HYPERTHYROIDISM AND PREGNANCY

(Report of a case and Review of Literature)

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The association of pregnancy and hyperthyroidism is uncommon as conception rarely occurs in patients with untreated hyperthyroidism. Severe hyperthyroidism is often associated with amenorrhea and infertility due to anovulation. However, when minor degrees of hyperthyroidism exist conception may occur. MacGregor and Goodwin, (1953) state that in their clinic 12 percent of thyrotoxic women between the ages of 16-40 years became pregnant during a period of observation lasting five days.

When conception does occur, the pregnancy usually terminates in spontaneous abortion. In rare cases that progress beyond twenty weeks, there is often premature labour, with a high incidence of foetal death (Herbst and Selenkow 1965). Physiologic regulation of hyperthyroidism is thus a prime consideration to the welfare of the foetus and the mother. The incidence of hyperthyroidism with pregnancy given by various workers varies from 0.025-1.4% (Hawe et al. 1962 and Portis et al., 1939). The average number of pregnancies in these patients is 3.35%. About 64% are multiparas and 36% primiparas (Ayromlooi et al., 1973). The same is reported by Javert and Hinton but Portis and Roth (1939) do not agree with this. Sometimes hyperthyroidism is noted for the first time when the patient comes for antenatal check up.

During the reproductive period the great majority of pregnant women with hyperthyroidism suffer from a Grave's disease and not the toxic adenoma.

It may be difficult to distinguish the physiologic alteration of pregnancy from those of mild hyperthyroidism if the patient is seen for the first time during pregnancy. Hyperthyroidism exaggerates the hypermetabolic symptoms and signs of pregnancy. During pregnancy the physician’s clinical judgement is vital to correct diagnosis since thyroid status cannot be evaluated fully by any single laboratory test. The effect of pregnancy on hyperthyroid state is unpredictable. It is postulated that the patients’ condition should improve during pregnancy as the free thyroxin level may fall as most of the thyroxin gets bound to the thyroxin binding globulin (T.B.G.) the level of which is raised during pregnancy because of raised levels of oestrogens. However, Mussey et al., (1948) are of the opinion that pregnancy does not seem to alter the course of hyperthyroidism in most of the cases. It seems that there is an individual variation as reported by Ayromlooi et al., (1973) that out of their 15 cases, 2 became worse and they needed an increased dosage of medication, 7.
had improvement of the condition and the rest 6 remained in the same state. Incidence of toxaemia is reported to be 14.3% by Ayromlooi et al., (1973). McLoughlin and McGoogan, (1943) also reported a higher incidence than in the general population.

Again the incidence of spontaneous abortion and premature delivery is higher even in those cases who are undergoing treatment. The total foetal loss as reported by Ayromlooi et al., was 14.3%.

The management of these patients presents a unique problem because of the foetus. The foetal thyroid gland begins to function at the 12th to the 14th week of gestation. (Chapman et al., 1948; Evans et al., 1967). Antithyroid medication prescribed for the mother may therefore affect the foetal thyroid gland from this period of gestation. Careful monitoring of the maternal thyroid function during the period of treatment is necessary for the successful management of the mother without adversely affecting the foetus.

There is no place for therapeutic abortion in the present day management of hyperthyroid cases. In the past the incidence of therapeutic abortion is reported to be 22% by Roth, (1935) whereas there was no need for therapeutic abortion in 28 pregnancies in the series reported by Ayromlooi et al., (1973).

As regards management of pregnancy there is no place for administration of iodine to these patients as it has been held responsible for the congenital goitre in the infants born to these mothers. The only indication for iodine administration is before the subtotal thyroidectomy for the preparation of the patient for surgery. The advocates of subtotal thyroidectomy are of the opinion that the antithyroid drugs cause hypothyroidism, mongolism and cryptorchidism in about 13.5% of infants (Burrow, 1965; Bell and Hall 1960). It is supported by Talbert et al., (1970) who feel that 4% incidence of intellectually damaged children in the medically treated patients along with scattered single case reports of such children emphasised the risks associated with the use of thiouracil during pregnancy. They feel that this incidence must represent a minimal value, since lesser degrees of intellectual impairment would be difficult to recognise. The incidence of congenital goitre, reported by Ayromlooi et al., was 7.1% but they feel that this was present in those infants whose mother had been given iodine along with antithyroid drugs.

Herbst and Selenkow, (1965) reported that the patients who are treated by antithyroid drugs alone have higher incidence of foetal mortality (12.2%) as compared to 9.4% in those who are given thiouracil and thyroid extract. Similarly, the incidence of goitre is reported to be higher in women treated with only thiouracil and other abnormalities were also found to be higher like hypothyroid, mongolism, hyperthyroidism and cryptorchidism. So they feel that for the welfare of the foetus the mother should be administered antithyroid drugs and thyroxine together. Hamburger, (1972) discussed this philosophy of combined medication logically and concluded that there is need to give both the drugs together.

Selenkow, (1972) cited the most striking example of the complications of antithyroid therapy alone for thyrotoxic pregnancy given by the report of Bokat. In this investigator's series of 37 patients who were observed through 41 pregnancies, 13 had clinical and laboratory evidence of hypothyroidism during some period of their pregnancy despite careful serial observation and relatively low
doses of antithyroid drugs. Another example given by Selenkow (1972) is that of a series reported by Burrow (1965), in which out of 41 pregnancies there were 5 neonates with goitres and an additional 4 with foetal complications. He thinks that maternal hypothyroidism caused by these drugs is certainly not conductive to normal foetal growth and development.

CASE REPORT

R.G., 32 years old, 3rd gravida, attended the gynaecological out-patient department on 29-8-73 for the first time with the diagnosis of 24 months' pregnancy with thyrotoxicosis. She had been attending thyroid clinic since October, 1972 and had been on antithyroid drugs when she conceived. She had been alright till 1968 when she started having symptoms like weakness on mild exertion, palpitation, feeling of warmth, insomnia, loss of weight and gradual enlargement of the thyroid gland. She started taking treatment from general practitioners for the enlargement of the thyroid gland till February, 1972. In 1972 she attended thyroid clinic of this Institute for the first time and she was put on antithyroid drugs. She stopped this treatment after 3 months but again resumed the same medication in October, 1972. Since then she has been on antithyroid drugs regularly. She continued to take Neomercazole 40 mgm. per day.

She got married in 1967. In 1968 she had a spontaneous abortion at 4½ months' gestation and had D & C for bleeding following abortion. In August, 1969 she had another abortion at 6 months of gestation and was admitted to hospital for retention of placenta and received one unit of blood for excessive bleeding.

On examination on 29th August, 1973 no exophthalmos was noticed, hands were warm but no tremors were found. Thyroid was enlarged bilaterally and was smooth but no bruit was heard. B.P. was 140/70 mm. of Hg, pulse 100/ml, regular and weight 45 kg. Height of uterus was 16 weeks which corresponded with the period of gestation. No evidence of pre-eclamptic toxæmia was noted. No evidence of premature leakage and started having mild labour pains which lasted for 9 hours. Artificial rupture of membranes were done following which the pains improved and she had full dilatation after 21 hours but the descent of the head was not satisfactory. So lower segment caesarean section was done and a normal healthy female baby weighing 4.2 Kg was taken out. Her post-operative period was uneventful. She was not allowed to breast feed the baby and was discharged on 5-9-1974.

Investigations:

Total weight gain during pregnancy was 12 Kg; she did not have pre-eclamptic toxæmia or any other complication. The haemoglobin remained 11 gms.% Urine examination revealed no abnormality. Blood group O +ve. T<sub>3</sub>, T<sub>4</sub> and T.S.H. values were as follows:—

- 23.3.1973 T<sub>3</sub> 14.6.73 T<sub>4</sub> 23.11.73
- 14.6.73 T<sub>3</sub> 2.08 mg/ml. 2.6 ng/ml. 3.6 mg/ml.
- 23.11.73 T<sub>4</sub> 176 ng/ml. 380 ng/ml.
- 2.08 mg/ml. T.S.H.-3.1 mcu/ml. 0.4 mcu/ml. 0.5 mcu/ml.

PBI assay on 11.12.1973 and 20.12.73 was 5.3 mcg% and 6.8 mcg% respectively. Urinary oestriol done weekly remained within normal limits. Total leucocyte count done every fortnight did not reveal and abnormality.

The dosage of neomercazole was continued as 40 mgm. per day up to 5 weeks of gestation at which time it was increased to 60 mgm. a day up to 26 weeks, then it was again reduced to 40 mgm. up to 32 weeks, and then 30 mgm. up to 36 weeks. From 36 weeks onwards up to onset of labour, and for two months thereafter the dosage was 20 mgm. and later it was reduced to 10 mgm. per day. The patient was last seen on 22.3.74 i.e. 3 months after delivery. The weight was 45.2 Kg, B.P. 120/80 mm Hg, pulse 122/ml. regular. The baby weight is 5 Kg. 200 gms. The baby is absolutely normal so far.

Discussion

The present case was known to have
hyperthyroidism as she had already been on treatment. She had had two abortions within 2 years and then did not conceive for 2 years until she was put on treatment regularly though there is no history of abnormal menstruation. The dose of antithyroid drug had to be adjusted from time to time during antenatal period. The patient was in a satisfactory condition even when she had a stress of labour and she did not have complication during caesarean section. The total weight gain was 12 Kg. which is normal during pregnancy (Chesley, 1944).

In the non-pregnant patient thyrotoxicosis can be controlled with either thiouracil drugs, radioiodine or subtotal thyroidectomy (Ingbar, 1968). However, in the pregnant patient the outlook is narrowed by the presence of a developing foetus. Radioactive iodine is absolutely contraindicated during pregnancy as it readily crosses the placental barrier and it would be taken up by the foetal thyroid after 12 weeks of gestation (Chapman et al., 1948; Shepherd, 1967).

The thiouracil group of drugs readily cross the placenta and so may affect the foetal thyroid function. Many thiouracil induced goitres, probably mediated by increased foetal thyrotropin secondary to depressed foetal hormone synthesis, have been reported (Elphinstone, 1953; Keynes, 1952; Piper and Rosen, 1954 and Werner, 1967). Thyroxine (T4) and L-triodothyronine (T3) have been shown to cross the placenta but the placental permeability to these hormones is limited and T3 crosses the placenta more rapidly than T4.

The maintenance of maternal euthyroidism by either endogenous or exogenous thyroid hormone may not provide sufficient thyroid hormones to the foetus to assure optimal foetal development if the foetal thyroid is compromised by drug therapy as shown by Dussault et al., (1969).

It is well known that foetal tissues, especially those of the brain and skeleton, are dependent on an adequate level of circulating thyroid hormone for normal development (French et al., 1964), but so far the minimal required levels of these hormones for normal development of brain and skeletal system are not known.

Even though the antithyroid drugs traverse the placental barrier freely the incidence of foetal damage is not great. However, there are reports of cretins and retarded children born to such mothers. (Becker et al., 1959; Hawe, 1962; Keynes, 1952; Herbst and Selenkow, 1965). Astwood, (1951) on the other hand has reported 12 normal children born to drug treated mothers. Concurrent administration of antithyroid drugs and desiccated thyroid or T3 will prevent maternal hypothyroidism but because of protein binding and delayed placental transfer, it is unlikely to assure normal circulating thyroid hormone in the foetus if foetal thyroid function is compromised. Herbst and Selenkow (1965) are of the opinion that the mother should be administered anti-thyroid drug along with the thyroxine so that if the thyroid of the foetus is compromised the exogenous thyroxine would prevent the development of congenital anomalies but it is just theoretical as the transport of thyroxin across the placenta is very minimal. Hamburger, (1972) on the other hand has disputed the school of thought of combined antithyroid thyroid drug treatment by theoretical but very understandable logic.

So we believe that antithyroid drug therapy alone is satisfactory but the patient should be under constant care in order to increase or decrease the dose...
in anticipation of the improvement or deterioration in the condition. But one must remember that the patient should never be allowed to become hypothyroid. As in the present case the use of antithyroid drug alone has assured the welfare of the mother as well as the foetus.

Summary
A case of hyperthyroidism successfully treated during pregnancy with antithyroid drugs alone with controlled dosage is described and available literature is reviewed.

REFERENCES
27. Roth, F. A.: (Quoted by Ayromlooi et al., 1973).