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Case Reports

A Baby Girl with Neonatal Thyrotoxicosis and Subsequent Pituitary Hypothyroidism

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Abstract A baby girl was delivered at 36 weeks of gestation. Antenatally her mother was diagnosed to have thyrotoxicosis in third trimester and was put on propyl-thiouracil for 2 weeks before delivery. Initially the baby had typical biochemical findings of thyrotoxicosis. In subsequent follow up she developed pituitary hypothyroidism. Treatment with L-thyroxine achieved normal serum free thyroxine level and the baby girl enjoyed normal growth and neuro-development during the 2 years of therapy. The case illustrated the need for early detection of neonatal thyrotoxicosis (especially with current or past maternal history of thyrotoxicosis) and the possibility of subsequent pituitary hypothyroidism.

Key words Neonatal thyrotoxicosis; Thyroxine treatment; Transient hypothyroxinaemia

Introduction

Graves' disease is not uncommon among women of childbearing age with occurrence of 0.2% in pregnant women. Neonatal thyrotoxicosis will develop among 1-1.4% of these newborn.[1] In the presence of maternal history, clinical symptoms and signs and the availability of thyroid function test, neonatal thyrotoxicosis should be readily detected and treated accordingly. In addition, a small proportion of patient will have the pituitary gland suppressed for a longer period. Until the full recovery of pituitary secretion of thyroid stimulating hormone (TSH) to drive the thyroid gland, L-thyroxine replacement is necessary in order to protect the growth and neuro-development of the infants.

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Case Report

A baby girl was the third child of a non-consanguineous couple delivered at 36 weeks of gestation (by maturity assessment) by normal spontaneous delivery. Apgar Score was 9 at both 1 and 5 minutes. Birth weight was 2.2 kg (appropriate for age).

The mother had late antenatal booking and was suspected to have Graves' disease at third trimester of pregnancy. Thyroid function test confirmed maternal thyrotoxicosis and she was prescribed propyl-thiouracil for 2 weeks until delivery. There was no previous history of abortion and the first 2 children were healthy all along.

Physical examination revealed a calm baby. No jitteriness or sweating were observed. Anterior fontanelle was measured to be 2 cm x 2 cm. There were no goitre, eye lid retraction or proptosis. Therefore, the baby was clinically euthyroid.

The baby was transferred to special care nursery after birth. She had hypoglycaemia with a plasma glucose of 2.1 mmol/L and required dextrose solution infusion. Later she became euglycaemic with establishment of milk feeding and dextrose infusion was weaned off. She had physiological jaundice on Day 3 requiring phototherapy

for 2 days. She was feeding well on formula milk and was afebrile all along. Her heart rate ranged from 128 to 158 beats per minute and respiratory rate ranged from 40 to 55 per minute. Electrocardiogram was normal for age. Birth weight was regained at 1 week of life. Weight gain was at 27 g per day during the second and the third weeks of life. No anti-thyroid drug was given to baby all along.

Cord blood TSH was <0.03 miu/L and total thyroxine (T4) was 104 nmol/L (reference range 110-254 nmol/L). Serum anti-microsomal and anti-thyroglobulin anti-bodies were negative. Bone age was between newborn and 3 months (Greulich and Pyle).

Serial thyroid function tests were performed and the result were as follows:

	Day 5	Day 7	Day 17	Day 50
TSH miu/L	0.03	<0.01		0.01
Free T4 pmol/L (ref 17-31)		54.5	29.4	8.9

Thyroid function test on cord blood and Day 7 showed that the baby had biochemical evidence of thyrotoxicosis. The mother declined treatment in view of lack of clinical symptoms. However, on Day 50, when the serum free T4 level was 8.9 pmol/L, the pituitary gland failed to respond with serum TSH remained suppressed. Therefore thyrotrophin-releasing hormone (TRH) stimulation test was performed in order to test the pituitary release of TSH. The basal and peak TSH were 0.83 miu/L and 1.96 miu/L respectively, hence pituitary hypothyroidism was confirmed.

Thyroid technetium scintiscan showed tracer uptake was found in both lobes of thyroid in normal anatomical position. Magnetic resonance imaging (MRI) study of the brain was performed. There was no mid-line defect and the hypothalamo-pituitary regions were normal.

L-thyroxine 25 μg once daily was started after TRH stimulation test and the same dosage was maintained until 2 years of age. She had no symptoms or signs of hypothyroidism or thyrotoxicosis. Her growth velocity was normal and neuro-development was appropriate for age. Both TSH and free T4 levels were monitored regularly while on L-thyroxine treatment. TSH ranged from 0.18 to 3.35 miu/L and free T4 ranged from 14.3 to 20.6 pmol/L. At 2 years of age the TSH and free T4 were 3.35 miu/L and 17.6 pmol/L respectively. As these results suggested that the pituitary thyrotrophs regained the capacity to secrete TSH, the patient was advised to stop taking the drug for 1 month. Blood test repeated after this period showed that the TSH and free T4 levels were at 3.48 miu/L (reference range 0.27-4.2) and 13.8 pmol/L (reference range 13-23) respectively.

Discussion

Graves' disease occurs in about 0.2% of pregnant women and neonatal thyrotoxicosis will develop in 1-1.4% of these newborns.[1] Asymptomatic women with Graves' disease and in rare circumstances, women with Hashimoto thyroiditis[2] or even women not known to have any thyroid disease may give birth to affected neonates. Fetal thyrotoxicosis starts to occur in the second half of gestation when the fetal thyroid gland becomes fully responsive to TSH and hence transplacental thyroid-stimulating immuno-globulin (TSI). The condition manifests as tachycardia (heart rate >160 per minute), craniosynostosis, frontal bossing, intra-uterine growth retardation or premature delivery.[3] In order to avoid the condition, pregnant women with thyrotoxicosis should receive treatment with propyl-thiouracil. The drug is preferred to carbimazole as the former decreases the conversion of thyroxine to tri-iodothyronine in peripheral tissue and the latter may be associated with cutis aplasia.[4]

In the reported case, Day 7 serum TSH level was suppressed while free T4 level was raised and was likely a result of fetal hyperthyroxinaemia which may be explained by 2 mechanisms. One mechanism was due to the transplacental transfer of thyroxine from mother. She was diagnosed to have Graves' disease late in the gestation and was prescribed anti-thyroid drugs for only 2 weeks before delivery. The other mechanism was the transplacental transfer of TSI causing fetal thyrotoxicosis and suppression of the fetal hypothalamo-pituitary-thyroidal axis.

However, the patient's serum free T4 level was in a decreasing trend after birth, from 54.5 pmol/L on day 7, to 29.4 pmol/L on day 17 and 8.9 pmol/L on day 50, with TSH remained suppressed. The decreasing trend demonstrated that the initial high thyroxine level was due to transplacental transfer and when the hormone was gradually metabolised, the serum level started to fall. In addition, there was no TSH response to TRH stimulation. The condition, described as transient hypothyroxinaemia,

had been found in infants whose mother had thyrotoxicosis which is not well under control during pregnancy, especially in third trimester.[5]

There were 3 possible mechanisms for the defect. Firstly, the prolonged suppression of the axis by hyperthyroxinaemia. The resumption of normal TSH secretion in childhood Graves' disease after treatment took 3-19 months[6] and might take up to 3.25 years in neonatal thyrotoxicosis.[5] Another mechanism was the altered set-point for pituitary-thyroid feed back control. Rats given large dose of L-thyroxine during the first week of life would as adults had low thyroxine level, low basal TSH level and diminished response to TRH.[7] The third mechanism would be a decreased capacity for TSH secretion. Animal studies had shown that hyperthyroxinaemia decreased the number of pituitary thyrotrophs[8] and the level of TRH receptors in pituitary gland.[9]

After the TRH stimulation test, the diagnosis of pituitary hypothyroidism was confirmed. L-thyroxine replacement was started as prolonged hypothyroidism in infancy could result in mental and growth retardation. In our patient, both her neuro-developmental milestone and growth parameters were normal during the 2 years under treatment. TSH level at 2 years old was 3.35 miu/L which was within the normal range. This suggested that she might regain her pituitary secretion of TSH. After a trial of stopping medication for 1 month, the TSH and free T4 were both within normal limits. These indicated that the patient did not need further L-thyroxine treatment, i.e. she recovered from suppressed pituitary-thyroidal axis.

In conclusion, clinicians should be alert to the possibility of neonatal thyrotoxicosis in newborns who presented with symptoms of irritability, tachycardia etc., especially if the mother has a history of thyrotoxicosis. Monitoring of patient's thyroid function should not be stopped even when treatment is finished, but should be continued until the full recovery of the pituitary-thyroidal axis is demonstrated (with normal basal TSH and free T4 levels) in order to ascertain that the patient does not suffer from prolonged suppression of the pituitary gland.

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