A case of neonatal Graves in a premature infant with negative thyrotropin receptor stimulating antibodies

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Background

The cause of neonatal hyperthyroidism is almost always transient and related to the passage of maternal thyrotropin receptor stimulating antibodies (TSAb). A positive thyrotropin receptor stimulating antibody level in a neonate is often diagnostic of neonatal Graves disease. Neonatal Graves occurs in infants born to mothers with Graves disease with an incidence of approximately 2%. The manifestation of symptoms has not been well characterized in premature infants.

Clinical Case

A 31 year old mother delivered a female infant at 27 weeks GA weighing 827 grams. The mother was diagnosed 2 weeks prior to delivery with Graves disease but was not started on any medication. Due to the maternal history of Graves disease, on day of life (DOL) 2 thyroid function tests (TFTs) were obtained on the baby. Labs showed a TSH of 0.009 mIU/mL and free T4 of 1.4 ng/dL and negative levels of thyrotropin receptor stimulating antibodies (TSAb). The infant was clinically doing as well as expected for an infant born at 27 weeks GA. By DOL 7 the infant began developing tachycardia in the 220s. Repeat laboratory evaluations showed a TSH of 0.005 mIU/mL, a free T4 of 4.3 ng/dL and a total T3 of 4.0 (0.6-1.6 ng/dL). Methimazole (MMI) (0.4 mg/kg daily), and propranolol (0.5 mg/kg/day) were started. Four days after starting anti-thyroid medication TSH was still low but free T4 had normalized to 1.3 ng/dL. The tachycardia had resolved. By DOL 14 rising liver function tests led to discontinuation of MMI.

By DOL 18 (four days off MMI) the tachycardia had recurred and free T4 was once again elevated to 4.7 ng/dL. Repeat levels of TSAb were negative. AST and ALT had decreased. MMI and propranolol at slightly smaller doses than before (0.25 mg/kg/day and 0.4 mg/kg/day respectively) were then restarted. Within 3 days free T4 normalized to 1.3 ng/dL. Other laboratory studies revealed an elevated thyroglobulin level of 131.9 ng/mL (2.8-40.9), anti-thyroglobulin levels were negative and anti-TPO antibodies were positive at 37.4 IU/mL. Thyrotropin receptor blocking antibodies (TBAb) levels were positive at 40% (normal less than 17%). Beta-blockers were discontinued, and the patient remained on MMI for approximately 3 weeks. Free T4 levels remained normal. The baby began to thrive. The baby had thyroid levels checked weekly and was allowed to outgrow her MMI dose. By DOL 45 MMI was discontinued. She had repeat TFTs a week later and was found to have a suppressed TSH of 0.013 mIU/mL and a normal free T4 of 1.3 ng/dL. Repeat levels of TBAb were decreased to 20%. She was restarted on MMI at a low dose of 0.15 mg 3 times per week. She was then sent home and seen in outpatient clinic 1 week later. Repeat TFTs showed an improved TSH of 0.022 mIu/L and a normal Free T4 of 1.1 ng/dL. She was then kept on MMI 0.15 mg twice a week for the next few weeks. At around 3 months of age her last TSH was 0.225 mIU/L and FT4 0.7 ng/dL, total T3 was 1.1 ng/dL, TBAb remained 20%. Her MMI was then discontinued and she was then lost to follow up.

Conclusion

This is an interesting case of TSAb negative neonatal Graves who was very sensitive to MMI. The suspected cause for this infant's neonatal hyperthyroidism were the TBAb, stimulating the TSH receptor, as has been previously reported. The patient's FT4 normalized almost immediately after starting the medication, and once MMI was held early in her course, her FT4 rose 3 fold in less than 72 hours. It was not until her TBAb declined significantly that MMI could be safely weaned. In a TSAb negative patient with suspected Graves disease, another lab study to be considered would be to measure TBAb.

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Thyroid
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