Neonatal hyperthyroidism with craniolacunia

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Background:
Overt neonatal hyperthyroidism is estimated to occur in 1-2% of offspring of pregnant women with Graves’ disease.
Preterm delivery, enhancement of bone including advanced bone age, craniolacunia and microcephaly can be present. Liver dysfunction, hepatosplenomegaly, thymic enlargement, hyperviscosity, and thrombocytopenia present rarely. Ventriculomegaly was reported in three cases previously. Hydrocephalus due to aqueductal stenosis and Arnold-Chiari malformation type I have not reported previously. Craniolacunia is a risk factor for hydrocephalus.

Craniolacunia is an abnormality of the calvarial bones of the skull, and is characterized by cavitation in the cranial vault as honey comb pattern. It is caused by non-ossification of the membranous skull due to intracranial decompression. It develops prenatally and is present at birth, while digital markings are caused by increased intracranial pressure and only appear after the first year of life. It is almost always associated with meningocoele, and rarely with craniolacunia, Arnold-Chiari malformation type II, and Klippel-Feil syndrome. However craniolacunia with neonatal hyperthyroidism has not previously been reported.

Purpose:
This is the first report of two cases with craniolacunia and one case with hydrocephalus and Arnold-Chiari malformation type I associated with neonatal hyperthyroidism due to maternal Graves’ disease, although neither of them had craniolacunia.

Conclusion:
Neonatal hyperthyroidism may be included in a differential diagnosis for craniolacunia.

Case 1:
Male
Mother: 27y/o: She developed Graves’ disease at age 13 years and treated with PTU at age 26 years because of persistent symptoms. She received L-thyroxine after PTU. She was pregnant after lost course of PTU, and added Thioumarine (MMI) at 20th wk. of pregnancy because of TRAb>30 U/L.
Gestational age: normal
TSH (mIU/mL): 0.39-4.01
FT3 (pg/mL): 2.13-4.27
FT4 (ng/dL): 0.83-1.71
TRAb (U/L): <2.0

3 hours: BT 37.2°C, HR 148/min, BP 50/24 mmHg, RR 41/min.
He had exophthalmos, goiter, thymic enlargement, hepatosplenomegaly (Fig 1), laboratory findings:
TSH 0.005 mIU/mL; FT3 11.45 pg/mL; FT4 6.14 ng/dL, TRAb 75.2 U/L; AST 44 U/L, ALT 12 U/L, LDH 1085 U/L, y-GT 395 U/L, CK 116 U/L, N/3 67 g/dL, WBC 7100/mL, Hb 11.3 g/dL

3 days: BT 37°C, HR 120-150/min, BP 70-90 mmHg, RR 40-60/min, immaturity, jitteriness, restlessness, exophthalmos, perinatal edema (Fig 2). Sunburst phenomenon. Anterior fontanelle 3cm.
TSH 0.005 mIU/mL; FT3 29.78 pg/mL; FT4 1.77 ng/dL.
Kl 30mg/day (1mg/kg/day)and MMI 1 mg/day 0.5 mg/kg/day were started.

Case 2:
Female
Mother: 36y/o: Leg edema and hypertension were recognized at 24w of pregnancy. She was diagnosed as having exophthalmos and goiter, and diagnosed as having Graves’ disease at 1 day post partum (TSH 0.005 mIU/mL; FT3 13.71 pg/mL; FT4 5.42 ng/dL, TRAb 23.5 U/L).

3 days: BT 37.5°C, HR 120-150/min, BP 70-90 mmHg, RR 40-60/min, immaturity, jitteriness, restlessness, exophthalmos, perinatal edema (Fig 3). Sunburst phenomenon. Anterior fontanelle 3cm.
TSH 0.005 mIU/mL; FT3 29.78 pg/mL; FT4 1.77 ng/dL.
Kl 30mg/day (1mg/kg/day)and MMI 1 mg/day 0.5 mg/kg/day were started.

Discussion:
1. Various rare clinical findings associated with Graves’ disease were observed in case 1. Although pathogenesis of those features remains to be elucidated, all those abnormalities were ameliorated by age 17 months but Arnold-Chiari malformation type I.
2. Hydrocephalus due to aqueductal stenosis and Arnold-Chiari malformation type I was found in case 1. Hydrocephalus due to aqueductal stenosis has not previously been reported in neonatal hyperthyroidism. Arnold-Chiari malformation type I with mild ventriculomegaly was reported in only one patient with mutation in thyrotrpin receptor gene. It is not known whether the presence of the both disorders was consequence of fetal and neonatal hyperthyroidism or they are just coincidental representations.

3. Craniolacunia was presented in both of our two cases. Craniolacunia has never been reported in neonatal hyperthyroidism. Neither encephalocele nor craniolacunia was observed in our cases. The cause of craniolacunia in our cases is not clear.
Craniolacunia might be a consequence of fetal hyperthyroidism, considering the following: 1) Intracranial decompression during the fetal life is assumed to be the etiologic factor in the development of craniolacunia. 2) Hyperthyroid state during fetal life is suggested to have adverse effects on brain growth. 3) Head circumstances of our cases at birth were slightly small for the gestational age.
Further study including more patients with neonatal hyperthyroidism is needed to elucidate whether craniolacunia is associated with neonatal hyperthyroidism or not.