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Neonatal Hyperthyroidism: Case Report and Literature Review

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Abstract **Case Report**

The onset of Graves' disease during pregnancy exposes the newborn to the risk of neonatal hyperthyroidism due to the transplacental passage of anti-thyroid-stimulating hormone (TSH) receptor antibodies. We report the case of a child whose mother was diagnosed with Graves' disease during pregnancy. Clinical hyperthyroidism appeared only a few days after birth and was confirmed by hormonal tests. Thanks to treatment with synthetic antithyroid drugs, the child's clinical and biological course was favorable. It is essential to systematically screen for neonatal hyperthyroidism in newborns of mothers with Graves' disease, as the absence of immediate clinical signs after birth does not rule out the diagnosis. The pediatrician must be aware of this thyroid condition even in the absence of an identified maternal history, in order to enable rapid therapeutic management.

Keywords: Neonatal Hyperthyroidism, Maladie de Basedow, Thyrotoxicose.

INTRODUCTION

Neonatal hyperthyroidism is a rare endocrine disorder, typically secondary to the transplacental passage of thyroid-stimulating antibodies of the IgG type, known as anti-TSH receptor antibodies (TRAb), originating from the mother. This phenomenon occurs primarily in mothers with Graves' disease, an autoimmune thyroid condition in which these antibodies inappropriately stimulate the fetal thyroid gland, leading to excessive thyroid hormone production in the fetus and subsequently the newborn. Although Graves' disease is relatively common in women of childbearing age, neonatal transmission of this hyperthyroidism remains rare and often presents with less pronounced clinical symptoms [1–3].

Nevertheless, in the absence of early diagnosis and appropriate therapeutic management, the consequences can be severe for both the fetus and the newborn. The most feared complications include cardiac disorders such as fetal tachycardia, heart failure, and neurological damage that can lead to long-term developmental delays. These complications result from the prolonged effect of TRAb antibodies, which remain in the newborn's circulation for several weeks after birth until they are completely eliminated. This makes the rapid recognition of neonatal hyperthyroidism signs all the more crucial to initiate adequate treatment [1–4].

The goal of early diagnosis is therefore based on monitoring mothers with Graves' disease, with particular attention required during pregnancy to assess the risk of transmission. Given the severity of potential complications, a multidisciplinary approach involving obstetricians, pediatricians, and endocrinologists is essential to optimize maternal and neonatal outcomes.

We report the case of a newborn with transmitted hyperthyroidism to illustrate the symptomatology and neonatal management of this condition.

OBSERVATION

This male infant was born at 37 weeks of gestation via vaginal delivery. His Apgar score was 7 at 1 minute and 10 at 10 minutes. At birth, he weighed 3000g. His 31-year-old mother had a medical history of an early miscarriage.

During the first trimester of pregnancy, the mother experienced nervousness, diarrhea, fatigue, the onset of exophthalmos, and maternal tachycardia. Graves' disease was suspected and confirmed by laboratory results: T3 at 32 pmol/l (normal: 2.8-6.5), T4

at 85 pmol/l (normal: 10.3-27), and TSH suppressed at 0.05 mUI/l (normal: 0.25-5), along with the presence of anti-TSH receptor antibodies (TRAK) at 71 U/l. The mother was started on carbimazole, with close monitoring of thyroid function.

At birth, the clinical examination and biological tests on day 1 were unremarkable. However, around day 9, the newborn exhibited incessant crying, hyperexcitability, sinus tachycardia at 180 beats per minute, with prominent eye gaze and retraction of the upper eyelid. The biological tests confirmed the diagnosis of neonatal hyperthyroidism with TSH suppressed at 0.05 mUI/l (normal: 0.25-5), T4 elevated above 100 pmol/l (normal: 10.3-27), T3 at 29 pmol/l (normal: 2.8-6.5), and positive TRAK.

The baby was placed on symptomatic treatment with a β-blocker (propranolol: 2 mg/kg/day in 3 doses) for 15 days, and etiological treatment with synthetic antithyroid drugs (carbimazole: 1 mg/kg/day in 3 doses) starting from day 11 for 5 months.

Clinical improvement was remarkable within 48 hours, with the resolution of tremors and hyperexcitability, and normalization of cardiac function within 15 days. Carbimazole treatment was continued until the baby was 5 months old, with the anti-TSH receptor antibodies becoming negative at 4 months of age. Eight months after discontinuing the treatment, the child is clinically euthyroid, with normal growth and development, and appropriate psychomotor development.

Table I: Evolution of Biological Parameters and Treatment Dosage by Age

Variable/Age	Day11	Day30	Day41	Month3	Month5	1Year
TSH mUI/L(N :0.25-5)	<0.05		0.28	1.69	1.02	0.86
T4L ng/dL(N :0.71-1.95)	⟩100	1.51	0.33	0.44	0.74	0.68
T3L pmol/L(N :2.8-6.5)	29					
Néomercazole(mg /kg/j)	1	1	0.6	0.2	0	0

DISCUSSION

It is estimated that 0.2% of pregnant women are affected by Graves' disease, and among these, only 1 to 2% of their newborns will present with hyperthyroidism due to the transplacental passage of maternal thyroid-stimulating autoantibodies of the IgG type [5].

Graves' disease in pregnant women can indeed lead to serious complications for both the mother and the newborn. Untreated or poorly controlled hyperthyroidism in the mother increases the risk of miscarriage, preterm delivery, and heart failure. Although less common, preeclampsia remains a possible complication [6, 7].

For the fetus, complications can include prematurity, growth restriction, accelerated bone maturation, and, in some cases, craniosynostosis [6]. Intrauterine death occurs in a minority of cases (12 to 20%). Fetal tachycardia is also frequently observed. The presence of maternal autoantibodies can lead to fetal goiter, which may be associated with mechanical complications such as compression of the trachea or esophagus, complicating the diagnosis.

In newborns, signs of hyperthyroidism generally appear after 10 days of life because synthetic antithyroid drugs (ATDs) taken by the mother during pregnancy can cross the placenta and mask the early symptoms of neonatal hyperthyroidism. Prematurity and growth restriction are common, regardless of sex [8].

À l'examen clinique, il est crucial de rechercher des signes comme la tachycardie, une craniosténose, un goitre, une exophtalmie, ou des signes d'insuffisance cardiaque congestive. D'autres signes évocateurs comprennent l'hypertonie, les trémulations et une polyphagie associée à une stagnation pondérale. D'autres manifestations, telles que la cholestase, l'ictère ou la thrombopénie, peuvent aussi être presents [8].

During clinical examination, it is crucial to look for signs such as tachycardia, craniosynostosis, goiter, exophthalmos, or signs of congestive heart failure. Other indicative signs include hypertonia, tremors, and polyphagia associated with weight stagnation. Additional manifestations, such as cholestasis, jaundice, or thrombocytopenia, may also be present [8, 9].

At birth, if neonatal hyperthyroidism is suspected, it is crucial to measure TRAK (anti-TSH receptor antibodies) from the umbilical cord or within the first 48 hours of life. It is also recommended to measure TSH, T3L, and T4L from the cord to identify at-risk newborns before discharge from the maternity unit. These tests help assess fetal thyroid function. In the case of significant disturbances in TSH levels, increased clinical and biological monitoring is necessary [5-10].

If TRAK are positive, a comprehensive thyroid assessment, including T3L, T4L, and TSH, should be conducted between the 3rd and 5th day of life. An additional check between the 10th and 14th day is recommended, especially if the mother took synthetic antithyroid drugs, as the half-life of TRAK is shorter than that of these medications. If maternal TRAK measured during the last trimester of pregnancy are above 7 U/L, there is a risk of transplacental passage and neonatal hyperthyroidism. Additionally, maternal use of synthetic

antithyroid drugs increases the risk of neonatal hypothyroidism.

In cases of neonatal hyperthyroidism, treatment is crucial to prevent severe complications. Treatment is generally initiated when the free thyroxine (T4L) level exceeds 35 pmol/L [10]. In this context, several therapeutic and monitoring measures are implemented to ensure effective management.

The medication treatment usually starts with the administration of synthetic antithyroid drugs, such as carbimazole, at a dose of 0.5 to 1 mg/kg/day. These medications are essential for reducing the excessive production of thyroid hormones by the newborn's thyroid gland. Additionally, if cardiac symptoms such as tachycardia or heart failure are present, symptomatic treatment with β-blockers or digoxin may be necessary to manage these complications [11].

Additionally, as soon as a decrease in T4L levels is observed, it is important to start L-thyroxine supplementation to prevent the risk of hypothyroidism secondary to suppression of thyroid function. This supplementation helps maintain an adequate hormonal balance and prevents the adverse effects of hypothyroidism.

Treatment with synthetic antithyroid drugs and L-thyroxine is generally continued until TRAK (anti-TSH receptor antibodies) disappear, which typically occurs between 6 and 12 weeks after birth [12]. This period corresponds to the time needed for maternal TRAK, transmitted to the fetus, to be completely eliminated.

It is important to note that the absence of treatment can lead to severe complications, such as acute heart failure with cardiogenic shock. Therefore, appropriate management is crucial to prevent such serious outcomes [13].

To ensure adequate monitoring, free thyroxine (FT4) and TSH levels should be measured 1 to 2 times per week until thyroid function stabilizes. Once thyroid function normalizes, these checks can be reduced to twice a month until TRAK levels return to normal [5].

Finally, regular follow-up is recommended during the first year of life to detect any potential complications, such as craniosynostosis, which may be associated with severe or poorly controlled hyperthyroidism. Close monitoring ensures that the newborn receives the necessary care for optimal long-term health.

Breastfeeding is generally permitted for mothers taking antithyroid drugs, provided that certain dosage limits are adhered to. Recommendations specify that the daily dose of propylthiouracil (PTU) should not exceed 300 mg, while methimazole should not exceed 20 mg per day. These thresholds have been established to minimize potential risks to the newborn while allowing the mother to continue her antithyroid treatment (6).

Studies have shown that neither PTU nor methimazole has a significant impact on the thyroid function or physical and cognitive development of breastfeeding children. However, methimazole is generally preferred due to the risks associated with PTU [14]. Biological monitoring of both the mother and the child is recommended 3 to 4 weeks after the start of breastfeeding to ensure the absence of adverse effects.

CONCLUSION

Neonatal hyperthyroidism of maternal origin presents a significant diagnostic and therapeutic challenge, especially in the context of a pregnancy complicated by Graves' disease. The observation of maternal-fetal tachycardia during pregnancy should systematically raise the suspicion of maternal hyperthyroidism, with Graves' disease being a primary consideration. Although this condition is relatively rare in newborns, it can have serious consequences if not detected and treated in a timely manner.

To ensure optimal management, close collaboration between obstetricians, endocrinologists, and pediatricians is essential. Once Graves' disease is confirmed in the mother, this multidisciplinary team must implement precise monitoring of the pregnancy, including regular assessments of maternal thyroid activity and detection of potential fetal anomalies such as tachycardia or thyroid hypertrophy. This coordination continues after birth with rigorous neonatal follow-up, including hormonal evaluations and thyroid gland ultrasounds of the infant. If neonatal hyperthyroidism is detected, prompt initiation of antithyroid treatments is necessary to prevent cardiac and neurological complications.

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