This suggests strongly that a large invasive cancer developed during the 26 months between the patient’s last normal Papanicolaou smear and her presentation with invasive cancer. McIndoe et al. found that 1.5% of 817 patients with normal cytology after treatment for CIS developed invasive cancer 4 to 19 years later (median, 9 years). Our case demonstrates a much more rapid progression to invasive cancer.

Immunosuppression predisposes women to preneoplastic changes of the cervix and increases the possibility of progression of these lesions to invasive cancer. This progression may be much more rapid than the slow process observed in immunocompetent women. Our case demonstrates not only the rapid progression to invasive cervical carcinoma in an HIV-positive woman but also the virulent nature of this tumor, as evidenced by its resistance to treatment. Frequent follow-up cytologic and colposcopic examinations are necessary in HIV-infected women treated for cervical dysplasia to rule out persistent or recurrent preneoplastic lesions.

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Ovulation induction and normal pregnancy after panhypopituitarism due to lymphocytic hypophysitis

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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.

Case: 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. Clinical course during puerperium was normal.

Conclusion: 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 relapse observed. (Obstet Gynecol 1998;91:850–2. © 1998 by The American College of Obstetricians and Gynecologists.)

Lymphocytic hypophysitis is a rare pituitary gland inflammatory disease of suspected autoimmune etiology. Since the first description in 1962 nearly 100 cases...
have been reported. Most of them occurred in young women, during pregnancy, puerperium, or the first postpartum year. Clinically, it is characterized by symptoms of a hypophyseal mass with varying degrees of hypopituitarism, often associated with other autoimmune diseases, and usually requiring surgical treatment.

We reviewed the medical literature recorded in the MEDLINE database from 1966 to April 1997 and found four pregnancies reported in women with pre-existing lymphocytic hypophysitis. In this literature review we did not find any report of ovulation induction in patients with this disease.

We report a case of successful ovulation induction in a woman with panhypopituitarism secondary to lymphocytic hypophysitis and the clinical course of her pregnancy, delivery, and puerperium.

Case
A 31-year-old woman was referred for infertility treatment. Five years before she had suffered lymphocytic hypophysitis and had been the subject of a clinical report. In brief, she developed a nonpregnancy-related compressive sellar mass, with panhypopituitarism (hypocortisolism, hypothyroidism, and hypogonadism with hyperprolactinemia) associated with Hashimoto thyroiditis. A transsphenoidal mass resection was performed to relieve the compressive symptoms. Permanent panhypopituitarism resulted, requiring hormonal replacement. The pathologic examination of the sellar mass revealed abundant lymphocytic infiltrate, with no giant cells or granulomas, together with extensive areas of hyalinized fibroblastic tissue and islands of pituitary cells. Glandular islets and intraepithelial lymphocytes were observed focally. Neurohypophysis was not identified. Isolated growth hormone–positive cells were detected in the immunohistochemical study, but no positive cells were observed for the other pituitary hormones. The lymphocytic infiltrate consisted of B cells and numerous T lymphocytes with predominance of CD 4 cells over CD 8 cells. In the ultrastructural study, abundant lymphoid cells were identified, as were occasional endocrine cells, with medium-sized granules. These findings were diagnostic for lymphocytic hypophysitis.

When first evaluated in our Reproductive Medicine Unit, the patient was being treated with hydrocortisone (30 mg daily), L-thyroxine (100 µg daily), desmopressin (2.5 µg twice a day), and an oral estrogen-progesterone combination (ethinyl estradiol 30 µg and levonorgestrel 150 µg daily).

General and gynecologic examination yielded normal findings. Serum biochemistry (sodium, potassium, calcium, glucose, urea nitrogen, uric acid, cholesterol, total protein, albumin, total bilirubin, alkaline phosphatase, lactate dehydrogenase [LDH], and transaminases) and complete blood count were normal. Endocrinologic evaluation showed undetectable pituitary hormones (ACTH, growth hormone [GH], FSH, LH, and TSH) with a slightly elevated prolactin level (57 ng/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 semenogram of her partner showed mild oligospermia with about 20 million motile spermatozoa in the total ejaculate. Nevertheless, postcoital test (Sims-Huhner test) was rich, and intrauterine insemination was not considered.

Ovulation induction treatment with human menopausal gonadotropin (hMG) and hCG was initiated. Micronized progesterone (300 mg twice a day) was used for luteal phase support. Treatment response was satisfactory: ovulation occurred in all but the second cycle, achieving a single intrauterine pregnancy in the fifth cycle. There were no significant side effects. The amount of hMG ampules used in each cycle averaged 33 (range 29–37).

Progesterone treatment was provided up to the 12th week of pregnancy. The rest of replacement hormonal therapy (hydrocortisone, L-thyroxine and desmopressin) also was maintained. L-thyroxine had to be increased (125 µg daily) during the first trimester to maintain free-thyroxine values at physiologic level. Desmopressin had to be increased (2.5 µg in the morning and 5 µg at bedtime) because of increasing polyuria and nocturia.

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 for low-risk pregnancies: antibodies to toxoplasma, rubella, syphilis, and human immunodeficiency virus at the first antenatal visit and hepatitis B surface antigen at the third trimester. Other laboratory examinations (complete blood count, sodium, potassium, calcium, glucose, urea nitrogen, uric acid, total protein, albumin, total bilirubin, alkaline phosphatase, LDH, transaminases, free-thyroxine, blood osmolarity, and urinalysis) were repeated every 4–6 weeks. Ultrasound examination was performed at weeks 10, 18, 28, 33, and 38. Nonstress test (NST) was first scheduled at 32 weeks’ gestation and then every 2 weeks.

Her pregnancy course was uneventful until the 38th week, when ultrasound scanning showed mild oligohydramnios with a reactive NST. After cervical ripening with prostaglandin E2 gel, labor was induced with amniotomy and intravenous oxytocin. Cesarean delivery was performed because of protracted active-phase dilatation. A healthy female infant weighing 2490 g was delivered.

Puerperal clinical course was normal, gynecologically and neurologically. Lactation began on the third postpartum day and breastfeeding was maintained for 3 months. L-thyroxine and desmopressin were reduced to pregestational 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.

Comment
Lymphocytic hypophysitis is an uncommon disorder that shows a striking female predilection of approximately 8.5:1 and is related to pregnancy in about 70% of
affected women. Etiology is unknown, but many facts—namely, its propensity to occur in women, the presence of anti-pituitary antibodies in the sera of some patients, and the association with other autoimmune disorders, thyroiditis in particular—strongly suggest an autoimmune pathogenesis.

We have not been able to find any previous case of ovulation induction in a case with pre-existing lymphocytic hypophysitis in our review of the literature. 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, but this is controversial. In our case, classical hMG/hCG treatment was used with a good response and ovulation in almost all cycles leading to pregnancy at the fifth cycle. We did not need co-treatment with GH, in spite of using normal amounts of hMG.

The natural course of lymphocytic hypophysitis remains unclear, and the impact of a subsequent pregnancy on its course is unknown. There is a close association between pregnancy and the initial occurrence of this disease, so the possibility of lymphocytic hypophysitis relapse during subsequent pregnancy was a matter of concern to us. We thought that this possibility could happen in our patient because, in spite of the previous hypophysectomy, residual pituitary tissue was likely to exist, as prolactin production suggested and normal lactogenesis confirmed.

Four spontaneous pregnancies in women with a history of lymphocytic hypophysitis have been reported. In all of these, cases pregnancy was normal with term delivery of healthy infants and without evidence of disease relapse. In our case, pregnancy was also normal. No manifestation of activity of her previous disease was observed.

As classically established, pregnancy outcome in women with panhypopituitarism is not different from that in a normal obstetric population when adequate replacement therapy is provided. 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.

References


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