Pituitary Tumors and Pregnancy

Mark E. Molitch, MD

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Summary

Pituitary adenomas may cause problems during pregnancy because of oversecretion of hormones and hypopituitarism. Hyperprolactinemia and Cushing’s syndrome may need to be controlled to allow conception. Maternal morbidity and fetal mortality and morbidity may be affected by the hormone oversecretion in Cushing’s disease, acromegaly, and TSH-secreting adenomas. Treatment of hyperprolactinemia and acromegaly during pregnancy is not necessary but resection of ACTH-secreting adenomas during pregnancy and medical treatment of hyperthyroidism are warranted. Reinstitution of dopamine agonists may be indicated in the 30% of macroprolactinomas that enlarge symptomatically during pregnancy. In hypopituitary patients, thyroid hormone levels should be increased empirically each trimester but no increase in steroid hormones is needed except during additional stress and labor. Lymphocytic hypophysitis may cause mass effects and hypopituitarism, both of which may need treatment. Sheehan’s syndrome has both acute and chronic forms which need appropriate evaluation and treatment.

Key Words: Pregnancy, Pituitary adenoma, Acromegaly, Prolactinoma, Cushing’s syndrome.

1. ANTENIOR PITUITARY GLAND AND PREGNANCY

Pituitary adenomas comprise 6% of intracranial (malignant and nonmalignant) neoplasms (1). They may cause problems because of oversecretion of hormones by the tumor besides causing hypopituitarism, thereby affecting
fertility and pregnancy outcome if pregnancy does ensue. In addition, the pregnancy itself alters hormone secretion and pituitary function, complicating the evaluation of patients with pituitary neoplasms. The influence of various types of therapy on the developing fetus also affects therapeutic decision making.

During pregnancy, the normal pituitary gland enlarges considerably, due to estrogen-stimulated hyperplasia and hypertrophy of the prolactin (PRL)-producing lactotrophs (2,3). Concomitantly, PRL levels rise gradually throughout gestation (4). The elevated PRL levels found at term prepare the breast for lactation. Thus, the finding of amenorrhea associated with hyperprolactinemia could well be due to pregnancy and not due to pathologic hyperprolactinemia. This lactotroph hyperplasia results in an increase in overall pituitary size as seen on magnetic resonance imaging (MRI) scans, with the peak size occurring in the first few days postpartum when gland heights up to 12 mm may be seen (5–7). Following delivery there is a rapid involution of the gland, so that normal pituitary size is found by 6 months postpartum (6,7). This stimulatory effect of pregnancy on the pituitary has important implications for the patient with a prolactinoma who desires pregnancy.

Beginning in the second half of pregnancy, pituitary growth hormone (GH) secretion decreases and the circulating level of a GH variant made by the syncytiotrophoblastic epithelium of the placenta increases to as high as 10–20 ng/ml (8,9). The decreased production of normal pituitary GH is likely due to negative feedback effects of insulin-like growth factor 1 (IGF-1), which is stimulated by the placentally produced GH variant (8,9). In patients with acromegaly who have autonomous GH secretion and become pregnant, both forms of GH persist in the blood throughout pregnancy (10).

Over the course of gestation, cortisol levels rise progressively, resulting in a twofold to threefold increase by term (11). Most of the elevation of cortisol levels is due to the estrogen-induced increase in cortisol binding globulin (CBG) levels (12). However, the bioactive “free” fraction is also elevated threefold and the cortisol production rate is increased, so that there is a twofold to threefold elevation in urinary free cortisol level (11,12). ACTH levels have been variously reported as being normal, suppressed, or elevated early in gestation (11,13). However, later in the pregnancy, there is a progressive rise, followed by a final surge of ACTH and cortisol levels during labor (11). ACTH does not cross the placenta but it is also manufactured by the placenta (13). The amount of ACTH in serum that is of placental as compared to pituitary origin at various stages of gestation is not known. Corticotropin-releasing hormone (CRH) is also produced by the placenta and is released into maternal plasma (14). The CRH is bioactive and may release ACTH both from the placenta, in a paracrine fashion, and from the maternal pituitary (14). The role of placental