date of tachycardia-induced cardiomyopathy secondary to hyperthyroidism due to selective pituitary resistance to thyroid hormone. Our patient experienced left chamber dilation combined with severe pulmonary artery hypertension which was caused by persistent sinus tachycardia and frequent ventricular extrasystoles secondary to hyperthyroidism.

Triiodothyroacetic acid is a T3 analogue with a predominant pituitary and hepatic effect which has been shown to be of value for the treatment of selective pituitary resistance to thyroid hormones at doses ranging from 1.4 to 2.8 mg/day,\(^1\) although partial or no response has been reported in some cases.\(^6\) Dextrothyroxine is another agent with a TSH-suppressing effect greater than levothyroxine which does not significantly affect cardiac function and has been shown to be effective in patients not responding to triiodothyroacetic acid. In the near future, new specific analogues of TRβ2 and TRβ1 receptors could be more effective for the treatment of pituitary resistance to thyroid hormones. On the other hand, ablative treatment with radioiodine and/or thyroid surgery may be detrimental in these patients, because it induces a chronic, sustained elevation of TSH levels with the probable subsequent occurrence of thyroid hyperplasia or adenoma.\(^5\)\(^,\)\(^7\) Treatment with bisoprolol 10 mg/day before the final diagnosis of our patient was unable to control tachycardia or extrasystole. Once the final diagnosis of selective pituitary resistance to thyroid hormones had been made, treatment was started with triiodothyroacetic acid at a dose of 1.4 mg/day, which achieved an excellent response at 6 months, with the disappearance of symptoms and thyroid hormone normalization. An adequate control of heart rate and 24-hour Holter monitoring (mean heart rate of 64 bpm, no extrasystoles) was also achieved. Echocardiography showed a significant improvement in pulmonary artery pressure, with a return to the baseline state of moderate pulmonary artery hypertension and the disappearance of left ventricular and atrial dilation. Systolic function also normalized.

In conclusion, tachycardia-induced cardiomyopathy associated with hyperthyroidism due to selective pituitary resistance to thyroid hormones is an exceptional and reversible cause of dilated cardiomyopathy and pulmonary artery hypertension. Triiodothyroacetic acid is currently a safe and effective drug for the adequate management and treatment of this condition.

References


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Management of acromegaly in pregnancy: Case report and literature review

Seguimiento de gestación en paciente con acromegalia: descripción de caso clínico y revisión de la literatura

Acromegaly is a disease diagnosed with increasing frequency\(^1\) and whose mean age of onset coincides to a great extent with the child-bearing life of women.\(^2\) Treatments currently available for acromegaly include surgery, drug treatment and, in some cases, radiotherapy. These therapeutic modalities achieve tumor growth control and minimize the clinical consequences of hypersomatotropism in most patients.\(^3\)

Despite the positive impact of current treatments on survival and quality of life, pregnancy in acromegaly continues to be an uncommon event and a challenge for clinicians. The largest case series reported required multicenter collaboration in France and included 59 pregnancies,\(^4\) while hardly one hundred pregnancies have been reported in other publications.\(^4\) The lack of retrospective data makes it difficult to anticipate potential complications. Such information is required to provide informed counsel to patients with acromegaly who want to bear children. We therefore report a patient with active acromegaly after surgery

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attending our department who completed a full-term pregnancy.

A 31-year-old woman attended the gynecology clinic in 2005 reporting oligomenorrhea and galactorrhea for approximately one year, with no hirsutism or other symptoms. Available biochemical test results included prolactin levels of 86.22 ng/mL (4.8–23.3 ng/mL) in the absence of drugs that could affect such measurement. Pituitary magnetic resonance imaging (MRI) revealed a pituitary macroadenoma with suprasellar extension and invasion of the right cavernous sinus. The patient was referred to the neurosurgery department for surgery, which was performed in 2006 by a transsphenoidal approach with no complications. She was subsequently evaluated at our department for postoperative follow-up. The patient had not shown at any time acral thickening, prognathism, diaphoresis, headache, arthralgia, high blood pressure, hyperglycemia, or other evidence suggesting acromegaly. However, basal hypothalamic-pituitary tests (Table 1) found consistently elevated IGF-I levels and there was an absence of growth hormone (GH) suppression in an oral glucose tolerance test. The pituitary profile also included decreased serum cortisol levels, for which the patient was treated with oral hydrocortisone. Additional tests performed included an echocardiogram, a polysomnographic study, and a colonoscopy, none of which suggested changes associated with acromegaly. Postoperative MRI revealed a residual tumor in the sella turcica and right cavernous sinus, and repeat surgery was decided upon after consultation with the neurosurgery department.

Endoscopic transsphenoidal surgery was performed at our hospital, and a significant decrease in IGF-I levels and tumor mass reduction were achieved. The pathological laboratory reported an adenoma with immunohistochemistry positive for GH and negative for prolactin, with a Ki 67 index of 5%. After surgery, the patient achieved regular menses and had no evidence of hypopituitarism. However (Table 1), biochemical criteria of disease activity persisted, as well as gross tumor remnants. Because of a slight increase in IGF-I levels, treatment was attempted with cabergoline, which improved biochemical control of the disease. At treatment start, the patient had been recommended to avoid pregnancy until biochemical normalization and tumor stability had been ensured.

In 2008, three months after the final control and at 35 years of age, the patient attended our department reporting a five-week pregnancy that she wanted to continue. Therefore, cabergoline treatment was discontinued, and three-monthly neurological and ophthalmological controls and monitoring of high-risk pregnancy at the clinic were scheduled. The patient was also advised to stop smoking, which she declined to do. She remained symptom-free during pregnancy until she delivered a healthy baby at 39 weeks. At the controls made (Table 1), IGF-I levels decreased during pregnancy to levels normal for age, except in the last measurement. The O’Sullivan test was normal in the first and third trimesters, and no treatment was required for blood pressure. At the end of pregnancy, MRI showed tumor stability (Fig. 1). However, postpartum IGF-I levels again exceeded physiological limits, although the patient reported no symptoms. In order to decrease the morbidity associated with excess GH, the patient started treatment.

### Table 1

<table>
<thead>
<tr>
<th>Laboratory test results of the patient.</th>
<th>IGF-I</th>
<th>GH nadir in</th>
<th>OGTT 75 g</th>
</tr>
</thead>
<tbody>
<tr>
<td>After initial surgery (January 2007)</td>
<td>407 ng/mL</td>
<td>115-307 ng/mL</td>
<td>0.87 ng/mL</td>
</tr>
<tr>
<td>Before surgery (June 2007)</td>
<td>328 ng/mL</td>
<td>109-284 ng/mL</td>
<td>-</td>
</tr>
<tr>
<td>After repeat surgery, 6 months postpartum (June 2007)</td>
<td>109-284 ng/mL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>After repeat surgery, 2 months postpartum, without treatment for nursing</td>
<td>109-284 ng/mL</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>At 7 weeks of pregnancy</td>
<td>2.15 mg/dL</td>
<td>0.87-307 mg/dL</td>
<td>-</td>
</tr>
<tr>
<td>At 14 weeks of pregnancy</td>
<td>2.15 mg/dL</td>
<td>0.87-307 mg/dL</td>
<td>-</td>
</tr>
<tr>
<td>At 26 weeks of pregnancy</td>
<td>2.15 mg/dL</td>
<td>0.87-307 mg/dL</td>
<td>-</td>
</tr>
<tr>
<td>At 36 weeks of pregnancy</td>
<td>2.15 mg/dL</td>
<td>0.87-307 mg/dL</td>
<td>-</td>
</tr>
</tbody>
</table>

GH: growth hormone; IGF-I: insulin-like growth factor-I; OGTT: oral glucose tolerance test.
with cabergoline, which led to a gradual improvement in the biochemical parameters and to tumor stability.

Acromegaly is a syndrome with high associated morbidity and mortality. Fortunately, we now have available an increasingly wide therapeutic armamentarium to improve patient prognosis and quality of life. However, despite these advances, little experience is available in pregnancy monitoring in patients with acromegaly. There may be several reasons for this:

- Hyperactivity of the somatotropic axis may alter hormonal cycles leading to ovulation. This, combined with the greater frequency of ovarian functional hyperandrogenism and increased insulin resistance in patients with acromegaly,\(^1\),\(^3\)\(^,\)\(^5\) may hinder ovulation and, thus, pregnancy. In addition, hypogonadotropic hypogonadism due to tumor compression or iatrogenic in nature (surgery and radiotherapy) may coexist, and will then require external hormonal induction of ovulation to achieve pregnancy.
- The burden of disease symptoms and the limited experience with most drugs available for acromegaly in pregnancy may discourage attempts at pregnancy in patients and their physicians. Discontinuation of somatostatin analogues and cabergoline is currently recommended when pregnancy is documented, but the clinical cases reported have not shown that these drugs are teratogenic or increase maternal or fetal risk. In addition, surgery involves a risk of pregnancy interruption, and radiotherapy is directly contraindicated in pregnant patients.
- The greater difficulty in the clinical and biochemical monitoring of the disease: during pregnancy, pituitary GH (GH1) secretion is physiologically replaced by placental GH (GH-V) secretion; healthy patients suppress GH1 secretion, while pregnant women with acromegaly maintain steady GH1 levels. In addition, gestational hypoestrogenism blocks IGF-I secretion in the liver, which explains the decreased IGF-I secretion in our patient.\(^3\)\(^,\)\(^6\) Moreover, the different GH variants and IGF-I do not cross the placental barrier, which prevents their having direct harmful effects on the fetus.\(^7\) The abovementioned physiological changes do not allow for the reliable monitoring of acromegaly in pregnancy based on these biochemical parameters, and the physical changes inherent in pregnancy (edema, limb swelling, etc.) may be confounded with disease symptoms. In addition, MRI should be performed without contrast, and only in cases with symptoms of potential visual involvement, which increases the uncertainty regarding the clinical course.

Based on the above considerations, the following should be taken into account when a patient with acromegaly inquires about the feasibility of a future pregnancy:

1) The patient should be monitored for tumor growth during pregnancy, and the specific risks to pregnancy of the available treatments (surgery, somatostatin analogues, and cabergoline) should be taken into account.
2) The patient should be monitored closely for gestational diabetes and pregnancy-induced hypertension, each with its own specific maternal and fetal risks, particularly in the presence of active disease.
3) There is no evidence that excess growth hormone and IGF-I on their own increase the maternal and fetal risks.
4) Biochemical monitoring is of less value during pregnancy, and clinical data are more difficult to interpret, because the typical changes of pregnancy may be very similar.

Despite the above, the experiences reported to date have been favorable in a majority of cases, although a publication bias cannot be ruled out. In the largest series reported to date,\(^4\) including 59 pregnancies, most patients were able to safely discontinue drug treatment. The offspring of these patients included six micromom and two macrosomic fetuses, and there was a slightly higher incidence of gestational diabetes and arterial hypertension induced by pregnancy, particularly in patients with active disease. Tumor volume remained stable in most patients. Despite these positive data, the currently available experience regarding pregnancy in acromegaly is scant, and consistent and comprehensive analysis of data from future pregnancies is therefore required, preferably in the setting of multicenter studies. Such studies would allow for more rigorous counseling about the feasibility of pregnancy
in patients with acromegaly, which should be part of the treatment of childbearing patients with any pathological condition.

References


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Diabetes insipidus induced by pregnancy.
A case report

Diabetes insipida inducida por el embarazo.
Comunicación de un caso

Diabetes insipidus (DI) is a rare endocrine disorder reported to occur in one per 25,000–30,000 people in the general population. The occurrence of this syndrome in pregnancy is even rarer, and only a limited number of cases of DI have therefore been reported during pregnancy. DI may be the continuation of the syndrome discovered before pregnancy, or may first occur during pregnancy and subsequently disappear.

We report the case of a 16-year-old female patient, a primigravida with no significant clinical history regularly attending antenatal visits. No medical problems were reported until the 38th week of pregnancy, when she was found to have high blood pressure (162/102 mmHg) associated with headache, epigastric pain, and proteinuria (650 mg/day). Laboratory test results were normal, except for a serum creatinine level of 151 mmol/L. An intravenous dose of clonidine was administered, and a magnesium sulfate infusion was started to stabilize the patient, after which a cesarean section was performed for fetal distress, delivering a live newborn weighing 3400 g.

A persistent increase in urine output (900 mL/h) and a urine specific gravity of 1005 were seen despite fluid restriction to 80 mL/h. The patient reported severe polydipsia. On further questioning, the patient reported polydipsia and polyuria three months before admission. Plasma osmolality was 289 mOsml/L, and decreased urinary osmolality (141 mOsm/L) and normal glucose, potassium and calcium levels were found. DI was therefore diagnosed. Treatment was started with L-deamino 8-d arginine vasopressin (LDDV; 10 µg intranasal twice daily), which resulted in decreased urine output within 60 min of administration and increased urinary osmolality. Urinary osmolality increased to 249 mOsm/L 48 h after delivery, and LDDV was therefore discontinued. The patient was discharged from hospital on the fifth postpartum day with no signs of DI or additional complications. Endocrinological follow-up confirmed that there were no underlying metabolic disorders.

The placenta normally secretes small amounts of vasopressinase (a cystinaminopeptidase produced by the trophoblast), which reaches peak levels at the end of pregnancy. The factors predisposing some women to have placental vasopressinase levels high enough to cause DI are unknown. The sudden occurrence and rapid disappearance of symptoms suggest a diagnosis of DI induced by vasopressinase secreted by the placenta. Since vasopressinase levels decrease by 25% one day after delivery, rapid recovery in the postpartum period is normal. The risk of recurrence in the next pregnancy is unknown.

The usual signs of DI are polydipsia and polyuria. Diagnosis is not simple because of changes in water metabolism during pregnancy. The initial step is confirmation of free water diuresis to exclude diabetes mellitus. During pregnancy and in the absence of glycosuria, hypokalemia, or hypercalcemia, diabetes insipidus may be diagnosed in a patient with polydipsia and polyuria with serum osmolality higher than 285 mOsm/L associated with hyposthenuria. The exclusion of organic diseases is essential to diagnose DI.

As seen in the reported case, DI is often associated with preeclampsia. Specifically, DI has been associated with acute fatty liver of pregnancy or other liver diseases (elevated transaminases), which are also manifestations of preeclampsia. A hypothesis relating DI and preeclampsia was postulated by Gordge et al.