**SUMMARY**

**Background**: Aplasia Cutis Congenita (ACC) is a rare congenital anomaly in which localized or widespread areas of skin are absent at birth. Defective lesions show complete absence of all layers of skin, occasionally extending to the skull or even the dura. ACC is etiologically heterogeneous; many different etiologies, including teratogenic substances, have been described. In the thyroid literature, ACC has been reported in infants born to women treated with methimazole (MMI) or carbimazole during pregnancy. There is one or two even more exceptional descriptions of ACC associated with PTU administration for Graves’ disease during pregnancy.

**Case Report**: The authors describe the first reported case of a monozygotic twin with ACC after in utero exposure to MMI. The girl was born at 36 weeks gestation as the first child of monozygotic twins. The mother received MMI between the 11th and 17th weeks of pregnancy because of transient hyperthyroidism. The MMI dose given was 30 mg/d for the first 3 days and thereafter 15 mg daily. The second child did not have ACC. The patient had defects of the scalp, skull, and dura (7 x 5 cm) on the sagittal line of the parieto-occipital region. No other malformation was noted. The scalp defect was treated daily with sterile physiological saline and petrolatum dressing in addition to intravenous antibiotics (ampicillin & amikacin). Trafermin, a recombinant human fibroblast growth factor, was sprayed from day 6 to promote epithelialisation of the scalp defect. On day 21, the patient had high fever due to infection of the defect lesion, which was controlled by povidone-iodine dressing and more intravenous antibiotics (ampicillin & cefotaxime). The defect of the scalp was well healed after 6 weeks, covered by ingrowth of skin from its margins, but the skull defect remained unclosed.

**Conclusions**: This is a rare discordant case report (only one of two twins affected) of a monozygotic twin (monochorionic & diamniotic) with ACC and major skull defect after MMI exposure in utero. These findings confirm that MMI is a potential teratogen of ACC.

**COMMENT**

Both thyrotoxicosis itself and the administration of antithyroid drugs (ATD) to pregnant women may raise concern with regard to the potential teratogenicity of disease and/or medications. To date, it remains uncertain whether untreated Graves’ disease is associated with a higher frequency of congenital abnormalities, but there have been reports of 2 distinct teratogenic patterns associated with the administration of MMI, namely aplasia cutis congenita and choanal/esophageal atresia. Data supporting these associations remain controversial but should nevertheless not be overlooked. Aplasia cutis has, so far, been reported only exceptionally in mothers treated for gestational hyperthyroidism using PTU. The so-called ‘methimazole embryopathy’ includes congenital abnormalities such as...
choanal and/or esophageal atresia, minor dysmorphic features and developmental delay. Reviewing the evidence linking ATD with such fetal abnormalities, the conclusion is that the prevalence of these malformations remains exceptional: less than 20 reported cases, 2/241 in MMI-exposed infants in a series reported by Di Gianantonio (Teratology, 2001). In view of the potential danger – both for mother and offspring – of not treating active Graves’ disease in pregnancy, the concern posed by these rare congenital abnormalities would not justify to withhold the administration of ATD. However, despite the fact that the link between severe congenital defects and in utero MMI exposure has not been formally established (nor understood), it appears prudent to avoid the use of MMI during embryogenesis and to prefer using PTU if available.

Concerning the present case report, it is certainly exceptional be several features: 1) only one of two twin babies affected (and why was it the premature one?) while both were exposed similarly; 2) the particular severity of scalp & skull defect; 3) the fact that MMI was given between 11th & 17th week (i.e. after the most active phase of organogenesis, thought to be the most sensitive period to teratogenic effects of drugs); and finally 4) the fact that the diagnosis of maternal Graves’ disease was far from certain: it is likely that transient hyperthyroidism was not of autoimmune origin and perhaps hCG-related, in which case the administration of ATD remains questionable.

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See Figure below

![APLASIA CUTIS CONGENITA AFTER METHIMAZOLE](image-url)