Aplasia Cutis Congenita and Antithyroid Drugs

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Introduction

A congenital defect of the scalp is an uncommon entity occurring in one in 2000 deliveries. It may present certain diagnostic problems in the newborn infants. In this era of invasive intrapartum fetal monitoring, Obstetricians should be made aware of this entity as in its limited form aplasia cutis congenita (ACC) could easily be mistaken for damage inflicted by spiral electrodes. The late scarring observed occasionally after the application of Willet's forceps may also mimic this defect. The defect tends to be familial in majority of the cases. Relation of this scalp anomaly with in utero exposure to antithyroid drugs is still a matter of debate. We report a child with ACC whose mother was treated with neomercazole during pregnancy. As there was no history of similar defects in other siblings, a causal role for neomercazole is suspected.

Case Report

A 28 year old woman, gravida 2, para 1, attended antenatal clinic with six weeks pregnancy. She was diagnosed to have thyrotoxicosis one year ago and was treated with neomercazole. The pregnancy was unplanned but welcome. She was taking neomercazole 20mg daily during periconceptional period. Her urine pregnancy test was positive and ultrasound showed single intrauterine gestation of eight weeks duration. Neomercazole was stopped and she was switched over to propyl thiouracil but she experienced severe nausea with its use and discontinued the drug after four days. She continued taking neomercazole 10mg daily throughout her pregnancy. Her pregnancy ran an uneventful course. The thyroid status remained normal. Ultrasound scans performed at 18 and 34 weeks gestation showed satisfactory fetal growth and failed to reveal any congenital anomaly. At 41 weeks gestation it was decided to induce her to prevent postmaturity. Prostaglandin pessary was inserted at midnight followed by another one six hours later. She started having regular uterine contractions seven hours after the insertion of second pessary. Labour proceeded normally and no further augmentation was required. External fetal monitoring was employed which showed a normal trace throughout the labour. Five hours later membranes were ruptured at 7cms. An easy outlet forceps delivery was performed after one hour due to maternal non-co-operation during second stage. An alive baby boy with good Apgar score was delivered. The baby showed multiple, small, punched out lesions of the scalp. The defects were seen at the vertex arranged in two groups, varying in size from one to two centimetres and round to oval in shape. The margins were sharply demarcated and surrounding skin was normal. No gap in the underlying bone was noted. No other congenital anomalies were observed. A clinical diagnosis of ACC was made. The thyroid profile of the neonate at 6 and 24 hours revealed hypothyroidism (TSH>10mU/I, T4<4mcg/dl) and treatment was instituted. Thyroxine was started in a dose of 1 micrograms/kg/24hours. Treatment was continued for one year.

Discussion

ACC is a rare lesion in which localised or widespread areas of skin are absent at birth. Depending upon the location of the defect and the presence of associated anomalies it has been classified into nine subtypes (Table).
Clinical outcome depends upon size and location of the defect. Small lesions confined to the cutis and subcutis usually heal spontaneously and require no treatment other than simple cleansing. They heal with scarring and leave bald patches behind. Extensive defects particularly those associated with an osseous defect require surgical closure. Most of the reported mortality occurred in the cases where extensive defects overlie the sagittal sinus and involved skull and dura. Anderson and Novy brought congenital defect of scalp into dermatological literature in 1942. According to Cutlip and colleagues this condition was first described by Campbell in 1826. Vigot and colleagues have claimed that the first report was by cordon in 1767. Roughly 500 cases have so far been described. The defect tends to be familial and may be a sign of chromosomal abnormalities and malformations syndromes. Only a few cases have been linked to teratogens. Herpes simplex virus infection, in utero exposure to valproic acid and antithyroid drugs are among the supposed risk factors.

Different authorities have discussed the causal or casual nature of association of scalp defect with antithyroid drugs. Milham and Elliges found 2 cases in association with methimazole in a series of 12 cases of ACC. In another series out of six infants with ACC one mother was exposed to methimazole. Farine et al have reported a case of scalp defect where mother was treated by tapezole. They have described ACC as another aetiology for elevated alpha feto protein. Kalb and Grossman (one case), Mandel and Brent (one case), Van Dijke et al (one case), Buchrach and Burrow (five cases) have also reported scalp defects in new-borns exposed to antithyroid drugs in utero. A significant increase in the incidence of isolated scalp defects in some regions of Spain was observed by Martinez-

Table. Nine subtypes of Aplasia cutis congenita (ACC).

<table>
<thead>
<tr>
<th>Category</th>
<th>Definition</th>
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<tbody>
<tr>
<td>1</td>
<td>Scalp ACC without multiple anomalies</td>
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<tr>
<td>2</td>
<td>Scalp ACC with associated limb anomalies</td>
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<tr>
<td>3</td>
<td>Scalp ACC with epidermal or organoid naevi</td>
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<tr>
<td>4</td>
<td>ACC overlying embryological malformation</td>
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<tr>
<td>5</td>
<td>ACC with associated placental infarcts or fetus papyraceus</td>
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<tr>
<td>6</td>
<td>ACC associated with epidermolysis bullosa</td>
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<tr>
<td>7</td>
<td>ACC localised to extremities without blistering</td>
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<tr>
<td>8</td>
<td>ACC caused by teratogens</td>
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<tr>
<td>9</td>
<td>ACC as a part of malformation syndrome</td>
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frías et al. in 1980s. They relate it with the illicit use of MZO in animal feed as weight enhancer.
There are reports that suggest that this association is not as strong as initially believed by these workers. Van Dijke et al.\textsuperscript{14} analysed data from all patients with congenital skin defects who were born in University hospital of Amsterdam between 1959 and 1986. They found 25 children with congenital skin defect in 4909 deliveries (0.05%). In 13 cases these defects were confined to scalp. None of the mothers of these 25 children had used antithyroid drugs. On the other hand, 24 mothers who received methimazole or carbimizole (which bioactivates rapidly and totally to methimazole) during first trimester had children who showed no sign of skin defects. Momotami and colleagues\textsuperscript{17} reported no case of congenital skin defect in 243 infants whose mothers had been treated with methimazole during pregnancy.

Other authors\textsuperscript{7,14} have concluded that even though there is little evidence either to establish or
eliminate a direct causal relationship between ACC and methimazole, it is perhaps safer to use Propylthiouracil during pregnancy. It is an equally effective antithyroid agent and has not been associated with ACC. Mandel and Brent\textsuperscript{13} indicated that impairment of neonatal thyroid function may be minimised by using a thioamide dose that is just sufficient to maintain the maternal serum free thyroxin concentration in the high normal or slightly thyrotoxic range. It is concluded that the condition is rare and establishing causality that fulfils the criteria for association is very difficult. It is important to make Obstetricians aware of this defect so that more cases could be identified and recorded.

References