

A Case of Transient Neonatalthyrotoxicosis - Case Report

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Abstract: Neonatal immune hyperthyroidism is a rare but potentially fatal condition. It occurs in 1–5% of infants born to women with Graves' disease. We present a case of neonatal thyrotoxicosis born to a mother with Graves disease (elevated thyroid stimulating immunoglobulins) which was detected early owing to high index of suspicion and resolved without any impairment.

Keywords: Transient neonatal thyrotoxicosis, Maternal Graves disease, Thyroid stimulating antibodies, TRAB (Thyroid receptor antibodies)

1. Introduction

Maternal graves disease is the most common cause of neonatal hyperthyroidism. In most of the cases, it is due to maternal antibodies transferred from the mother into the fetal compartment, stimulating the fetal thyroid by binding thyrotropin (thyroid-stimulating hormone, TSH) receptor. In 1–5% of the babies born to these mothers, these antibodies will stimulate the thyroid by binding thyrotropin (thyroid-stimulating hormone, TSH) receptor, causing a clinical hyperthyroidism. (1) In infants born to mothers taking antithyroid drugs, the clinical onset is usually delayed to 5–10 days after birth.

Symptoms may include intrauterine growth restriction, prematurity, goitre, exophthalmos, vacant stare, craniosynostosis (usually coronal), flushing, heart failure, tachycardia, arrhythmias, hypertension, hypoglycaemia, thrombocytopenia and hepatosplenomegaly. (2) Thyrotoxicosis disappears with the clearance of the maternal antibodies and usually signs disappear during the first 6 months of life.

The AAP (American academy of Paediatrics) recommends to start treatment early when free T4 levels exceed 2.7 ng/dl and TSH < 3 mU/L to prevent clinical hyperthyroidism with its potential morbidity and mortality. If left untreated, it can lead to death in up to 12% of patients, usually from heart failure. (3) Early diagnosis and treatment are required for a good prognosis.

2. Case Report

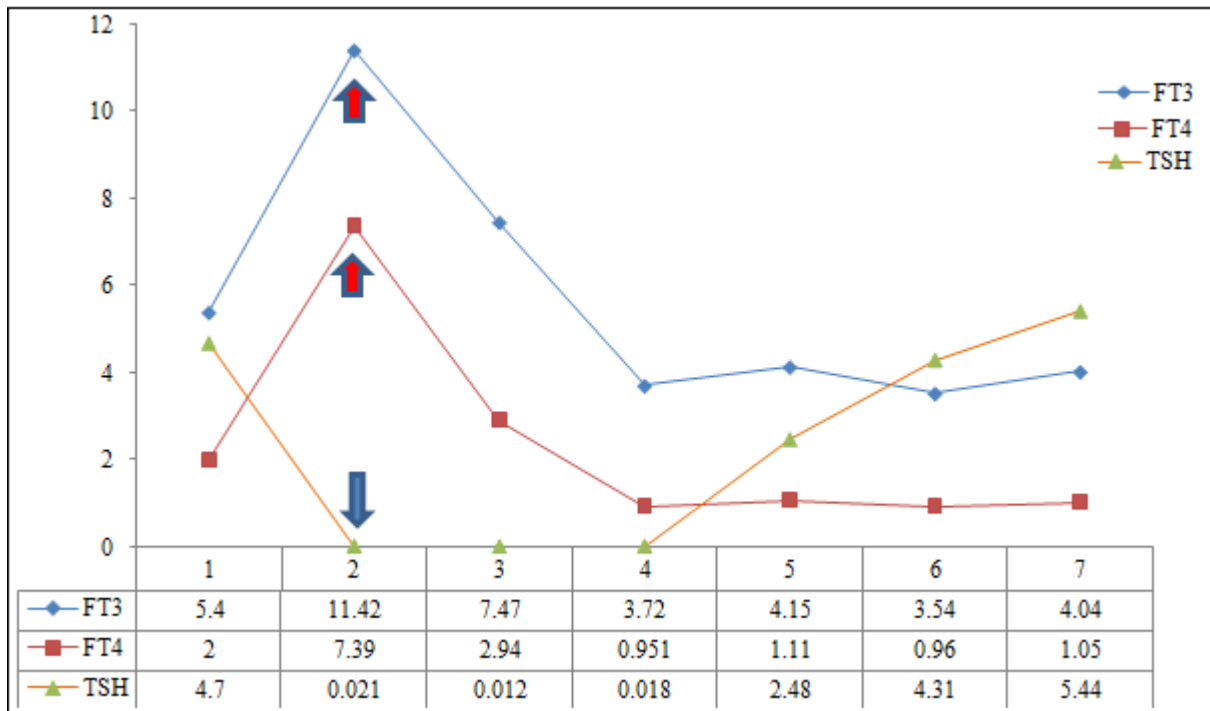
We present the case of a singleton late preterm female baby born to 34 yr, second gravida mother who was diagnosed as a case of Graves disease during 2nd trimester (16 weeks) owing to her complaints related to excessive sweatings and palpitations for which she was on antithyroid drugs (Carbimazole 10mg twice daily) and beta blockers. (Propranolol 20mg once daily). The mother had elevated

thyroid stimulating immunoglobulins (460%; N < 130%) and negative antithyroid peroxidase antibodies and antithyroglobulin antibodies during pregnancy.

The baby was delivered by caesarean section in view of previous LSCS at 36 weeks gestation with an Apgar score of 8/10 and 9/10 at 1 and 5 min, respectively. She had a birth weight of 2300g (centile less than 50th centile in the WHO growth charts), a length of 50cm (centile 50 in the WHO growth charts); head circumference 33.5 cm (centile less than 50 in the WHO growth charts).

In view of maternal history of Graves disease with low TSH, TRAB (Thyroid receptor antibodies) was done on day 1 which was abnormal (6.73, N < 2), thyroid profile was done at 72 HOL which was found to be normal. Baby was discharged by day 5 of life as she was asymptomatic and was advised regular weekly followups. Baby was brought to the OPD by day 12 of life for follow up. Although, the baby was clinically asymptomatic, thyroid profile was repeated which was found to be abnormal showing elevated free T4 (7.3 ng/dl) and free T3 (11.4 ng/dl) and low TSH (0.02 mu/L). In order to prevent complications related to hyperthyroidism, baby was started on Carbimazole (0.75 mg/kg) and was monitored regularly during the subsequent follow ups weekly for any clinical manifestations and vital parameters. Baby was monitored for growth pattern in terms of weight, length and head circumference which were found to be normal. While the baby was on Carbimazole, thyroid profile was screened weekly which showed serial improvement in the thyroid parameters. By 4 weeks of life, thyroid profile improved and Carbimazole was tapered over a period of 2 weeks (Total duration- 6 weeks). By 6 weeks of life, TRABs were repeated which was found to be negative. As such, Carbimazole was stopped by 6 weeks.

Baby was under regular follow up during infancy showing normal growth and development. Currently, baby is 9 months old having no issues related to thyrotoxicosis.



DOL	Day3	Day 12	Day 21	Day 28	Day 35	Day 42	Day 49
Weight	2.3 kg	2.58kg	2.86 kg	3.1 kg	3.28kg	3.4 kg	3.52 kg
Weight gain	-	28 gm/day	28 gm/day	34 gm/day	25 gm/day	20 gm/day	20 gm/day
RR (/min)	30	35	34	38	36	34	38
HR (/min)	170	140	150	166	154	148	146
NIBP (95 th centile 82/50)	-	71/24	86/42	73/54	59/46	77/46	74/40
ft3 (ng/dl)	5.4	11.42	7.47	3.72	4.15	3.54	4.04
T4 (ng/dl)	2.0	7.39	2.94	0.951	1.11	0.96	1.05
TSH (mu/L)	4.7	0.021	0.012	0.018	2.48	4.31	5.44
Drugs	-	2mg (0.75 mg/kg)	2mg (0.75 mg/kg)	1.5mg (0.5 mg/kg)	0.8mg (0.25 mg/kg)	0.8mg (0.25 mg/kg)	stop

3. Discussion

Transient Neonatal thyrotoxicosis

- 1) Rare condition caused by the transplacental passage of TSH receptor antibodies (TRAb) from mothers with Graves disease.
- 2) Prevalence: 2-3% of mothers with graves disease (4) 1 in 50, 000 newborns
- 3) Mostly self-limited, with duration determined by the rate of disappearance of maternal TRAb (Thyroid receptor antibodies) from the infant circulation usually by 3-6 months.
- 4) Most babies born to mothers with Graves disease have normal thyroid function.
- 5) Any evidence of elevated thyroid stimulating immunoglobulins or thyroid receptor antibodies in mother is of great concern and mandates serial monitoring of thyroid profile in a neonate.
- 6) The time of onset and severity of symptoms are variable, depending upon whether the mother is taking an antithyroid drug at the time of delivery. Initial thyroid profile in a neonate may be normal in case of maternal

usage of antithyroid drugs prior to delivery. Hence, serial monitoring of thyroid profile in neonates is advised.

- 7) Treatment should be initiated at the onset of clinical or biochemical hyperthyroidism to avoid:
 - a) Short term (cardiac failure)
 - b) Long term (craniosynostosis, growth retardation, intellectual impairment, hyperactivity, and developmental and behavioral problems) complications.
- 8) The AAP recommends to start treatment when f T4 levels exceed 2.7 ng/dl and TSH < 3 mU/L to prevent clinical hyperthyroidism with its potential morbidity and mortality.
- 9) Neonatal thyrotoxicosis may not be detected by newborn screening programme, as low TSH levels are not reported by Guthrie card.
- 10) An even more uncommon type of nonautoimmune hyperthyroidism has been described, resulting from activating mutations of the TSH receptor gene. (5) Neonates with this disorder have the same symptoms of neonatal thyrotoxicosis, but more prolonged and severe, requiring a more aggressive treatment

Treatment				
TRAb	Biochemical Hyperthyroidism	Clinical Hyperthyroidism	Complications	Management
+	-	-	-	• Wait and watch
+	+	-	-	• Oral antithyroid drugs
+	+	+	-	• Hospitalisation • Oral antithyroid drugs • B blockers if required
+	+	+	+	• Hospitalisation • Oral antithyroid drugs • B blockers • Anti failure therapy, if necessary

4. Conclusion

We would like to highlight the importance of the history of maternal Graves Disease, including the evolution of the thyroid function, antibody levels and medication during pregnancy. If the mother has a history of Graves Disease, a serum determination of TRABs or thyroid stimulating immunoglobulins should be obtained at 20–24 weeks gestation. High index of suspicion of neonatal thyrotoxicosis must be kept in mind in case of abnormal maternal thyroid profile. (TRAB/TSII) (6)

After birth, careful evaluation and surveillance of the newborn must be carried out. As thyroid function tests performed in the first week of life often reflect maternal disease status, it is important to repeat them at 5–7 days of life despite initial thyroid function tests being normal. (7, 8). If symptomatic, and the diagnosis is confirmed, iodine / antithyroid agents are administered to decrease thyroid hormone secretion.

The parents should be warned about suggestive clinical signs in a neonate. Even though it is transient, symptomatic neonatal hyperthyroidism should be treated to avoid short-term (heart failure) and long-term morbidity (craniosynostosis and intellectual impairment). (7, 8)

5. Key Message

- Most babies born to mothers with Graves disease have normal thyroid function.
- Neonatal thyrotoxicosis due to maternal GD requires early recognition and treatment to prevent potential morbidity or mortality.
- Role of TRAB in screening of neonatal graves is crucial in management.
- Treatment should be initiated at the onset of clinical or biochemical hyperthyroidism to avoid unwanted complications.
- Neonatal thyrotoxicosis may not be detected by newborn screening programme, as low TSH levels are often not reported.

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