

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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Endocrinol Metab Clin N Am 44 (2015) 181–197

<http://dx.doi.org/10.1016/j.ecl.2014.10.015>

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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 adrenocorticotrophic 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}

It is generally advised to discontinue DA treatment as soon as pregnancy has been confirmed, particularly in patients with microadenomas.²⁰ When used in this fashion, in more than 6000 pregnancies, bromocriptine has not been found to cause any increase in the incidence of abortion, ectopic pregnancy, trophoblastic disease, or multiple pregnancies, and only 1.8% of the births were affected by congenital malformations, compared with the 3.0% expected in the general population.^{21,22}

In recent years, the data concerning cabergoline safety during pregnancy have increased, and more than 800 cases have been published.^{23–28} Fetal exposure to cabergoline in early pregnancy seems to be as safe as exposure to bromocriptine (**Table 1**).^{23–28} Given the safety profile and the tolerability of cabergoline, this agent has been increasingly used as the first-line therapy in women with prolactinoma who want to become pregnant.²⁹

Treatment of Prolactinoma During Pregnancy

The primary goal of prolactinoma treatment during pregnancy is to maintain the adenoma away from the optic chiasm. A review by Molitch³⁰ pooled information from 514 women with either microadenoma or macroadenoma of any type and showed that only 1.4% of the women with microadenoma presented symptomatic enlargement of the adenoma. Regarding macroadenoma, the behavior of the tumor was more aggressive: 26.2% of the subjects presented symptomatic tumor enlargement. Of the 67 women with macroadenomas with a previous history of surgery or radiation, only 2 women (3%) had symptomatic tumor enlargement.

Therefore, the DA can be safely withdrawn shortly after pregnancy confirmation in patients with microadenoma (**Fig. 1**).^{23–28,30,31} These patients should be carefully followed to detect symptoms of tumor enlargement. Visual field testing and MRI (without gadolinium), at any trimester,³² should be performed only in those cases. This recommendation should be followed for any type of pituitary adenoma that exhibits enlargement during pregnancy.

Because macroprolactinomas have a higher risk of symptomatic tumor enlargement during gestation,^{26,30,31} the discontinuation of DA must be individualized, though DA is withdrawn in most patients with intrasellar macroadenomas.¹⁶ In this setting, close surveillance must be performed on a monthly basis. Furthermore, visual field testing is recommended every 2 to 3 months, and MRI is reserved for patients with documented changes in visual field and symptoms of tumor growth.^{20,33,34} Maintenance of DA throughout pregnancy may be preferred when previous treatment with DA was administered shortly before conception or when the tumor is located outside of the intrasellar boundaries. Macroprolactinomas with a history of successful surgery or radiation therapy can be managed as microprolactinomas.

If the tumor increase is confirmed for either microadenomas or macroadenomas, treatment should be restarted, more specifically using bromocriptine, according to the published literature.¹⁶ If the enlarged tumor does not respond to DA, alternatives include delivery if the pregnancy is far enough or, during the second trimester, surgical decompression. Periodic evaluation of prolactin levels offers no diagnostic benefit and is not recommended (**Box 2**).¹⁶

ACROMEGALY

Patients with acromegaly diagnosis frequently have fertility impairment because of the cosecretion of prolactin and the mass effects of the tumor affecting the gonadotrophic axis.³⁷ Nevertheless, pregnancy among acromegalic patients is becoming more common due to improvements in treatment as well as in fertility therapies.

Table 1
Summary of the series reported about cabergoline use during pregnancy in subjects harboring a prolactinoma

Series	Number of Subjects/ Pregnancies	Sellar Images (Available)	Time of Exposition	Dose Range (Per Week)	Maternal Complications (Number of Cases)	Gestational Outcomes	Deliveries (Known Duration)	Fetal Outcomes
Robert et al, ²³ 1996	205/226	118 Microadenomas 15 Macroadenomas 5 Empty sella 65 Normal (ID)	1 to 144 d	0.125–4.0 mg	None	23 Spontaneous abortions 31 Terminations (3 for malformation) 1 IUFD 1 Ectopic pregnancy	129 Term 17 Premature 2 Missing data All single births	148 Live births (10 SGA and 10 LGA) 7 Malformations (3.1%) (2 major) 22 Unknown
Ricci et al, ²⁴ 2002	50/61	25 Microadenomas 12 Macroadenomas 2 Empty sella 5 Normal (ID)	7 to 266 d (mean 39.3 d)	0.25–7.0 mg (mean dose 1.1 mg)	None	6 Spontaneous abortions 5 Terminations (1 for malformation) 1 Hydatidiform moles	38 Term 3 Premature 8 Missing data All single births	49 Live births (6 SGA) 2 Malformation (3.3%) (1 major)
Colao et al, ²⁵ 2008	329/329	N/A	<1 mo in 33% 1–2 mo in 47%	Mean dose 0.98 mg	N/A	31 Spontaneous abortions 40 Terminations (9 for malformation)	193 Term 45 Premature 12 Unknown (8 twin)	250 Live births (17 SGA and 9 LGA) 23 Malformations (6.9%) 4 Stillbirths 4 Unknown
Lebbe et al, ²⁶ 2010	72/100	45 Microadenomas 15 Macroadenomas 12 Normal (ID)	7 to 154 d (median 28 d)	0.25–1.5 mg (median dose 0.5 mg)	3 Hypertension 1 Preeclampsia 4 Gestational diabetes	10 Spontaneous abortions 5 Terminations (3 malformations; 1 twin)	76 Term 8 Premature (4 twin)	88 Live births (9 SGA) 3 Malformations (3.0%) (All major)

						2 Ectopic pregnancies)		
Ono et al, ²⁷ 2010	80/93	53 Microadenomas 27 Macroadenomas	<4 wk in all pregnancies	Maximum dose of 3.0 mg (mean dose 2.29 mg)	1 Hypertension	1 Spontaneous abortion 1 Termination 1 IUFD	82 Term 1 Premature All single births	83 Live births (9 SGA) 7 Ongoing pregnancies No malformations
Auriemma et al, ²⁸ 2013	91/143	76 Microadenomas 10 Macroadenomas 5 Normal (ID)	<6 wk in all pregnancies	(Mean dose 0.69 mg)	None	13 Spontaneous abortions 4 Terminations (1 therapeutic)	126 Term 0 Premature All single births	126 Live births (2 SGA) No malformations
Total	827/952	317 Microadenomas 79 Macroadenomas 7 Empty sella 87 Normal (ID)	N/A	N/A	4 Hypertension 1 Preeclampsia 4 Gestational diabetes	83 Spontaneous abortions 86 Terminations 6 IUFDs 3 Ectopic pregnancies 1 Hydatidiform mole 4 Unknown status	644 Term 74 Premature	744 Live births 35 Malformations (3.7%)

Abbreviations: ID, idiopathic disease; IUFD, intrauterine fetal death; LGA, large for gestational age; SGA, small for gestational age.

Data from Refs.²³⁻²⁸

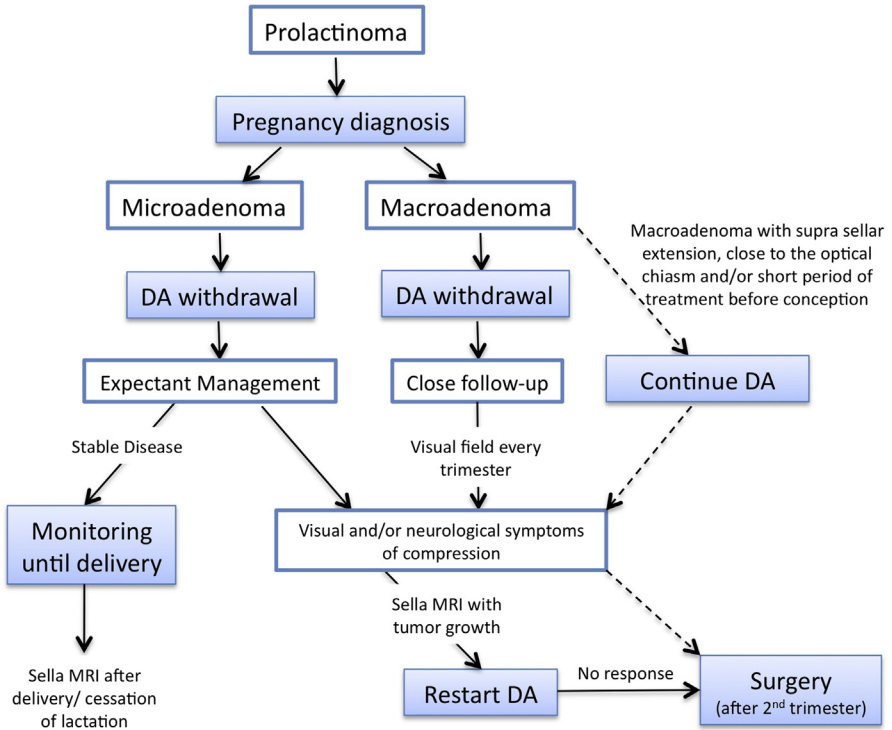


Fig. 1. Prolactinoma management during pregnancy. DA, dopamine agonist.

Box 2

Lactation and follow-up after delivery for women with prolactinoma

- Women who wish to breastfeed their infants should not be given DA because the resulting decrease in serum prolactin levels will impair lactation.¹⁴
- Patients who must receive DA to prevent tumor growth should continue their treatment, although lactation will be impaired.
- No data suggest that breastfeeding leads to an increase in tumor size. Furthermore, prolactin levels are often lower than before pregnancy.
- The recent studies by Domingue and colleagues³⁵ and Auriemma and colleagues²⁸ showed that 41% and 68% of women with prolactinoma, respectively, were in remission of hyperprolactinemia after pregnancy and lactation at a median time interval of 22 months and up to 60 months, respectively. In both studies, breastfeeding did not increase the risk of recurrence of hyperprolactinemia.
- Patients should be reassessed 2 months after delivery or after cessation of lactation, and a pituitary imaging is recommended to evaluate the adenoma.²⁹
- If MRI is necessary during lactation, it can be performed using gadolinium. Less than 1% of this contrast is excreted into the breast milk.³⁶ Therefore, the decision to continue or to suspend breastfeeding for 24 h after a scan should be determined by the doctor and the mother.³⁶

The occurrence of pregnancy associated with acromegaly is concerning because the risk of complications, such as gestational diabetes and hypertension, are increased, especially in women with growth hormone (GH) or insulinlike growth factor-1 (IGF-1) not controlled before conception.³⁸ Regarding the fetus, limited publications have reported normal full-term infants in most cases, with a few cases of low birth weight, which is often related to treatment using somatostatin analogue (SA).^{38–40}

No tumor enlargement was diagnosed in subjects with prior surgery and/or radiotherapy of macroadenomas in series of acromegalic pregnant subjects.^{39–42} However, in the presence of a high Ki-67 labeling index and low aryl hydrocarbon receptor-interacting protein expression, tumor enlargement may occur during gestation even after transsphenoidal surgery.⁴³ Most women with untreated acromegaly have uneventful pregnancies, especially those with microadenomas; however, several subjects required transsphenoidal surgery for pituitary apoplexy associated with GH-secreting macroadenomas or advancing visual loss (**Box 3**).^{38,42}

Treatment of Acromegaly During Pregnancy

Among the medications available for treating acromegaly, SAs are more efficacious than DAs^{50,51}; however, SAs have not been used frequently during pregnancy. Women planning to get pregnant should discontinue medical therapy with a long-acting SA 2 to 3 months before conception, depending on their clinical status.^{46,52}

In several recent series,^{38–41} pregnant women with acromegaly received SA during pregnancy, sometimes with concomitant DA; however, in most cases, the medication was stopped as soon as gestation was diagnosed. Even considering cases in which there was prolonged use of SA during gestation, no serious adverse events regarding pregnancy, delivery, and newborn development were observed (**Table 2**).^{38–41,53} The GH-receptor antagonist use is restricted to exceptional case reports of uncomplicated pregnancies in acromegalic subjects.^{54,55}

Box 3

Pregnancy and acromegaly

- In pregnant acromegalic women, the secretion of placental GH induces an increase in plasma IGF-1 level but not a decrease in the autonomous secretion of GH by the pituitary adenoma.⁴⁴
- To diagnose acromegaly in pregnancy, an interference-free immunofluorometric assay specific for placental GH variant is required to differentiate the pituitary GH and the placental GH.⁴⁵
- The presence of both maternal GH and placental GH in the maternal blood, along with elevated IGF-1, makes it difficult to definitively diagnose acromegaly during gestation. Therefore, biochemical monitoring is of limited use.⁴⁶
- Despite additional placenta-derived GH during pregnancy, acromegalic patients often report an improvement in their clinical signs and symptoms, especially during the first trimester of pregnancy.
- A reduction in IGF-1 levels during pregnancy of acromegalic patients is often noted even without medical therapy,^{38–41,47} whereas a variable decrease in pituitary GH concentrations has been reported in the second half of pregnancy.⁴⁸
- The improvement in IGF-1 could be attributed to the effect of the marked increase in estrogen levels during pregnancy, which inhibits GH signaling, an action that is mediated by the suppressor of cytokine signaling (SOCS) proteins, resulting in a state of GH resistance.^{47,49}

Table 2
Summary of the series reported about acromegaly during pregnancy with use of somatostatin analogue

Series	Number of Subjects/Pregnancies	Adenoma Size (Available)	Time of Diagnosis	Nonmedical Treatment Before Pregnancy	Treatment During Pregnancy	Acromegaly Course During Pregnancy	Maternal Complications or Gestational Outcome	Fetal Outcome
Cozzi et al, ⁴¹ 2006	6/7	4 Macro 2 Micro	All subjects diagnosed before pregnancy	3 Neurosurgeries 1 Neurosurgery and radiotherapy	2 Subjects discontinued depot SA after confirmation of pregnancy Others stopped medication 3–4 mo before conception (DA and/or SA)	GH status: increased in 11, stable in 3, and decreased in 3 subjects IGF-1 status: stable, close to normal range in all subjects 1 Subject refused surgery before pregnancy and was on depot SA, presented tumor enlargement, but no visual field defects	No complications 7 Term pregnancies	7 Live births, all normal newborns
Caron et al, ³⁸ 2010	46/59	39 Macro 7 Micro	6 Subjects had acromegaly diagnosis during pregnancy	39 Neurosurgeries 9 Conventional radiotherapies 5 Gamma-knife radiotherapies	25 Subjects conceived using DA treatment and 14 subjects conceived using SA treatment (8 used both drugs) In most cases, medical treatment discontinued when pregnancy was diagnosed	GH status: mean values were stable IGF-1 status: significant reduction during the 1st and 2nd trimesters 4 Cases of visual field defect (leading to diagnosis of acromegaly in 3 cases, 1 submitted to neurosurgery at 2nd trimester)	4 Cases of GD, 4 cases of hypertension, 1 case of preeclampsia 2 Spontaneous abortions 2 Terminations 55 Term 4 Premature 5 Twin	64 Live births (6 SGA and 2 LGA) No malformations

Cheng et al, ³⁹ 2012	12/13	5 Macro 3 Micro 4 N/A	All subjects diagnosed before pregnancy	6 Neurosurgeries	3 Subjects conceived using SA treatment 1 Case, SA used during 1st trimester 2 Cases, SA used for 20 wk of gestation	IGF-1 status: remained stable or decreased	No complications 13 Term pregnancies	13 Live births (1 SGA, from a subject treated during pregnancy) No malformations
Dias et al, ⁴⁰ 2014	8/10	8 Macro	All subjects were diagnosed before pregnancy	8 Neurosurgeries	9 Pregnancies started with SA treatment 4 Pregnancies started with SA and DA treatment Pharmacologic treatment withdrawn at pregnancy diagnosed (5–6 wk)	GH status: levels assessed in 5 subjects with no significant changes (significant decline in GH was observed in normal pregnant controls) IGF-1 status: mean levels remained unchanged, although the range has increased significantly after midgestation	3 Cases headache, 1 case of GDM and 1 case of hypertension, followed by preeclampsia 9 Term 1 Premature	10 Live births (1 SGA, from subject with preeclampsia) No malformations

Abbreviations: GH, growth hormone; IGF-1, insulinlike growth factor-1; LGA, large for gestational age; SGA, small for gestational age.
Data from Refs.^{38–41}

Nevertheless, a clinical approach to pregnant acromegalic patients is usually expectant, and the withdrawal of any medical therapy for acromegaly treatment is recommended in most cases, along with close follow-up during gestation (Fig. 2).^{46,52}

In patients with GH-secreting macroadenomas, although tumor enlargement rarely occurs,^{38–41} close follow-up and visual field testing are recommended every trimester, independent of the development of compressive symptoms and with the use of MRI limited to confirming tumor enlargement.^{46,52} For patients with a macroadenoma diagnosed during pregnancy or after a short medical treatment (less than 1 year), monthly follow-up visits should be proposed.⁵² Patients with macroadenomas at high risk for tumor growth can be maintained on treatment with DA and/or SA throughout the pregnancy.^{43,46,53} In patients with evidence of tumor growth, transsphenoidal surgery during the second trimester and/or medical treatment should be considered, and breastfeeding is contraindicated.^{34,52}

There are only 2 reports of transsphenoidal surgery in acromegalic pregnant patients.^{56,57} In both cases, the diagnosis of acromegaly was made at the last trimester due to visual complaints: 1 patient had acute visual loss and the other had pituitary apoplexy. Both underwent emergent transsphenoidal surgery. One patient delivered at term, whereas the other patient had a cesarean section at 34 weeks. Both babies were healthy.

In uneventful pregnancies, breastfeeding is allowed before the commencement of pharmacologic treatment because of the lack of complications documented in

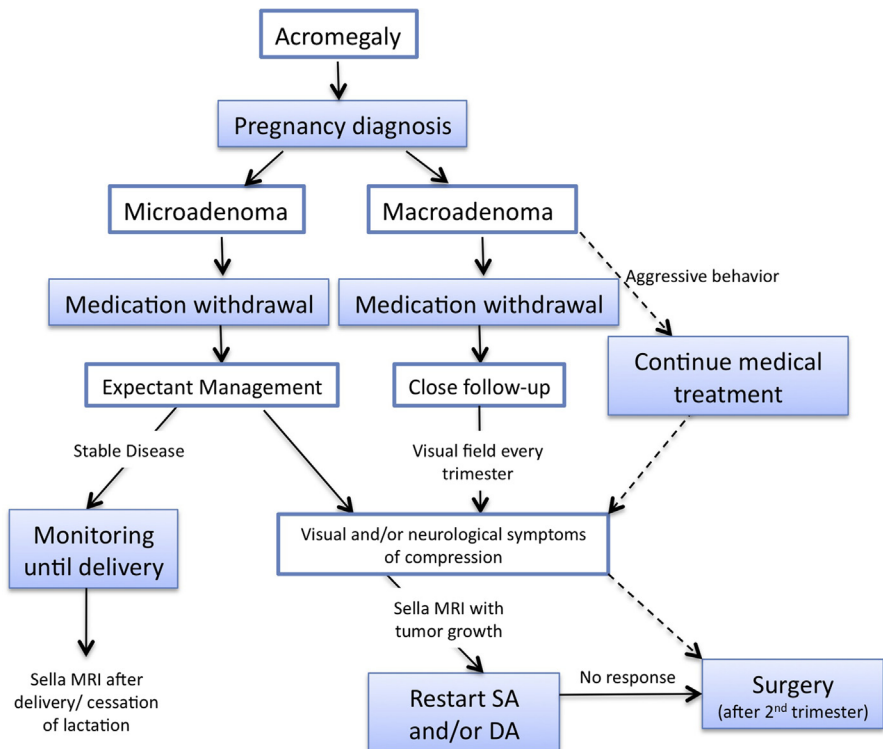


Fig. 2. Acromegaly management during pregnancy. DA, dopamine agonist; SA, somatostatin analogues.

lactating women with acromegaly.^{38–41} After delivery, MRI must be repeated in all patients with GH-secreting tumors to evaluate the tumor size.³⁴

CUSHING SYNDROME

Pregnancy rarely occurs during the course of Cushing syndrome (CS) because the disease leads to a state of hypercortisolism and hyperandrogenism that suppress the gonadotroph function. This condition results in oligomenorrhea and amenorrhea in most female patients, frequently accompanied by infertility.⁵⁸

Different from cases of prolactinoma and acromegaly, in which the disease is usually diagnosed before pregnancy, CS was diagnosed during the course of pregnancy in most reported cases.⁵⁹ An adrenal adenoma is responsible for most of these cases, with only 40% related to an adrenocorticotrophic hormone (ACTH)-producing pituitary adenoma.²⁹

Cushing Syndrome Diagnosis and Differential Diagnosis During Pregnancy

The clinical diagnosis of CS during pregnancy may be missed because of the overlapping features of weight gain, hypertension, fatigue, hyperglycemia, and emotional changes characteristic of pregnancy.⁶⁰ Clues that can lead to suspicion of CS include large purple instead of white striae, hirsutism, acne, the presence of hypokalemia, muscle weakness, and pathologic fractures.^{61,62}

The diagnostic tests for CS become less reliable during gestation (**Box 4**), and the normal physiology of pregnancy makes it difficult to biochemically diagnose CS (see **Box 1**). The differential diagnosis among all possible causes of CS is mandatory to address the therapeutic approach. Therefore, plasma ACTH measurement should be the initial step to guide the subsequent evaluation with pituitary or adrenal MRI.⁵⁹

Treatment of Cushing Syndrome During Pregnancy

The association of pregnancy with CS increases maternal morbidity in approximately 70% of cases and also impairs fetal outcome (**Table 3**).^{11,29} Therefore, there is a rationale for treating CS during pregnancy. However, treating pregnant patients with CS has been done only sporadically, generally late in the course of the pregnancy.

Box 4

Establishing Cushing syndrome diagnosis during gestation

- Low-dose dexamethasone administration usually fails to suppress cortisol secretion during pregnancy.²⁹ According to the guidelines for diagnosis of CS, the use of this test during pregnancy should not be preferred because of false-positive results due to blunted response to dexamethasone.⁶³
- Another problem is that plasma cortisol will be elevated because of an increase in CBG.⁶⁴
- UFC should be used as the best choice in screening for CS during pregnancy. Values greater than 3 times the upper limit should be taken into consideration in the last 2 trimesters.⁶³
- Because serum cortisol circadian variation is altered in women with CS but preserved in normal pregnancy, late-night cortisol greater than 5 mg/dL or greater than 50% of morning cortisol is suggestive of CS.¹¹
- Nighttime salivary cortisol measurement is the best test to evaluate the circadian rhythm of cortisol and theoretically could be a good screening test for CS during pregnancy, although there is no specific study that defines the cutoff during gestation.^{65,66}

Maternal Morbidity	Fetal Morbidity
Hypertension	Spontaneous abortion or intrauterine death
Diabetes mellitus	Prematurity
Preeclampsia	Stillbirth
Osteoporosis and fracture	Intrauterine growth retardation
Cardiac failure	Infant death
Pulmonary edema	Hypoadrenalism
Psychiatric disorder	Intraventricular hemorrhage postpartum
Wound infection	Malformation
Maternal death	—

Consequently, the ability of treatment to prevent adverse outcomes is not well-established,⁶⁰ although a trend toward better fetal outcome in treated patients compared with nontreated patients has been observed.⁵⁹

Concerning ACTH-secreting adenomas, which is the scope of this article, the treatment of choice is transsphenoidal surgery during the second trimester of pregnancy.^{29,67} Despite that recommendation, among all cases of CS reported in a review by Lindsay and colleagues,⁵⁹ only 20% of the patients underwent transsphenoidal surgery; the remainder of the treated patients received medical therapy (metyrapone or ketoconazole) and/or adrenalectomy. A high proportion (54%) of the patients was untreated.

In cases in which surgery cannot be performed, such as severe CS, medical treatment can be considered. The primary medical therapy was reported in 20 women, most using metyrapone, which seems to be well tolerated although it is occasionally associated with preeclampsia. Therefore, its use must be limited to a transient period, pending a definitive approach.⁵⁹ Ketoconazole has been successfully used in 3 pregnancies without adverse events.⁵⁹ However, because of its antiandrogenic effects and teratogenicity demonstrated in rats, this medication should be reserved for individuals who need emergent medical therapy and who cannot tolerate metyrapone.⁵⁹ A recent case report concerning the use of cabergoline in high doses throughout pregnancy showed a favorable outcome, suggesting a possible role for DA in the treatment of pregnant patients with CS.⁶⁸

THYROTROPIN PITUITARY ADENOMAS

Thyrotropin is also called thyroid-secreting hormone (TSH). TSH pituitary adenomas (TSH-omas) account for approximately 0.5% to 3% of all pituitary adenomas.⁶⁹ They are often large and invasive lesions associated with symptoms of hyperthyroidism.⁶⁹ Pregnancy in women harboring TSH-omas is, therefore, exceedingly rare, with only 4 cases reported in the literature. The pituitary adenoma diagnosis occurred before pregnancy in 3 cases and during pregnancy in 1 case, all of which resulted in healthy newborns.^{70–73}

As with other pituitary adenomas, patients with TSH-omas require close follow-up for mass-related tumor symptoms. Because this adenoma subtype is rare, a general management strategy cannot be established. Nevertheless, successful outcomes from previously reported cases demonstrate that pregnancy is feasible in these patients.

NONFUNCTIONING PITUITARY ADENOMAS

Nonfunctioning pituitary adenomas (NFPAs) represent approximately 30% of all pituitary tumors.⁷⁴ They are usually diagnosed at the sixth decade, being rare in women of reproductive age.⁷⁵ Because fertility is usually impaired due to hypopituitarism, pregnancy rarely occurs in women with NFPAs.

Pregnancy rarely increases the size of clinical NFPAs. The enlargement of the pituitary adenoma may be due to tumor growth or apoplexy of the tumor during pregnancy.²⁹ The best approach for patients with asymptomatic NFPA is the wait-and-see policy. However, in cases of symptomatic tumor enlargement, medical treatment using DA can be considered to reduce physiologic lactotroph cell hyperplasia, and surgery should be considered during the second trimester.^{29,34}

SUMMARY

The general recommendation for pituitary adenoma patients is to withdraw medical therapy as soon as pregnancy is diagnosed. However, in cases of macroadenomas, this decision must be individualized. Moreover, when medical therapy is imperative, commonly used medications (eg, DA and SA) seem to be safe. Surgery, when indicated, must be performed during the second trimester of gestation. Those recommendations are not applicable to pregnant women with CS in which there is a high risk of complications for both mother and fetus, independent of the pituitary adenoma size, due to the deleterious effects of high cortisol levels. In this setting, either medical or surgical treatment can be considered during pregnancy.

Available data show that microadenomas often exhibit a favorable course and that macroadenomas occasionally increase in size. A concern regarding visual compression exists primarily because the pituitary gland suffers an estrogen-induced lactotroph hyperplasia; however, this physiologic phenomenon is usually not enough to lead to compressive symptoms, unless the tumor itself suffers an enlargement. Nevertheless, close follow-up is the best approach for ensuring early recognition of complications.

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