

## An Atypical Case of Congenital and Neonatal Grave's Disease

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### Abstract

Neonatal Grave's disease is associated with maternal Grave or Basedow's hyperthyroidism, which is a rare endocrinopathy in pregnant women. In this report, we present and discuss the case of an infant with congenital and neonatal hyperthyroidism with neurological manifestations. Such presentations are rare, with congenital onset and neurological signs not often at the front line, although tremor sometimes mentioned in the literature may be expected. However, repeated and persistent myoclonus is exceptional, and the certitude of complete resolution of abnormal movements, even with a well conducted treatment is not always guaranteed.

**Keywords:** Congenital hyperthyroidism, Neonatal hyperthyroidism, Grave Disease.

### Introduction

Congenital and neonatal hyperthyroidism or thyrotoxicosis are principally auto-immune hyperthyroidisms, also known as neonatal Grave's disease by some authors [1]. It affects infants with an incidence around 1-5% neonates from women with active or past history of Grave's hyperthyroidism. It takes place as a result of the trans-placental passage of maternal Thyroid Stimulating Hormone (TSH) receptor-stimulating antibodies (TRab) to the fetus as from the 17<sup>th</sup> to 20<sup>th</sup> weeks of gestation. This coincides with the time when fetal thyroid receptors of TSH become responsive [1-3].

### Case presentation

This is the case report of a 14 days old female neonate who was brought to consultation presenting with repeated spontaneous intermittent myoclonus of the upper limbs, evolving from the first day of life, with onset immediately after delivery. They were predominant during sleep without alleviating factor. They lasted for about 10 to 15 minutes in an afebrile context and were accompanied with sweating. This led to a first consultation in a health center where the baby was treated with neonatal meningitis protocol: Ampicillin, Gentamycin, Cefotaxim for 10 days. The neonate was also given phenobarbital and clonazepam at adequate doses for 2 days. The evolution was marked with the persistence of the abnormal movements and the baby was then referred to our setting for better management.

Concerning past history, the baby was delivered at 39 weeks of Gestation (GA) of an uneventful pregnancy with 8 antenatal consultations. The mother had complained about regular fetal active movements and fetal tachycardia sometimes noted during prenatal consultations. Delivery was normal, with baby's birth weight 2800g. The mother was 29 years old, being followed-up for Grave's disease over 8 months before the pregnancy. She had been on antithyroid drug methimazole during 4 months before being operated upon with partial thyroidectomy indicated for goiter. She was then prescribed levothyroxine at 100mg daily for post-operative hypothyroidism. Methimazol was discontinued in the meantime and pregnancy was planned in accordance with the gynecologist-obstetrician. Systemic enquiry revealed irritability, agitation, sweating, sleeplessness and intermittent diarrhea in the neonate.

On physical exam, the general state was normal but the baby was hyperactive. The weight was 3200g. The heart rate was accelerated with 175 cycles/minutes tachycardia. The neurological exam revealed explosive intermittent myoclonus of the upper limbs with slight trembling, exaggerated Moro reflex prolonged with myoclonus, increased deep tendon reflexes.

Serum electrolytes showed mild hypokalemia, Thyroid Stimulating Hormone (TSH) was decreased at 0.0274µu/ml, TSH receptor antibodies (TRab) was positive at 4.1 IU/l and blood thyroxin (T4) level was as high as 25mU/l. This

enabled to confirm the diagnosis of neonatal hyperthyroidism with other possible etiologies excluded. The infant was put on propranolol at 1 mg/kg per day and Methimazol at 1 mg/kg per day as well, but was to be introduced 2 days after the initiation of Propranolol.

The neonate was seen 2 weeks later on and 6 weeks thereafter with no more myoclonus, nor sweating. There was regression of hyperactivity and improvement of sleep. However, constipation was reported. TSH control at 8 weeks after the start of treatment was 25.4  $\mu$ u/ml, Propranolol and methimazol were discontinued; TSH and TRab controls were to be done the 12<sup>th</sup> week.

## Discussion

Although we could not find evidence for preconceptional TRAb elevation as a predictive factor for fetal and neonatal autoimmune hyperthyroidism in our patient, cessation of ATDs in the mother was a non-negligible risk factor [4,5]. The notions of fetal tachycardia as from the 5<sup>th</sup> month of pregnancy and the recurrence of early active fetal movements accounted for fetal or congenital hyperthyroidism [1, 3].

The diagnosis was delayed in this neonate firstly because of the non-systematization of TSH sampling in our context, which is contrary to norms. The second reason was the atypical presentation with paroxysmal myoclonus, for which a neurological disease absolutely had to be ruled out. Nevertheless, the pathophysiology of movement disorders in neonates with Grave's disease is still unclear [6-9].

The management of our patient consisted of Methimazol and propranolol, which is the actual recommended therapy. The outcome was favorable with marked regression of myoclonus and other hyperthyroidism signs and symptoms. Hormonal inversion was noted after 8 completed weeks of treatment, with rising TSH which permitted to discontinue methimazol and propranolol. [3,10,11].

## Conclusion

Neonatal hyperthyroidism may be preceded by congenital manifestations, and both presenting with atypical neurological semiology, of which paroxysmal myoclonic dyskinesia. These signs tend to subside with an adequate management of underlying hyperthyroidism. However, the pathophysiological mechanisms of neurological signs in neonates with Grave's disease are poorly described, indicating the need for further empirical research or review

of the existing literature on the topic. likewise, the search for congenital manifestation and early systematical TSH sampling of newborns in all settings may contribute to prompt diagnosis and management, thereby preventing eventual complications.

## Conflict of Interest

The authors declare that they have no competing interest.

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