Maternal Hypothyroidism in Autoimmune Thyroiditis and the Prognosis of Infants

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Abstract. We evaluated the developmental prognosis of 31 infants born to mothers with autoimmune thyroiditis. Four of the babies developed transient neonatal hypothyroidism. Their mothers all had low thyroid hormone concentrations during pregnancy. Neonatal thyroid function tended to correlate with maternal thyroid function at delivery in babies born to mothers with Graves’ disease who were taking antithyroid drugs. Since severe fetal hypothyroidism sometimes results in neurological damage, it is important to maintain normal maternal thyroid function during pregnancy.

Key words: Atrophic thyroiditis, Maternal Graves’ disease, Antithyroid drugs, Fetal hypothyroidism, Neonatal hypothyroidism

The role of thyroid hormones on fetal brain development is yet to be determined. The prognosis of infants born to mothers with autoimmune thyroiditis may be related to maternal thyroid function. We studied maternal thyroid function and treatment in an effort to evaluate the developmental prognosis of babies born to mothers with autoimmune thyroiditis.

Case reports

Case 1

At 3 months gestation, the mother was diagnosed with Graves’ disease and she took 30 mg/day of MMI until delivery. She had a large goiter and her thyroid function was fT4 0.4 ng/dl, TSH 73.8 µU/ml, and negative TRAB 2 days after delivery. The baby was born at 38 weeks gestation, with an Apgar score of 7/8 and a body weight of 2474 g. She was inactive from birth and had difficulty in feeding. At 2 days of age, her TSH was more than 1000 µU/ml and her fT4 was 0.4 ng/dl. The epiphysis of her distal femur was not visible. She received 10 µg/kg/day of L-T4 from 2 days until 38 days after birth. Her developmental milestone was head control at 5 months and DQ 70 at the age of 8 months, but her physical development was normal.
Case 2

The mother had Graves' disease and took 100 mg of PTU and 50 μg of L-T4 at delivery. Her thyroid function was fT4 0.68 ng/dl, TSH 6.5 μU/ml and TRAB negative. Her baby was born with fetal distress at 37 weeks gestation, with a body weight of 2026 g. His thyroid function at birth was fT4 0.32 ng/dl and TSH 491 μU/ml, and the epiphysis of his distal femur was not visible. He took 12.5 μg/kg/day of L-T4 from 2 days until 44 days after birth. At 3 years of age, his motor development was normal.

Case 3

The mother had Graves' disease and took 10 mg of MMI at delivery. Twenty-one days before delivery, her thyroid function was fT4 0.4 ng/dl, TSH 37 μU/ml, and negative TRAB. Her baby was born after 39 weeks of gestation, with a body weight of 2884 g. She had apnea on days 0 and 1. At 1 day of age, fT4 was less than 0.2 ng/dl and TSH was more than 500 μU/ml, and the epiphysis of her distal femur was not visible. She was given 12 μg/kg/day of L-T4 from 5 days to 3 months of age. At 4 years of age, her neurological development was normal.

Case 4

The mother had juvenile myxoedema. She had experienced intolerance to cold, loss of hair, and fatigability several years ago, but had received no medical attention during pregnancy. Twenty-three days after delivery, her thyroid function was undetectable fT4, TSH 123 μU/ml, TRAB 84% and TSBAB (thyroid stimulating blocking antibody) 85%. Her thyroid gland was atrophic and a thyroid scan revealed no notable accumulation of 123I around the neck. She has been treated with L-T4 since then. Her baby was born in distress after 41 weeks of gestation. Her body weight was 2649 g and she needed mechanical respiration for 3 days. In neonatal screening at 8 days, her TSH was more than 120 μU/ml. At 17 days of age, she was inactive and had generalized edema, peripheral coldness, and jaundice. At that time, fT4 was undetectable, TSH was 550 μU/ml, and TRAB was 87%, and the epiphysis of her distal femur was not visible. In utero, she became hypothyroidism due to transfer of TSBAB from mother and she had a nearly complete absence of thyroid hormone. She took L-T4 from 17 days to 8 months and after that her thyroid function was normal. At the age of 2 months, her brain was atrophic on MRI and the auditory brainstem response was less than 100 dB. At 4 years of age, sensorineural deafness of 70~80 dB was identified. At 6 years of age, her height was −1.5SD, and motor development remained the same as it was at the age of 4 months (head control and roll over).

Discussion

Infants born to mothers with Graves' disease may suffer from either hyper-or hypothyroidism due to transfer of TRAB and/or antithyroid drugs. TRAB is transferred from mother to fetus and maternal and fetal TBII level at term are well correlated. Anti-thyroid drugs are also transferred from mother to fetus, and there is a correlation between maternal and fetal PTU concentrations at delivery. Adequate antithyroid drugs from mother to fetus may be necessary to treat fetal hyperthyroidism due to TRAB, but excessive drugs may result in fetal hypothyroidism. Table 1 is a comparison of case 1 with another case. Both were born to mothers who were TRAB negative and were receiving 30 mg of MMI until delivery.

<table>
<thead>
<tr>
<th>Case</th>
<th>1</th>
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<tbody>
<tr>
<td>Mother</td>
<td>TSH (μU/ml)</td>
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<tr>
<td></td>
<td>fT4 (ng/dl)</td>
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<td></td>
<td>TRAB (%)</td>
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<tr>
<td></td>
<td>fT4 (ng/dl)</td>
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<tr>
<td></td>
<td>Development</td>
<td>DQ70</td>
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Table 1. Two neonates born from mothers with TRAB negative and receiving 30 mg of MMI. Case 1 was born to a mother with hypothyroidism. The infant suffered neonatal hypothyroidism and delayed development. The other baby was born to a mother with normal thyroid function and showed normal neonatal thyroid function. The difference in these two cases was maternal thyroid function during pregnancy.
Case 1 was born to a mother with hypothyroidism and she had neonatal hypothyroidism and delayed development. The other baby, born to a mother with normal thyroid function, showed normal neonatal thyroid function. The difference in these two cases was maternal thyroid function during pregnancy. Momotani et al. reported that in mothers who continued taking antithyroid drugs through delivery, maternal fT4 and fetal fT4 concentrations were closely correlated. We also found that neonatal fT4 levels were closely correlated with maternal fT4 levels, irrespective of antithyroid drug dose.

In chronic thyroiditis with TSBAB, fetal thyroid function is inhibited by a blocking type antibody, and infants sometimes become severe hypothyroidism and suffer irreversible damage. Our case with undetectable thyroid hormone concentration confirms the recent nationwide study in Japan by Matsuura et al., which suggested that maternal hypothyroidism during pregnancy may be an important cause of delayed physical, mental, and psychomotor development in infants.

In conclusion, maternal thyroid function is important in the prognosis of infants born to mothers with autoimmune thyroiditis, and severe fetal or neonatal hypothyroidism in these babies may result in neurological damage.

References