Pregnancy Associated with Recurrent Acromegaly: A Case Report

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ABSTRACT
BACKGROUND: Acromegaly is an uncommon endocrine disorder. Pregnancy is an unusual event in acromegalic females because fertility is often reduced. With the advent of advanced surgical and medical management, more acromegalic women will achieve pregnancy. Reports of pregnancy in acromegaly and recurrent acromegaly postpartum are rare.

OBJECTIVE: To present a rare occurrence of pregnancy in acromegaly after macroadenectomy and recurrent acromegaly postpartum.

METHODS: Clinical and biochemical evaluation of a 39-year-old female Nigerian with features of acromegaly before and after macroadenectomy and postpartum was done. Investigations carried out included oral glucose tolerance test with serial growth hormone assays and insulin-like growth factor 1 as well as computed tomography scan and magnetic resonance imaging of the pituitary.

RESULTS: There was a history of menorrhagia, swelling of the feet and increasing coarsening of the facial appearance. She had biochemical evidence of acromegaly and subsequently had a transsphenoidal macroadenectomy. There was postoperative clinical and biochemical remission. Magnetic resonance imaging done six months postsurgery showed no evidence of tumour regrowth. Clinical and biochemical evidence of acromegaly recurred after pregnancy. Magnetic resonance imaging confirmed tumour regrowth.

CONCLUSION: Pregnancy in treated acromegaly, though a rare occurrence, is achievable but is capable of provoking recurrence of acromegaly. WAJM 2010; 29(2): 120-122.

Keywords: Recurrent acromegaly, Pituitary macroadenoma, transsphenoidal macroadenectomy, pregnancy.
INTRODUCTION

Reports of pregnancy occurring in acromegalic patients are uncommon. In 1998, Herman Bonert et al had in a review of the literature reported 24 cases of pregnancy and acromegaly. This was subsequent to the 34 cases initially reported in the 1950s. Their report revealed that pregnancies occurred in varied clinical settings of acromegaly, ranging from undiagnosed, untreated acromegaly, to patients treated with bromocriptine, octreotide and trans-sphenoidal surgery without specific fertility treatment. The majority of reported cases were treated with bromocriptine only or in combination with radiation or surgery. Pregnancy has occurred after surgical intervention alone and despite the persistence of GH hypersecretion. This report is of a Nigerian who became pregnant after successful surgical removal of a GH-secreting macroadenoma.

Case Report

A 39-year-old female Nigerian clerical officer presented with a six-month history of amenorrhea, swelling of feet and increasing coarsening of her facial appearance. There were no headaches, visual disturbances, or symptoms of heart failure. She was a known case of acromegaly, which was diagnosed in 1999 after a two-year history of amenorrhea, galactorrhea, increase in the size of the hands and feet, deepening of the voice and mild degree of hirsutism. Serum prolactin level was 1986mIU/L (normal 40–700). She had a transsphenoidal hypophysectomy in the United Kingdom in September 1999 for a macroadenoma with suprasellar extension. Tumour histology showed an acidophil adenoma. There was postoperative clinical and biochemical remission (see Table 1 for results of postoperative evaluation). Serum prolactin level dropped to 363 mIU/L post surgery. The rest of the anterior pituitary function was well preserved and no hormonal replacement therapy was indicated. Magnetic resonance imaging (MRI) of the pituitary fossa done six months postsurgery showed no evidence of tumour regrowth.

She had four successful pregnancies before the diagnosis of acromegaly. Seven months after surgery she became pregnant. She had declined the use of intra-uterine contraceptive device because of the attendant menorrhagia and also refused any form of hormonal contraceptive for fear of regrowth of the pituitary tumour. After an uneventful antenatal care under a consultant obstetrician, she was delivered of a live normal male baby at term by elective caesarian section on patient’s request to avoid the ‘stress of labour’. She breastfed for about a year.

Physical examination showed a lady prognathism, macroglossia, large hands and feet, and ankle edema. Arterial pulse rate was 88 beats per minute, blood pressure was 130/80mmHg, and apex beat was not displaced. There was a midline subumbilical scar in the abdomen but no organomegaly. There was no cranial nerve deficit or ophthalmoplegia. Chest and visual field examinations were normal. Clinical impression was that of recurrence of growth hormone hyper-secretion in an acromegalic patient possibly secondary to regrowth of tumor.

Investigations done showed that human growth hormone levels were elevated during a 75g oral glucose tolerance test (Table 1). Prolactin level was 59ng/ml (normal 1.2–22). The serum electrolytes, urea and creatinine, and heamatological indices were within normal limits. Computed tomography (CT) scan of brain showed no significant enlargement of sella turcica or evidence of intraluminal glandular enlargement or erosion of the adjacent bony structure. There was delay in doing MRI (not readily available in Nigeria), but showed evidence of tumour regrowth. Abdominal and pelvic ultrasound scans were normal.

Treatment was commenced with bromocriptine 5mg daily and long-acting octreotide (Sandostatin®) given intramuscularly at a dose of 20mg 4-weekly. However compliance with octreotide has been poor due to irregular procurement on account of financial constraints and non-availability of the drug in Nigeria.

DISCUSSION

Until recently, pregnancy was considered an uncommon event in acromegalic females but with the advent of better medical and surgical therapy, more acromegalis are becoming pregnant and having similar survival to that of age and sex-matched controls. There is however concern that pregnancy may aggravate acromegaly or lead to regrowth of GH-secreting adenomas in previously treated patients.

Mechanisms contributing to the impaired fertility in acromegaly include hypopituitarism and decreased gonadotropin reserve caused by the expanding pituitary tumour mass. Hyperprolactinemia that occurs in 30–40% of acromegalic patients results in hypothalamic-pituitary-ovarian axis dysfunction including reduction in pulsatile gonadotropin-releasing hormone. Our patient had a macroadenoma with suprasellar extension and

Table 1: Growth normal and IGF-1 Response to Oral Glucose Preoperation, at sixth Day and six months Post Surgery and Postpartum

<table>
<thead>
<tr>
<th>Period</th>
<th>Time (min)</th>
<th>0</th>
<th>10</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative:</td>
<td>BG(mmol/L)</td>
<td>5.6</td>
<td>7.1</td>
<td>8.3</td>
<td>7.4</td>
<td>7.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GH(mIU/L)</td>
<td>65.0</td>
<td>76.0</td>
<td>&gt;104</td>
<td>&gt;104</td>
<td>91.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IGF-1(mmol/L) (Ref.range of IGF-1: 13.91–40.30)</td>
<td>157.56</td>
<td>159.25</td>
<td>147.60</td>
<td>166.01</td>
<td>151.82</td>
<td></td>
</tr>
<tr>
<td>6 days post surgery:</td>
<td>BG(mmol/L)</td>
<td>4.5</td>
<td>7.5</td>
<td>7.0</td>
<td>5.2</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GH(mIU/L)</td>
<td>4.0</td>
<td>6.0</td>
<td>5.0</td>
<td>4.0</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>6 months post surgery:</td>
<td>BG(mmol/L)</td>
<td>4.8</td>
<td>6.4</td>
<td>5.8</td>
<td>5.7</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>GH(mIU/L)</td>
<td>2.4</td>
<td>1.6</td>
<td>1.9</td>
<td>1.8</td>
<td>1.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>*IGF-1(mmol/L)</td>
<td>74.2</td>
<td>66.3</td>
<td>64.3</td>
<td>66.8</td>
<td>69.5</td>
<td></td>
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<tr>
<td>Postpartum:</td>
<td>BG(mmol/L)</td>
<td>4.7</td>
<td>5.3</td>
<td>5.6</td>
<td>4.5</td>
<td>4.4</td>
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<td></td>
<td>GH(mIU/L)</td>
<td>17.5</td>
<td>18.0</td>
<td>5.6</td>
<td>36.0</td>
<td>30.5</td>
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</tr>
</tbody>
</table>

GH, Growth hormone; BG, Blood glucose; IGF-1, Insulin-like growth factor – 1 Normal value of GH: up to 7ng/ml. *Ref range (13 – 64 nmol/L). This was from a different laboratory.

Delayed diagnosis of Leptomeningeal Cyst
hyperprolactinemia prior to surgery. Postsurgery prolactin levels normalised and fertility was apparently restored.

In pregnancy in normal women, the maternal circulating GH levels are derived from the pituitary during the first trimester, thereafter placental GH contributes the major component of circulating GH. IGF-1 is elevated during normal pregnancy. Circulating placental GH induces maternal hepatic IGF-I production, which in turn, inhibits pituitary GH secretion. In acromegalic patients, pituitary GH persist during the entire pregnancy because the autonomous adenomatous somatotrophs are resistant to factors that usually inhibit pituitary GH secretion during the second trimester of normal pregnancy. Thus serum IGF-I concentration is less useful in the diagnosis of acromegaly in pregnancy. To diagnose acromegaly in pregnancy specific radioimmunoassays for the placental variants are required to differentiate elevated GH levels from pituitary vs placental sources. Our patient was lost to follow-up six months after macroadnectomy and was only seen when she came for elective caesarian section. Facilities for measurement of IGF-I and placental GH are however not readily available in our environment.

The pituitary gland enlarges during normal pregnancy. The implication of this for an acromegalic patient with a pituitary tumour is the possibility of development of visual impairment resulting from the mass pressure effect on the optic nerve. Patients with macroadenomas are at increased risk of developing visual loss during pregnancy. In this patient there was no visual impairment noted during the pregnancy and postpartum. CT scan did not show any evidence of tumour regrowth postpartum. Pituitary MRI showed evidence of tumour regrowth. MRI is more sensitive than CT scan in visualization of hypothalamo-pituitary anatomy.

It is not known with certainty if pregnancy exacerbated acromegaly in this our patient because this patient did not have GH and IGF-I measurement before and during pregnancy. She did not have clinical evidence of acromegaly during pregnancy. However, it should be noted that in the review of all cases reported in the literature, pregnancy exacerbated acromegaly in 4 of 24 patients. It is highly probable that pregnancy provoked the recurrence of acromegaly in our patient.

Medical treatment of acromegaly has no adverse effect on the outcome of pregnancy. Because the safety of continuous bromocriptine and octreotide treatment during pregnancy has not been established, it is recommended that these drugs be discontinued very early in pregnancy despite the rare risk of tumour regrowth. Serial evaluation of the visual field every six weeks is advocated. Pituitary MRI for patients with pituitary tumours should be done before conception and thereafter repeated during pregnancy only if there is evidence of headache or visual field loss. Occurrence of these features is an indication for an emergency transsphenoidal resection.

In the Nigerian environment where the cost and availability of facilities for regular assessment and monitoring of anterior pituitary function are limited, it may be better to recommend the use of adjuvant pharmacotherapy rather than irradiation, which is associated with a high incidence of panhypo pituitarism.

The patient was commenced on octreotide therapy, having agreed to have contraception to prevent unplanned pregnancy. There is a need to regularly have biochemical evaluation for treated acromegalics so that aggressive therapy can be instituted to normalise GH levels whenever any recurrence of GH hypersecretion is detected in order to improve survival in these patients. She will benefit from referral to a centre experienced in management of acromegaly.

It is therefore concluded that pregnancy, though a rare occurrence, is achievable in treated acromegaly but is capable of provoking recurrence of acromegaly.

REFERENCES

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