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Pregnancy and Acromegaly: About 2 Cases

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Abstract **Case Report**

Introduction: Pregnancies in women with acromegaly are rare. Literature reports indicate the absence of fetal malformations, rarely symptomatic increases in adenoma volume, and a possible risk of gestational diabetes and pregnancy-induced hypertension in women not adequately controlled by medication before pregnancy. Variations in somatotrope function have been rarely studied. ***Observations***: Our two patients had previously undergone surgery for somatotrope adenomas and were treated with somatostatin analogs before pregnancy, with treatment discontinued upon pregnancy diagnosis. All pregnancies were normal without gestational diabetes, pregnancy-induced hypertension, or pituitary tumor syndrome. No newborns had congenital malformations. ***Conclusion***: Pregnancy does not appear to worsen acromegaly in young patients well-controlled with somatostatin analogs before pregnancy.

Keywords: Acromegaly, Pregnancy, Growth Hormone, Somatostatin, Octreotide, Lanreotide, Somatotropinoma, Pituitary.

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INTRODUCTION

Acromegaly is a rare condition caused by excess growth hormone (GH) from a somatotrope macroadenoma, leading to significant changes in insulin-like growth factor-1 (IGF-1) and insulin concentrations and actions. These hormonal changes, along with processes like methylation, are crucial during pregnancy. The condition often disrupts the gonadotrope axis, causing menstrual disorders and infertility in women.

Despite these challenges, effective treatments for somatotrope hypersecretion have restored fertility in many young patients. Over 150 full-term pregnancies in women with acromegaly have been documented. A recent French multicenter study involving 59 pregnancies found increased risks of gestational diabetes and hypertension in patients with uncontrolled somatotrope hypersecretion. The study also showed that discontinuing treatments upon pregnancy diagnosis is generally safe, as adenoma growth rarely causes symptoms during pregnancy [1].

In normal pregnancies, increased estrogen and progesterone reduce liver sensitivity to GH. During the second half of pregnancy, placental GH secretion rises while pituitary GH secretion decreases, explaining why acromegaly patients do not usually experience a biochemical escape when treatment is stopped. Consequently, continuing medical treatment for acromegaly during pregnancy is often unnecessary [2].

Through these two observations, we describe the evolution and management of a full-term pregnancy in two women with progressive acromegaly.

OBSERVATIONS

PATIENT 1:

A 34-year-old female patient has been followed in our clinic since September 2017 for acromegaly, initially revealed by secondary amenorrhea and acromegaloid features. Her initial IGF-1 level was elevated at 1285 ng/ml (3.5 times the upper limit of normal). Pituitary MRI showed a macroadenoma measuring 24x18x19 mm, with slight T1 hyperintensity, homogeneity, and marked hypointensity on T2, unchanged after contrast injection. The tumor caused compression of the pituitary parenchyma and bulging of the diaphragma sellae, displacing the pituitary stalk to the right while preserving the integrity of the optic chiasm.

The patient underwent endonasal surgery on January 25, 2018. Postoperative MRI showed a left-lateralized pituitary lesion measuring 17x5.7 mm,

appearing as a postoperative residual. Post-surgery IGF-1 levels were 174 ng/ml.

She was started on Lanreotide therapy, which led to the resumption of regular menstrual cycles. Two years later, she conceived and carried the pregnancy to term without complications, successfully breastfeeding. Lanreotide treatment was discontinued during pregnancy.

Postpartum MRI was not performed. The latest MRI on January 2, 2024, showed a quasi-stable left-lateralized sellar formation, poorly defined, measuring 9.7x4.2 mm, with iso-signal on T1, marked hypointensity on T2, and no enhancement after contrast injection.

PATIENT 2:

A 34-year-old patient was admitted for a 6-month postoperative evaluation of a silent somatotrope pituitary macroadenoma, initially revealed by disconnection hyperprolactinemia. Postoperative assessment showed an IGF-1 level of 131 (normal) with a stable tumor volume except for some necrotic areas. Initially, the patient was on LT4 and hydrocortisone (HC), and post-surgery, she was prescribed 15 mg of HC.

The patient experienced an unplanned but desired progressive pregnancy, currently at 23 weeks gestation (23 SA), with no abnormalities detected on the 21-week obstetric ultrasound. She exhibited galactorrhea and asthenia but had no signs of thyrotropic insufficiency, tumor syndrome, or polyuria-polydipsia syndrome. An MRI with contrast of the hypothalamic-pituitary region was performed at the end of the first trimester.

The pregnancy proceeded without complications such as gestational hypertension or diabetes. The patient delivered a healthy full-term newborn. Postpartum MRI showed that the tumor mass remained almost stable

DISCUSSION

Around 150 cases of pregnancy in women with acromegaly have been reported in the literature, illustrating the rarity of this condition in young women and the associated hypofertility [3].

Growth hormone-producing tumors commonly lead to infertility due to the tumor mass effect on gonadotropins and possible associated hyperprolactinemia causing anovulation [5].

Under the influence of estrogens, lactotrope cells undergo hyperplasia, resulting in a physiological 45% increase in pituitary volume in normal women [4].

In acromegaly, the pituitary tumor (a macroadenoma in 80% of cases) can exert a mass effect on the optic pathways, threatening visual prognosis during pregnancy [6]. Estrogen-induced tumor expansion can also risk apoplexy, particularly if the adenoma exceeds 12 mm in diameter. Therapeutic pregnancy termination occurs in 4% of cases, often due to worsening clinical signs of acromegaly or the emergence of a tumor syndrome [4].

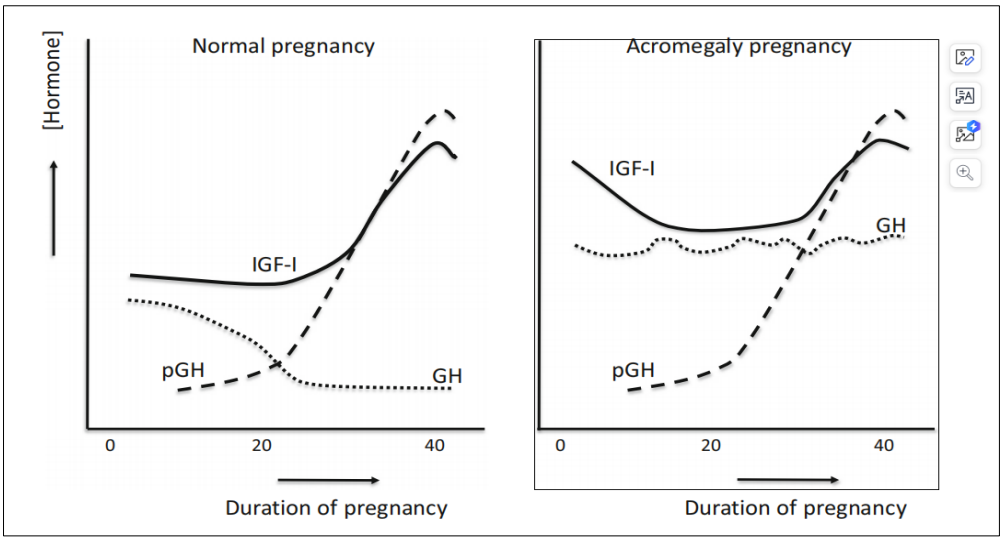

Figure 1: Semi-qualitative conceptual changes in GH, IGFI and placental GH (pGH) during normal pregnancy and during pregnancy in women with acromegaly

Breastfeeding stimulates normal pituitary cell growth, and four patients in Cozzi *et al.*,'s series [7], breastfed without incident. Bronstein *et al.*, [6], indicated that breastfeeding is permissible if the pregnancy was complication-free.

IGF-1 monitoring during pregnancy must consider the placental GH effect [8], which increases

IGF-1 levels. In normal pregnancy, placental GH inhibits pituitary GH secretion and stimulates hepatic IGF-1 production from the second trimester, raising IGF-1 levels in the second and third trimesters. In acromegalic pregnant women, pituitary GH secretion persists, also elevating IGF-1 from the second trimester. In our patient, IGF-1 levels tripled by the third trimester. However, not all reported cases show this IGF-1 increase. Cozzi *et al*., found stable IGF-1 levels during pregnancy in seven acromegalic women [6]. More recently, Lau *et al*., reported three full-term pregnancies without complications in a young woman with progressive acromegaly, noting clinical improvement and significant IGF-1 reduction, possibly due to estrogen-induced GH resistance [9].

Acromegaly during pregnancy also poses maternal and fetal complications. GH's antagonistic effect on insulin promotes gestational diabetes, and preeclampsia and cardiovascular complications are possible, although not unusually frequent in pregnant acromegalic women [7]. Fetal macrosomia, however, is significantly more common, with an average birth weight of about 4700 g, though our patient did not experience this complication [10].

Our patients treatment was stopped upon conception. Somatostatin analogs cross the placental barrier [11], and while somatostatin receptors are expressed in the fetus, their functionality is doubtful [7]. Therapeutic doses of octreotide do not bind to placental somatostatin receptors [12], and no adverse effects on newborns from mothers treated with octreotide have been reported, mainly with short-acting forms [11]. Prolonged-release forms might result in longer fetal exposure, but no intrauterine growth retardation or postnatal developmental anomalies have been reported [13]. An observation demonstrated the efficacy and safety of a GH antagonist (pegvisomant) during pregnancy in an acromegalic woman [14].

CONCLUSION

The occurrence of pregnancy in women with acromegaly is becoming increasingly common. The effectiveness of somatostatin analogs in controlling GH secretion, along with careful monitoring of these patients, makes pregnancy a feasible and relatively low-risk event for these young women. However, due to insufficient long-term data, it remains prudent to discontinue this type of treatment during pregnancy unless it is absolutely necessary.

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