CASE REPORT

Delayed Recognition of Central Hypothyroidism in a Neonate Born to Thyrotoxic Mother

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We describe a neonate born to a mother with uncontrolled thyrotoxicosis, who was euthyroid during first week of life and later developed central hypothyroidism.

Key words: *Thyrotoxicosis, Central hypothyroidism, Neonate.*

Central hypothyroidism is characterized by impaired secretion of thyroid hormone due to a defect in the hypothalamic-pituitary-thyroid (HPT) regulatory system. Exposure of fetal HPT system to a higher thyroid hormone concentration might impair its physiologic maturation leading to central hypothyroidism in neonates born to thyrotoxic mothers(1). It is usually detected during first week of life. We report delayed recognition of central hypothyroidism in a neonate born to a mother with uncontrolled thyrotoxicosis during pregnancy.

CASE REPORT

A male infant was born at 38 weeks of gestation (birth weight, 2084 grams) to a 25 years old primigravida mother, who had been on irregular treatment for Graves' disease. Mother was diag-nosed to have Graves' disease during her tenth week of gestation and advised 30 mg/day of carbimazole. Although she was compliant to the medications initially, took medicines irregularly during third trimester. She was hospitalized at 37 weeks of gestation with pregnancy induced hypertension and congestive cardiac failure. On admission her total triiodothyronine (TT3), total thyroxine (TT4) and TSH were 3.80 nmol/L, 308.88 nmol/L and 0.01 mIU/mL, respectively. After ensuring drug compliance and stabilization of general condition, baby was delivered by cesarean section.

Infant cried immediately after birth and was asymptomatic till third day of life, when he developed jaundice; peak serum bilirubin was 22.4 mg/dL on seventh day of life. Infant's T4 and TSH were 123.55 nmol/L (9.6 mg/dL) and 0.014 mIU/mL, respectively on fifth day of life. Hyperbilirubinemia was managed by phototherapy and baby discharged home on tenth day of life with the advice to follow up in Endocrinology out patient department after a week with repeat thyroid hormone evaluation. The infant was followed at sixtieth day of life. The diagnosis of central hypothyroidism was confirmed with free thyroid hormone profile which showed low FT3 and FT4 [FT3: 2.7 pmol/L and FT4: 6.435 pmol/L]. Infant was started on 50 µg of thyroxine. Follow up after two months of therapy showed the infant to be euthyroid (T3- 2.1 nmol/L, T4-114.07 nmol/L) with 50 µg of thyroxine.

DISCUSSION

First reported in 1988(2), incidence of neonatal central hypothyroidism in infants of mothers with Graves' disease is at least 1 per 35,000 neonates, but the exact mechanism has not been fully elucidated(3). It is usually seen with uncontrolled maternal

thyrotoxicosis, though rarely associated with well controlled disease also.

Mitsuura, *et al*.(4) showed higher thyroxine (T4) levels at birth than on fifth day of life in infants born to mothers with uncontrolled Graves' disease. Higuchi, *et al*.(5) also reported a phase of transient hyperthyroxinemia before settling down to a hypothyroid phase in infants born to mothers with Graves' disease. There are case reports of neonates with low TSH, low normal/normal FT4 levels in cord blood which subsequently declined to subnormal levels, on serial monitoring (at days four and seven of life)(6). The above studies suggest that fetal thyroxine may be elevated due to passive transfer of maternal thyroxine during the last trimester leading to suppression of fetal pituitary-thyroid axis.

The minimum duration of passive hyperthyroidism during fetal life that can lead to central hypothyroidism is unknown. In a previous review of case reports was suggested that the possibility of central hypothyroidism can not be excluded in term infants who are born to euthyroid mothers with Graves' disease, but exposed to maternal thyrotoxicosis before 32 weeks' gestation(5). They also proposed that maternal thyrotoxicosis before 32 weeks of gestation may be critical for development of central hypothyroidism in the offspring(5). Tamaki, *et al*.(7) showed that neonates born to mothers with Graves' disease with cord TSH levels below the normal range have a high predilection to develop thyrotoxicosis or central hypothyroidism. In this infant, TSH on fifth day of life was below normal range, which suggested the need for serial monitoring.

In most of these infants, recovery of the HPT axis varies from months to years(5). It is prudent to continue L-thyroxine replacement therapy until 2–3 years of age, to prevent possible delay in mental and motor faculties. We planned to continue thyroxine till three years of age in our patient.

It is recommended that all infants born to mothers with Graves' disease should not only have both fT4 and TSH measured in the cord blood, but also be monitored serially (such as at days 4 and 7), even if either of the cord measurements appear normal(8). There are no specific guidelines on the frequency and timing for further monitoring of these infants. We suggest monitoring once in a week till TSH normalizes to watch for delayed development of central hypothyroidism.

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