Pituitary Tumor Management in Pregnancy

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KEYWORDS

• Pituitary adenoma • Prolactinomas • Acromegaly • Cushing syndrome
• Cushing disease • TSH-secreting pituitary adenoma
• Nonfunctioning pituitary adenoma • Pregnancy

KEY POINTS

- The general recommendation for pituitary adenoma management is to withdraw medical therapy as soon as pregnancy is diagnosed; however, in cases of aggressive macroadenomas or adenomas close to the optic chiasm, this decision must be individualized according to the patient's status.
- Surgery, when indicated, must be performed during the second trimester of gestation.
- Microadenomas often exhibit a favorable course, and macroadenomas occasionally increase during pregnancy.
- Cushing disease usually leads to a high-risk pregnancy, independent of the size of the pituitary adenoma, because of the deleterious effects of high cortisol levels.
- Close follow-up is the best approach for ensuring the early recognition of complications.

INTRODUCTION

Clinically relevant adenomas have a prevalence of approximately 1 per 1000 in the overall population.[1,2] The adenomas can be functioning or nonfunctioning, and they can impair women's fertility because of the tumor mass and oversecretion of hormones. The improved management of pituitary tumors, either by medical or surgical therapy, has led to an increasing number of pregnancies in patients harboring pituitary adenomas.

The authors have nothing to declare.

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Pregnancy produces several physiologic changes to the endocrine system, especially to the pituitary gland (**Box 1**). The anterior pituitary gland enlarges by 2-fold to 3-fold during this period,[3] mostly because of hypertrophy and hyperplasia of the lactotrophs stimulated by marked increases in the estrogen levels.[4] Therefore, the endocrinologist faces the challenge of considering the patient's physiologic changes for the effective management of pituitary adenomas during pregnancy to guarantee the wellbeing of the fetus.

PROLACTINOMA

Prolactinomas have an estimated prevalence of 40% of all pituitary adenomas and are primary causes of hyperprolactinemia, which leads to infertility and gonadal dysfunction.[13] Prolactinomas present a peak incidence during childbearing years and are predominantly benign tumors measuring less than 10 mm (microprolactinomas) in more than 90% of cases.[14] Medical therapy with a dopamine agonist (DA) is the first-line treatment and normalizes prolactin levels in 86% of cases,[15] restoring fertility in most patients.[14,16] Transsphenoidal surgery is reserved only for select cases. Thus, pregnancy in these women is a frequent occurrence.

Pregnancy may lead to an increase in prolactinoma size, mainly in pregnant patients with macroprolactinomas.[17] Therefore, these patients should avoid pregnancy by using either hormonal or nonhormonal contraceptive methods until tumor shrinkage occurs.[18] Moreover, women with macroprolactinomas who do not experience pituitary tumor shrinkage during DA therapy or who cannot tolerate DA must be counseled regarding the potential benefits of surgical resection before attempting pregnancy.[16]

Safety of Dopamine Agonists

There are few DAs available for treating these patients; all have been shown to cross the placental barrier.[19] Most studies on pregnancy evaluate bromocriptine and cabergoline, so this article focuses specifically on these.

Box 1
Pituitary gland during normal pregnancy

- Prolactin levels increase up to 10-fold during pregnancy, parallel to the increase in the size of the pituitary gland.[5]
- Although there are hyperplasia and hypertrophy of the lactotrophs, gonadotrophs reduce in number, and corticotrophs and thyrotrophs remain constant.[4]
- The maternal placenta secretes a growth hormone (GH) variant by the end of the first trimester, leading to increased plasma levels of insulinlike growth factor-1 during the second half of pregnancy (up to 2–3 times the upper limit of normal). This leads to somatotroph suppression.[6,7]
- Plasma corticotropin-releasing hormone (CRH) levels (primarily synthesized by the maternal placenta) increase several hundred-fold by term,[8] stimulating the pituitary adrenocorticotropic hormone (ACTH) production.
- The ACTH levels consequently increase throughout gestation, accompanied by increased cortisol levels following the same pattern.[9]
- The increase in total plasma cortisol concentration (up to 2-fold to 3-fold by term) is mostly attributed to a concomitant increase in cortisol-binding globulin (CBG) levels, secondary to estrogen stimulated production.[10]
- The plasma and urinary free cortisol (UFC) start to increase approximately in the 11th week of gestation, incrementing 2 to 3 times during the last 2 trimesters; however, pregnant women normally do not exhibit any overt clinical features of hypercortisolism.[10–12]