Topic: **GOITROUS CONGENITAL HYPOTHYROIDISM**

Title: Goitrous congenital hypothyroidism in a twin pregnancy causing respiratory obstruction at birth: implications for management.

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SUMMARY

Objective: The authors report a twin pregnancy complicated by fetal goitrous hypothyroidism secondary to dyshormonogenesis caused by thyroglobulin deficiency.

Patients: Antenatal treatment with intra-amniotic thyroxine was considered but not performed, given the late gestational age at diagnosis and the multiple nature of the pregnancy. Both twins developed airway obstruction at delivery, requiring intubation and ventilation for 2 to 12 days.

Context: The authors review the literature and describe the practical issues relating to the antenatal assessment and perinatal management of fetal goiter.

COMMENT

A dichorionic twin pregnancy was confirmed at 12 weeks gestation in a healthy primiparous woman. At 18 weeks of gestation, fetal ultrasonography revealed no abnormality. A subsequent ultrasonography, at 24 weeks gestation, identified a neck mass in one of the twins, assumed to be a fetal goitre. At 31 weeks gestation, the goiter was enlarging (antero-posterior diameter: 43 mm) and was highly vascular, raising concern about a possible teratoma. One week later, ultrasound examination showed that the second twin also had a neck mass. MRI was performed (33 weeks gestation), allowing to confirm that the neck masses were goiters (tracheal compression was not reported at this stage). The mother had a normal thyroid function status, with slightly positive TPO-Ab titers. In the absence of maternal thyroid disease, the diagnosis was goitrous congenital hypothyroidism due to dyshormonogenesis. In view of the late gestational age and presence of twins, therapeutic thyroxine intra-amniotic administration was not performed. At 36 weeks gestation, one twin developed polyhydramnios. Delivery by caesarian section was carried out at 37 weeks gestation. Twin N°1 was intubated at 2 min of age, because she did not maintain regular respiratory efforts; clinical examination revealed a moderate goiter. Twin N°2 had clear evidence of airway obstruction and was also intubated at 2 min of age; her clinical examination revealed a large goiter. Both twins were given l-thyroxine (50 µg/day; 19 µg/Kg). One of twins was extubated on day 2; a thyroid ultrasound on day 5 showed a diffuse bilateral goiter with thyroid volume (TV) of 6.5 ml (normal: 0.3-1.7 ml). The other twin required external ventilation for a longer period and was extubated on day

12; her TV was 3 ml. Both twins remained well after these initial events with normal development. Concerning thyroid function, both twins had a raised serum TSH at birth (46 & 59 mU/L) with slightly decreased serum free T4 (8.1 & 8.5 pM/L) and very low serum TG values (paradoxical in a context of prolonged thyroidal stimulation). Therefore, the presumptive diagnosis was that of a thyroglobulin synthesis defect, and the diagnosis was confirmed by molecular genetic studies, showing in both twins the same pattern of compound heterozygocity with presence of two mutations .

The authors indicate that, retrospectively, they probably failed to gain maximal information from the MRI, in particular concerning potential airway obstruction associated with fetal goiter. Obstetric care providers felt that the potential risks of intra-amniotic thyroxine administration outweighed the benefits and the treatment was therefore not given. Perhaps now, with the knowledge that there was tracheal compression, neonatal hypothyroidism, and evolving polyhydramnios, they should have considered antenatal treatment at 34-35 weeks of gestation.

Fetal goiters can arise secondary to the transplacental passage of maternal thyroid autoantibodies (for instance, TSH-receptor blocking-type Abs) and also secondary to the effects of antithyroid drugs, given to treat maternal Graves' disease. In the absence of maternal thyroid disease, fetal goiter is usually due to dyshormo-nogenesis.

Was there a case for performing cordocentesis or amniocentesis? Such procedures carry a small (but significant) risk but would have provided direct information on fetal thyroid function (serum TSH, free hormone levels, serum Tg levels). Given that the diagnosis of dyshormonogenesis had already been suspected clinically, the additional information would probably not have added much to help clinicians decide on the best therapy.

With regard to fetal goiter imaging, fetal ultrasonography (US) is the first line test. Its accuracy can be further improved by the use of high-resolution US, three-dimensional US, and color flow Doppler. There is not much reported experience with MRI in the assessment of fetal goiter, but in the present cases it failed to disclose the possibility of upper airway obstruction.

Finally with regard to therapy, the administration of intra-amniotic thyroxine (alone or combined with l-T3) has been reported in several publications (as early as 1991). In all reported cases, thyroxine treatment led to goiter shrinkage, reduction in amniotic fluid volume in cases of polyhydramnios, and normalization of fetal thyroid function. The risk and hazard of intra-amniotic instillation of large doses of thyroxine must be balanced against the risk of untreated fetal thyroid function and goiter development (not an easy balance for clinicians).
(***Daniel Glinoer, M.D.; Ph.D.***)