Spontaneous Postpartum Regression of Pituitary Mass With Return of Function

Sara Leiba, MD; Bella Schindel, MD; Ruth Weinstein, MD; Iaron Lidor, MD; Shmuel Friedman, MD; Shoshana Matz, MD

- A 37-year-old woman undergoing endocrine evaluation during her seventh pregnancy because of headaches, weakness, and hyponatremia was found to have central hypoadrenalism and hypothyroidism. Computed tomography showed a pituitary mass with suprasellar extension but her visual fields were intact. She was treated conservatively with hydrocortisone acetate and levothyroxine sodium until 38 weeks of gestation, when healthy twins were delivered by cesarean section. A few months later, her pituitary function improved, with a significant increase in the adrenocorticotropic hormone level, normal values of basal thyroid-stimulating hormone, growth hormone, and gonadotropins and of their functional reserves, and only a slight elevation in the prolactin level. A repeated computed tomographic scan showed disappearance of the pituitary mass.

(JAMA 1986;255:230-232)

THE INTRODUCTION of the radio-diagnostic technique of computed tomography (CT) has provided the means for better evaluation of intrasellar pituitary tumors and made it possible to obtain a more accurate picture of the evolution of such tumors. Herein is presented the case history of a patient in whom a CT scan visualized an intrasellar mass with suprasellar extension in the seventh month of pregnancy, when she showed signs of hypopituitarism, but demonstrated disappearance of the mass three months after delivery, when there was also an improvement in pituitary function.

Report of a Case

A 37-year-old woman had already experienced six normal pregnancies. Following the sixth delivery, she noted galactorrhea...

<table>
<thead>
<tr>
<th>Results of Laboratory Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Normal values</td>
</tr>
<tr>
<td>Before pregnancy</td>
</tr>
<tr>
<td>26th week of pregnancy</td>
</tr>
<tr>
<td>3 mo after delivery</td>
</tr>
<tr>
<td>8 mo after delivery</td>
</tr>
<tr>
<td>11 mo after delivery</td>
</tr>
</tbody>
</table>

*GH indicates growth hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; ACTH, adrenocorticotropic hormone; TSH, thyroid-stimulating hormone; T₄, thyroxine; Na, sodium; 17-OH, 17-hydroxyenosteroid; and IV, intravenous.
†Adrenocorticotropic hormone and blood cortisol levels were determined from a single blood sample obtained at 8 AM after one hour of rest. Thyroid-stimulating hormone and T₄ levels were also determined from the same sample.
‡During pregnancy, the normal level of plasma cortisol is increased (>20 µg/dL) due to increased transcortin.
§During pregnancy, the normal level of total T₄ is increased (>10 µg/dL) due to increased thyroxine-binding globulin.

Reprint not available.
compared with previous determinations but was still insufficient to stimulate the level of cortisol, which remained lower than normal.

At this stage, the patient was receiving 10 to 20 mg/day of hydrocortisone acetate with the addition of 2.5 mg/day of bromocriptine mesylate. Three months later, the level of ACTH had increased; the plasma cortisol level was still low but showed a response to corticotropin stimulation. The level of 17-hydroxyestrogen was also low but showed a response to prolonged corticotropin stimulation. The delayed recovery of the pituitary-adrenal axis was probably due to the long-term maintenance treatment with hydrocortisone. Computed tomography one year after delivery again demonstrated a normal sella turcica without an intrasellar tumor (Fig 3). Menstrual bleeding recommenced one month after the patient began to receive bromocriptine and has remained regular ever since.

Simultaneously, antibodies were sampled using pituitary immunofluorescence, prolactin cell testing, gastric parietal cell immunofluorescence, thyroglobulin hemagglutination, and microsomal hemagglutination, with normal results. During this period, the patient continued to receive 10 to 15 mg of hydrocortisone acetate daily.

Methods

The following dynamic tests were performed: arginine hydrochloride stimulation test—determination of basal level of GH and those found at 30-minute intervals for two hours after intravenous (IV) infusion of 30 g of arginine hydrochloride in a 300-mL solution of 0.9% sodium chloride; gonadorelin test—determination of basal levels of follicle-stimulating hormone and luteinizing hormone and those found at 15-minute intervals for 90 minutes after bolus IV injection of 0.1 mg of gonadorelin; protirelin test—determination of basal levels of plasma prolactin and serum TSH and those found at 15-minute intervals for one hour after bolus IV injection of 0.2 mg of protirelin; corticotropin test—determination of plasma levels of cortisol before and four hours after four-hour IV infusion of 0.25 mg of cosyntropin (Synacthen) in a 500-mL solution of 0.9% sodium chloride; and prolonged corticotropin test—determination of urinary 17-hydroxy steroid levels in 24-hour urine samples collected before and 24 hours after intramuscular injection of 1 mg of cosyntropin depot preparation.

Comment

In considering the course of events in this patient, it is evident that the first signs of a pituitary disorder were the galactorrhea and the oligomenorrhea that appeared after she had undergone six pregnancies uneventfully. Although her prolactin level was within the upper limit of normal, conception took place only after treatment with small doses of bromocriptine, suggesting a state of discrete hyperprolactinemia. The headaches, weakness, and vomiting, which in the eighth week of gestation were moderate and transitory but which dramatically reappeared in the 26th week, proved to be due to a state of hypoadrenalism and hypothyroidism of central origin: all of these symptoms disappeared immediately after the administration of substitution therapy. The transitory polyuria and correction of the hyponatremia, along with the dramatic improvement in her condition, that followed institution of substitution therapy strongly suggest a transitory state of inappropriate secretion of antidiuretic hormone, also due to T, and glucocor-
ticoid deficiency. As for the radiological findings, the initial roentgenograms of the sella turcica taken before and during her pregnancy were normal but the CT scan taken during the third trimester revealed an intrasellar tumor with suprasellar extension (Fig 1). At that time, we could only conclude that the hypopituitarism was due to a pituitary tumor. The postpartum disappearance of the intrasellar mass and the improvement in pituitary function led us to consider a number of possibilities in the differential diagnosis of this patient, as follows.

Rapid growth of a microprolactinoma during pregnancy into a macroadenoma is suggested by the galactorrhea and menstrual disorders prior to pregnancy, with conception achieved following short-term treatment with bromocriptine, and by the subsequent discovery of a sellar and suprasellar mass on a CT scan. Although a macroadenoma is usually associated with much higher serum levels of prolactin (>200 ng/mL) than in our patient, there have been rare cases in which levels were normal. However, the rapid disappearance of the mass after delivery seems to argue somewhat against this possibility, although postpartum pituitary necrosis of a macroadenoma would have to be considered.

A hemorrhagic insult in or around the area of the pituitary and pituitary stalk could have occurred. This kind of accident is known to occur more frequently during pregnancy and could explain the state of hypopituitarism and would also be compatible with the disappearance of the mass after delivery. Sufficient pituitary tissue may have been spared to maintain normal or partial function of the pituitary, although this is uncommon in such circumstances of pituitary apoplexy. However, neither the image on the CT scan nor the density of the mass resembled what is usually seen with a hemorrhage.

Expansion of a pituitary tumor during pregnancy with compression of the pituitary stalk and portal vessels could also result in infarction and necrosis of the tumor and could cause a moderate increase in prolactin secretion due to decreased delivery of prolactin inhibiting factor to the adenohypophysis. The clinical and laboratory picture in our case might be explained by the presence of a pituitary tumor causing a state of low to normal secretion of pituitary hormone with little if any functional reserve. If tumor infarction occurred during pregnancy, these deficiencies could become more manifest transiently, leading to the discovery of hypopituitarism in this patient. Subsequently, however, with the disappearance of the tumor, amelioration instead of deterioration of pituitary function could occur.

Lymphoid hypophysitis, an autoimmune disease that may mimic a pituitary tumor and is associated with various degrees of hypopituitarism, is another possible diagnosis in this patient. Until now, all reported cases have been women and, in most cases, manifestations of the disease were observed during pregnancy or in the postpartum period. Antipituitary antibodies or selective antibodies to specific pituitary cells, particularly to prolactin-secreting cells, have been found in some of these cases and also in patients with other autoimmune diseases. In our case, a hypophysectomy was not performed, so there is no morphological information; furthermore, results of tests for autoantibodies against pituitary and prolactin-secreting cells as well as to gastric parietal and thyroid cells were all normal. Thus, there is no clear evidence of autoimmune disease in this patient. It should also be noted that there was no information on any autoimmune disease in the patient's family. Although long-term treatment with glucocorticoids has been shown to be effective in suppressing autoimmune disease, this is unlikely to have occurred in our case, as maintenance rather than pharmacologic doses of steroid were used. The evolution of the disease in this patient is highly suggestive of lymphoid hypophysitis, but without pathological examination of the pituitary and/or supportive immunologic evidence this diagnosis must remain a supposition.

In regard to treatment, it must be stressed that the diagnosis of a pituitary tumor is usually followed by hypophysectomy or pituitary irradiation and hormonal substitution therapy. Our experience with this patient shows that hypopituitarism and pituitary enlargement during pregnancy, and possibly in the postpartum period, is likely to be transitory, and a similar case has been reported by Zeller et al. It is therefore suggested that in such cases surgical intervention or irradiation not be undertaken before considering the possibility of a transitory disturbance and that such patients be kept under close observation while receiving adequate hormonal replacement therapy as their only form of treatment.

We wish to express our thanks and appreciation to Deborah Doniachi, MD, FRCPE, of the Department of Endocrinology of the Middlesex Hospital Medical School, London, for having performed the tests for autoantibodies.

References

Regression of Pituitary Mass—Leiba et al