumed.

Patients with subclinical hypothyroidism usually present no anesthetic problems and elective surgery can proceed without special preparation. Elective surgery should probably be deferred in the patient with symptomatic hypothyroidism. If emergency surgery is necessary, the potential for severe cardiovascular instability intraoperatively and myxedema coma in the postoperative period is high. Regional anesthesia, if possible, is an appropiate selection for the hypothyroid patient, provided that intravascular fluid volume is well maintained. Although supporting evidence is not avaible, theoretically the dose of local anesthetic necessary to performance a peripheral nerve block could be decreased. Furthermore, metabolism of an amide local anesthetic that is absorbed into the systemic circulation could be slowed, possibly predisposing to hypothyroid patient to the development of drug-induced systemic toxicity. [13]

Diabetes insipidus reflects the absence of ADH owing to neurogenic etiology. Classic manifestations are polydipsia and high output of poorly concentrated urine despite increased plasma osmolarity. Treatment of neurogenic diabetes insipidus is with vasopressin administered intramusculary or by intranasal administration of desmopressin. Management of anesthesia for patients with diabetes insipidus should include monitoring of urine output and plasma electrolyte concentrations during the perioperative period. [13] Side effects of desmopressin such us hyponatremia, hypotension or coronary spasms must be considered.

Our patient showed total panhypopituitarism with partial diabetes insipidus but with preserved vasopressin production. This endogenous production was evidenced by the low doses of desmopressin needed. Pregestational hormone replacement therapy was maintained, and only adjustments in L-thyroxine and desmopressin dosages were needed. L-thyroxine had to be increased to counteract the pregnancy-induced rise in the thyroxine binding globulin concentration. Although desmopressin is not metabolized by placental vasopressinase, its dose had to be increased too, likely in relation to increased catabolism of endogenous vasopressin.

In summary, we are reporting the first case of ovulation induction on a woman with previous LH. The patient run a course similar to that of other cases of panhypopituitarism. Therefore a history of LH should not be considered a contraindication to pregnancy.

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