Advanced Pregnancy in a Severely Myxoedematous Patient

A Case Report and Review of the Literature

E. J. BLIGNAULT

SUMMARY

A case of advanced pregnancy in a myxoedematous patient is described. This is a relatively rare occurrence. The physiology of the maternal thyroid gland in pregnancy and the fetal thyroid is briefly described.


A 34-year-old woman, para 5, gravia 6, had a history of hypertension, pedal oedema and gross proteinuria. In June 1973 she had become pregnant for the fifth time. Her menses did not recur after the birth of the child, although she only breast-fed for 3 months, and after several months she attended hospital and was found to be myxoedematous. After treatment with thyroxine (Eltroxin; Glaxo) menstruation recurred, but she stopped taking the thyroxine and did not attend hospital again. Her menses subsequently became scanty and irregular and eventually ceased.

On examination on 12 January 1979 the patient, who was now pregnant for the sixth time, was clearly myxoedematous. Her blood pressure was 180/100 mmHg, and the pulse rate 72/min and regular. There was no thyromegaly. The fundal height corresponded to 32 weeks' gestation, and the fetal heart rate was 140/min and regular. There was moderate pedal oedema and severe proteinuria.

The patient was admitted to hospital with strict bed rest ordered. She was given monohydrallazine (Aprcioline; Ciba-Geigy) 50 mg·h·hourly, and dihydrallazine (Nepresol; Ciba-Geigy) when the systolic blood pressure was higher than 160 mmHg or the diastolic blood pressure higher than 110 mmHg. Thyroxine 0.1 mg twice daily was given, and this was subsequently increased to 0.2 mg twice daily. The blood pressure was maintained at about 150/90 mmHg.

Fetal wellbeing was monitored by measuring serum human placental lactogen (hPL) and oestriol (E3) levels on 4 occasions. Results were found to be normal. The results of thyroid function tests are shown in Table I, and these reflect the severity of her disease. It is important to note that the test for thyroid antibodies was negative.

The results of routine blood and renal tests are shown in Table II. The serum protein and electrolyte levels were within the normal range. The serum cholesterol level was 729 mg/dl (normal 160 - 250 mg/dl) and the serum carotene level 5.6 ml/dl (normal 0.9 - 3.8 mg/dl). During her short stay in hospital there was no appreciable fetal growth and there appeared only to be a very small quantity of liquor amnii.

TABLE I. RESULTS OF THYROID FUNCTION TESTS

<table>
<thead>
<tr>
<th>Normal range</th>
<th>12 Jan.</th>
<th>22 Jan.</th>
<th>(after delivery)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T3 30 - 40%</td>
<td>23</td>
<td>25</td>
<td>27</td>
</tr>
<tr>
<td>T4 60 150 nmol/l</td>
<td>8</td>
<td>29</td>
<td>47</td>
</tr>
<tr>
<td>T7 17 - 60</td>
<td>2</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>TSH 1.5 - 8 IU/ml</td>
<td>47.3</td>
<td>74.4</td>
<td>46.1</td>
</tr>
</tbody>
</table>

Because of the decreasing renal function and difficulty in controlling the blood pressure, it was decided to terminate the pregnancy by caesarean section. Radiography of the abdomen showed a small fetus with the breech presenting. Unfortunately, on 31 January the fetal heart beat disappeared. A diagnosis of intra-uterine death was made and the caesarean section was cancelled. The patient went into spontaneous labour a few hours later and delivered a fresh stillborn female infant, weighing 1 440 g. The baby and placenta appeared normal.

TABLE II. RESULTS OF ROUTINE BLOOD AND RENAL FUNCTION TESTS

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>11.5 - 16.4 g/dl</td>
<td>14.0</td>
<td>15.1</td>
<td>14.1</td>
<td>13.1</td>
<td>10.8</td>
</tr>
<tr>
<td>Platelets</td>
<td>150 - 400 × 10^9/µl</td>
<td>117</td>
<td>103</td>
<td>109</td>
<td>90</td>
<td>109</td>
</tr>
<tr>
<td>Urea</td>
<td>10 - 25 mg/dl</td>
<td>26</td>
<td>33</td>
<td>32</td>
<td>42</td>
<td>24</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.1 - 1.5 mg/dl</td>
<td>1.3</td>
<td>1.6</td>
<td>1.4</td>
<td>1.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Uric acid</td>
<td>1.5 - 6.0 ml/dl</td>
<td>8.3</td>
<td>9.0</td>
<td>8.3</td>
<td>8.3</td>
<td>8.6</td>
</tr>
<tr>
<td>Creatinine clearance</td>
<td>70 - 170 ml/min</td>
<td>64</td>
<td>58</td>
<td>55</td>
<td>47</td>
<td>19</td>
</tr>
</tbody>
</table>
Since this patient had been under our care for such a short time it was difficult to assess her weight gain. It is of interest, however, that in 1 week after delivery her weight decreased from 73 kg to 58 kg, i.e. a loss of 15 kg. The blood pressure dropped to 130/90 mmHg and the blood urea level to 24 mg/dl. The proteinuria cleared rapidly, leaving only a trace of protein from time to time.

**DISCUSSION**

The commonest causes of myxoedema without goitre are: (i) chronic lymphocytic thyroiditis (Hashimoto's disease); (ii) pituitary hypothyroidism (Sheehan's syndrome); (iii) pituitary tumours; (iv) idiopathic hypothyroidism; (v) iodine deficiency or excess; (vi) developmental abnormalities; (vii) endemic cretinism; and (viii) postablative surgery or radiation.

The clinical syndrome of myxoedema is rarely encountered in pregnancy because the disease usually starts after the child-bearing years. It is often accompanied by loss of libido, menstrual disorders and impaired fertility. Pregnancy, if it does occur, is often followed by early abortion. Bercovici and Ehrenfeld assessed 2 patients with hypothyroidism associated with advanced pregnancy and found reports of 20 similar cases in the literature. He found that these pregnancies rarely progress to term. In addition, while some of the patients become euthyroid in pregnancy, they generally become worse as the pregnancy advances. 

**The Thyroid in Pregnancy**

The thyroid gland may triple in size during pregnancy because of the increased number of follicles and glandular hyperplasia. A hypothesis for the glandular enlargement is that: (i) there is an increase in the renal glomerular filtration rate in pregnancy and hence an increased loss of iodine by the kidney; and (ii) in pregnancy a placental thyroid-stimulating hormone (TSH), which is immunologically distinct from pituitary thyroid hormone, may be produced.

Because the thyroid gland enlarges during pregnancy one would expect myxoedema to improve in the pregnant patient, but this is not so. The increase in the oestrogen level in pregnancy results in an increase in the level of thyroid-carrying proteins. This increase begins at the 10th week of pregnancy, peaks in the 2nd trimester, and may last up to 12 weeks after delivery. The increased level of thyroid-carrying proteins subsequently causes an increase in the serum thyroxine (T4) level and a decrease in the triiodothyronine (T3) level. If this does not occur in pregnancy one should suspect the presence of subclinical hypothyroidism. While this may be a cause of recurrent abortion and should be investigated in such patients, there is no justification for empirical thyroxine therapy in recurrent aborters. If myxoedema (diagnosed by an increase in TSH levels) does develop in a pregnant woman, she will of course require thyroxine therapy.

It should be noted, however, that there is a marked similarity between the chemical structures of TSH and β-subunit human chorionic gonadotrophin and this similarity causes technical difficulties in assessing TSH levels in pregnancy. 

**Effects of Myxoedema on the Fetus**

In the embryo the thyroid gland develops from an epithelial growth on the pharyngeal floor on the 17th day. By the 7th week the gland is in the normal adult position. The fetal pituitary-thyroid axis functions from the 15th week and is under control of the fetal thyroid-stimulating hormone. Three important points involving the physiology of the fetal thyroid gland are: (i) maternal TSH does not cross the placental barrier (cf. long-acting TSH (LATS) which does cross the placenta); (ii) iodine does cross from mother to fetus and is then concentrated in the fetal thyroid gland far more efficiently than in that of the mother — this factor may explain the deterioration of thyroid function in most myxoedematous pregnant patients; and (iii) T4 and T3 both cross the placenta, but only in physiologically insignificant amounts, and the fetus is dependent on hormones from its own glands — the fact that athyrotic cretins have euthyroid mothers implies that a normal rate of maternal thyroid secretion cannot compensate for inadequate synthesis by the fetus.

**CONCLUSIONS**

Relatively few cases of advanced pregnancy associated with myxoedema have been recorded. The exact cause of myxoedema in this patient was not found. The negative test for thyroid antibodies tends to exclude Hashimoto's thyroiditis, and the diagnosis may turn out to be idiopathic hypothyroidism. This case must be distinguished from those now being reported in the literature as cases of postpartum amenorrhoea-galactorrhoea syndrome with hypothyroidism. It must be stressed that in the case presented the patient was myxoedematous during pregnancy; from her history it is likely that she was myxoedematous before she fell pregnant.

**REFERENCES**