Aplasia Cutis Congenita after Methimazole Exposure in Utero; A case Report and Literature Review

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Abstract

Objective: Aplasia Cutis Congenita (ACC) is a rare disorder with a complicated pattern of inheritance. Babies are born with the absence of certain layers of skin. It most commonly manifests as a solitary defect on the scalp, but sometimes it may occur as multiple lesions. The affected area is typically covered with a thin, transparent membrane. The skull and/or underlying areas may be visible and be abnormally developed. ACC may be the primary disorder or it may occur in association with other underlying disorders.

Case presentation: This article presents a case of ACC in a newborn whose mother was treated with methimazole due to thyrotoxicosis during the first trimester of pregnancy. He was born term with midline scalp defects. This case report is presented to highlight the steps to successful management and review the relevant literature.

Conclusion: Management strategies are based on the size and presence of an underlying skull defect. A review of the literature seems to support the hypothesis that methimazole is a potential teratogen. Although the risk of birth defects is low with clinically applied doses of the drug, it cannot be regarded as safe and should therefore be avoided pregnant women. Propylthiouracil should be considered as the first choice drug for hyperthyroid pregnant women until further data on the safety of methimazole are available.

Key Words: Aplasia cutis congenita, Scalp, Methimazole

Introduction

Aplasia cutis congenita (ACC) is a heterogeneous group of disorders characterized by well circumscribed focal absence of epidermis, dermis and occasionally subcutis at birth [1]. The majority of cases involves the vertex of the scalp overlying the sagittal sinus, in proximity to the...
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hair whorl, and may be associated with other congenital anomalies. However, skin defects may also occur on other regions such as the face, trunk and limbs, sometimes symmetrically. The diameter of the scalp defect ranges between 0.5 and 10 cm. The lesions are non-inflammatory and well demarcated, superficially eroded to deeply ulcerated and occasionally already healed with scarring alopecia at birth. ACC may be round, oval, linear or stellate. Larger defects are often deeper and may extend to the dura or the meninges, complicating the clinical course of the disease. The lesions may be single or multiple.

The etiology of this group of diseases is not completely understood and may be different in the subtypes. Viral infections, ischemic/thrombotic events, involution of an intraterine hemangioma, amniotic adherence, autosomal dominant and recessive varians and teratogenic medications such as methimazole, misoprostol, carbimazole, valproic acid may be also responsible for ACC. In the relevant medical literature some cases of embryopathies are described in association to the treatment with methimazole for hyperthyroidism in pregnant women. We describe a further case of ACC of the vertex in a newborn exposed to methimazole during the first trimester of pregnancy.

Case report

A male child born at term was noticed at birth to have a single and large scalp defect in vertex along the midline. The lesion was 5 x 3.5 cm in size (Fig 1). He was born of a non-consang-uneous marriage and there was no family history of congenital anomalies. He was the second child of parents, with mother aged 26 and father aged 34. The mother was treated with methimazole from the age of 24 years due to thyrotoxicosis. The methimazole was stopped at 8 weeks of gestation and replaced with propylthiouracil. Ultrasonography and routine laboratory tests during pregnancy were normal. The delivery by cesarean section was performed in the 38th week of gestation. Neurologically, the infant had no any obvious neurological deficit. The serum levels of TSH and T4 were normal range. Routine laboratory tests and Skull X-ray were normal. Initially regular dressings were performed. However, the scalp defects did not heal completely. The lesion was covered by a densely adherent yellow scar (Fig 2).

The infant had continued dressing with Mupirucine ointment. The lesion did not heal despite repeated dressings and there were several episodes of bleeding from the lesion. A thorough saline-wash was performed and the scars were gently separated. A full thickness pedicle rotation flap from the adjacent scalp was performed. The wound healed well over the following 2 weeks without residual defects.

Fig 1- Aplasia cutis congenital at birth time. A single and large scalp defect (5 x 3.5 cm) in midline.

Fig 2- Aplasia cutis congenital after initial dressing. A densely adherent yellow scar covered the scalp defects.
Discussion

ACC is a skin defect of multivariate etiology occurring at birth [1, 2]. Typically, the lesions appear as small ulcerations that usually heal spontaneously. Larger lesions may be associated with underlying bony lesions and can cause death secondary to infection or hemorrhage, especially if from the venous sinuses [3-8]. In the past, birth trauma, congenital syphilis or skin avulsion by attached amniotic bands was considered a causative factor [1,9]. Frieden classified ACC based on etiology and manifestation into nine groups [10]. Approximately 25% of the reported cases are familial, a vast majority (69%) showing an autosomal dominant inheritance [10]. Our case fits into group 8, which is caused by specific teratogens (Methimazole) [10-18]. Eighty-four percent cases of ACC involve the scalp, of which 75% are single. Most are situated in the midline [1-3]. Our patient had a solitary and large ACC of the vertex. Extension through dermis, galea and bony calvarium occur in 35% of cases [1,4]. Frequent dressings tend to pull the scar and cause frequent bleeds. If a tear occurs over the sagittal sinus, a life-threatening hemorrhage can result. The site often becomes secondarily infected [1,7]. If there is a dural tear and the subarachnoid space is exposed, meningitis can result [1,4].

Management strategies are based on the size and presence of an underlying skull defect. Smaller scars with intact calvarium can be allowed to heal spontaneously with routine wound care. Large lesions with an underlying skull defect require surgical closure to prevent massive hemorrhage [1,7]. In our patient there were several episodes of bleeding from the lesion that had needed to surgical treatment. When primary closure is not possible, a full thickness vascularized pedicle graft can be utilized [1,7]. In our patient a full thickness pedicle rotation flap from the adjacent scalp was performed. In untreated hyperthyroid pregnant women fetal loss, intrauterine growth retardation, premature labor, heart failure, preeclampsia and thyroid storm have been observed more frequently than in normal population [11]. For this reason treatment has been advocated. Moreover, maternal normal hormone levels allow normal development of thyroid function in the fetus. It was thought that methimazole crossed the placenta three times more than propylthiouracil, but Mortimer demonstrated that both drugs have similar kinetics of placenta transfer [12]. It is possible to have a transient hypothyroidism in the newborn that usually improves spontaneously [12].

Our patient had normal thyroid function at birth. Some reports have advised against the use of methimazole in pregnant women with hyperthyroidism because of its association with ACC in exposed fetuses. In these cases the most common associated defects described are choanal atresia, intestinal anomalies as imperforate anus, esophageal atresia, scalp defects and cardiovascular defects [13,16]. Karg et Al. describe a patient exposed to methimazole during the first 6 weeks of gestation who was born with scalp and skull defects associated with facial asymmetry [17].

Our patient exposed to methimazole during the first 6 weeks of gestation. Recently a prospective cohort study came to the conclusion that choanal as well as esophageal atresia may have a higher incidence rate than expected in fetuses exposed to methimazole between 3 and 7 gestational weeks [18]. Moreover, in some Spanish regions, during the eighties, a significant increase of isolated scalp defects was observed. They were not related to the intake of methimazole by mothers, but the drug had been added to animal feed in order to enhance the weight of the animals [19]. There are no reports of propylthiouracil associated to ACC.

Conclusion

Management strategies are based on the size and presence of an underlying skull defect. Observations suggest that methimazole has teratogenic potential. As up to now no cases of ACC have been reported since the use of propylthiouracil therapy during pregnancy, It is important that propylthiouracil should be considered as the first choice drug for hyperthyroid pregnant women, while methimazole should be reserved to cases of intolerance, poor response or allergic reactions.
References


