CASE REPORT

Neonatal thyrotoxicosis caused by maternal autoimmune hyperthyroidism

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SUMMARY

Neonatal immune hyperthyroidism is a rare but potentially fatal condition. It occurs in 1–5% of infants born to women with Graves' disease (GD). 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. We present a case of neonatal thyrotoxicosis due to maternal GD detected at 25 days of age and discuss the potential pitfalls in the diagnosis.

BACKGROUND

Neonatal hyperthyroidism is less frequent than neonatal hypothyroidism, but its impact on growth and development can be as dramatic.¹ The prevalence of clinical hyperthyroidism in pregnancy has been reported to be about 0.1–0.4%,² being the most common cause of neonatal hyperthyroidism. In most cases, it results from the transfer of thyroid-stimulating immunoglobulins from mother to fetus through the placenta, in women with history of Graves' disease (GD) or, more rarely, Hashimoto thyroiditis.³ 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 that may present at birth.⁴ In infants born to mothers taking antithyroid drugs, the clinical onset is usually delayed to 5–10 days after birth.⁵

Symptoms may include intrauterine growth restriction, prematurity, goitre, exophthalmos, stare, craniosynostosis (usually coronal), flushing, heart failure, tachycardia, arrhythmias, hypertension, hypoglycaemia, thrombocytopaenia and hepatosplenomegaly.² Thyrotoxicosis disappears with the clearance of the maternal antibodies and usually signs disappear during the first 4 months of life. Left untreated it can lead to death in up to 12% of patients, usually from heart failure.⁶ Early diagnosis and treatment are required for a good prognosis.

Recently, an even more uncommon type of non-autoimmune hyperthyroidism has been described, resulting from activating mutations of the TSH receptor gene.⁷ Neonates with this disorder have the same symptoms of neonatal thyrotoxicosis, but more prolonged and severe, requiring a more aggressive treatment.

CASE PRESENTATION

We present the case of a male newborn at 25 days of age referred by his family physician because of poor weight gain. The gestation was unknown until 24 weeks and was followed in the high-risk

consultation due to gestational diabetes, which was controlled with diet, and maternal GD, which was medicated with propylthiouracil (300 mg daily) with poor control.

The mother had positive thyrotropin receptor antibodies (TRABs) of 21 IU/L and negative antithyroid peroxidase antibodies and antithyroglobulin antibodies during pregnancy. The baby was delivered by caesarean section at 40 weeks with an Apgar score of 8/10 at 1 and 5 min, respectively. He had a birth weight of 3070 g (centile 50 in the WHO growth charts), a length of 48.5 cm (centile 50 in the WHO growth charts); head circumference 33 cm (centile 15 in the WHO growth charts). No sample of thyroid function test was taken from the umbilical cord blood or the newborn blood at the maternity ward.

The baby was discharged at day 4 with exclusive breast milk feed and referenced to his family physician. In the first week of life the physician performed a 'heel prick test', following the national metabolic screening programme protocol, which was normal.

The baby had progressive weight loss (maximum 13.5% on day 12), which led to the introduction of formula milk (200 mL/kg/day) with no recovery. At this stage, at 25 days of age, the baby was referred to our paediatric emergency department.

The physical examination revealed a malnourished infant (weight 2885 g) with a great irritability, hyperhidrosis and an ocular protrusion (video 1). He also had tachycardia (HR>170 ppm) with a normal blood pressure.

INVESTIGATIONS

The child was admitted to the neonatal intensive care unit (NICU) under close surveillance. The blood

Video 1 Video at admission. The physical examination revealed a malnourished infant (weight 2885 g) with a great irritability, hyperhidrosis and an ocular protrusion.

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work revealed low level of TSH 0.01 mUI/L (range value (RV) 0.70–18.10), high level of free thyroxine (FT4) 6.91 ng/dL (RV 0.66–2.36) and a high level of TRABS 22.50 IU/L (RV <1.0 IU/L). The cervical ultrasound and echocardiogram were normal.

TREATMENT

The patient started treatment with a 5% Lugol's solution and propranolol. On day 2 of admission the patient was transferred to a central hospital with a paediatric endocrinology department. Treatment with Lugol's solution was stopped and tiamazol was initiated with clinical improvement and normalisation of the thyroid hormone levels.

OUTCOME AND FOLLOW-UP

The baby was discharged at 37 days of life, medicated with propranolol and tiamazol until 2 and 7 months, respectively. The thyroid function normalised during the NICU stay and TRABS were negative at 4 months of age. Presently at 12 months the child remains euthyroid (FT4 1.18 ng/dL and TSH 1.703 µUI/mL) without any treatment and with excellent development and growth.

DISCUSSION

The main lesson we believe that can be extracted from this case is that when evaluating a newborn it is extremely important to obtain an accurate maternal/gestational history. That was not the case with this baby, who was discharged home from the maternity ward without any investigation or planned follow-up. The baby had his appointments at his family physician who also did not realise that the mother had GD. Moreover, we believe that a false sense of security comes from the normal national metabolic screening programme, which, by means of the Guthrie card, only tests for congenital hypothyroidism and does not mean the baby has a normal thyroid function.

It was only with the progressive weight loss that led to the referral to our hospital that the serious condition was diagnosed and the proper treatment was initiated.

We would like to emphasise the importance of the history of maternal GD, including the evolution of the thyroid function, antibody levels and medication during pregnancy. If the mother has a history of GD, a serum determination of TRABS should be obtained at 20–24 weeks gestation. Also, FT4 and TSH should be monitored approximately every 2–6 weeks; the primary goal is a serum FT4 at or moderately above the normal reference range.⁸ In high-risk pregnancies (uncontrolled hyperthyroidism or more than 3 times the upper normal value for TRABS), an experienced obstetrician should monitor by ultrasound the heart rate, growth, amniotic fluid volume and fetal goitre.⁸

After birth, careful evaluation and surveillance of the newborn must be carried out. As thyroid function tests (thyroid hormone and antibodies screening) performed in the first week of life often reflect maternal disease status rather than neonatal disease, it is important to repeat them at 5–7 days of life.⁹

If symptomatic, and the diagnosis is confirmed, iodide and antithyroid agents are administered to decrease thyroid hormone secretion. A combination of Lugol's solution (5% iodine and 10% potassium iodide) is given in a dose of one drop (8 mg of iodine) three times daily. In combination, agents such as methimazole or carbimazole are administered in doses

of 0.5–1 mg/kg/day or propranolol is given in a dose of 2 mg/kg/day. A therapeutic response should be observed within 24–36 h, but care must be taken to maintain euthyroidism (to avoid inducing hypothyroidism) in the infant.¹⁰

The parents should be warned about suggestive clinical signs (hyperexcitability, poor weight gain, stare and/or eyelid retraction), and a vigilance programme for the ambulatory should be made.¹¹ 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).¹

Learning points

- ▶ When evaluating a newborn it is extremely important to obtain an accurate maternal/gestational history.
- ▶ Thyroid function tests (thyroid hormone and antibody screening) carried out in the first week of life should be repeated at 5–7 days of life.
- ▶ The parents should be warned about suggestive clinical signs (hyperexcitability, poor weight gain, stare and/or eyelid retraction).
- ▶ Symptomatic neonatal hyperthyroidism should be treated to avoid short-term and long-term morbidity.

Contributors MFC and ATM were responsible for the conception and drafting of the manuscript. SP and CL were responsible for the critical revision of the manuscript.

Competing interests None.

Patient consent Obtained.

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