Aplasia Cutis Congenita in a Newborn Child Associated with Two Fetus Papyraceous

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ABSTRACT Aplasia cutis congenita (ACC) is a rare inborn lesion, presenting with absence of skin. The etiology is unknown and is probably not attributable to a single cause but to a combination of genetic factors. Multiple causes have been suggested for ACC: syndromes and teratogens, intrauterine infection – varicella zoster virus, herpes simplex virus – fetal exposure to cocaine, heroin, alcohol, or antithyroid drugs. The most common site is the scalp. We report a case with multiple lesions on the trunk, resembling an instance with ACC group 5. This form of ACC occurs in association with the *in utero* death of a twin or more (in this case triple) fetus. Histological findings are available in very few reports. Therapy options depend on the characteristics of the lesion, but conservative treatment is usually chosen.

KEY WORDS: aplasia cutis congenita, skin lesions, fetus papyraceous, histological findings

INTRODUCTION

Aplasia cutis congenita (ACC), first reported by Cordon in 1767, is a heterogeneous group of disorders characterized by well demarcated absence of a part of the skin at birth and benign lesion. Diagnosis is primarily clinical, while the histological appearance varies; however, most cases of ACC have not been studied histologically (1,2).

The disease can be associated with physical anomalies or malformation syndromes. Heredity has been proposed as a cause but with little evidence (3). Skin lesions, solitary or multiple, round, oval, or linear, may occur on the face, trunk and extremities, sometimes symmetrically, but most commonly as a solitary lesion on the scalp (4). Larger lesions are often deeper and may complicate the clinical course of the disease. Most commonly skin lesions are non-inflammatory, of variable extent, well circumscribed, and superficially eroded to deeply ulcerated (5). Lesions of the skin which were formed early in gestation may heal before delivery and appear as an atrophic, membranous, bullous, or parchment like scar, whereas less mature lesions present as ulcerations, which can later be revised if necessary (6). The depth may involve the epidermis and the upper dermis only. However, the

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lesion may extend to the deep dermis, the subcutaneous tissue, or even rarely to the periosteum, the skull, and the dura (7). ACC lesions are always congenital without racial and sexual predilection. The etiology of ACC is not completely understood and it is likely that more than one disease process mechanism is involved. Many cases of ACC that manifested on the trunk and limbs were associated with a mummified dead fetus or fetus papyraceus present at delivery (8). Mechanisms that contribute to the appearance of ACC include viral infections, genetic factors, teratogens, compromised vasculature to the skin, trauma, and fetus papyraceus. Teratogenic medication, such as methimazole, misoprostol, carbimazole, and valproic acid may be also responsible for ACC (3). No unifying theory can account for all ACC lesions. Truncal ACC has been reported with biliary atresia, distal duodenal atresia, intestine infarction, and multiple hepatic hematomas (2). Bilaterally symmetric ACC has been reported in association with fetus papyraceus. The main complications of larger lesions include infection, bleeding, and thrombosis that may be fatal. Therefore, prompt diagnosis and appropriate treatment are critical for avoiding adverse outcomes (4,7).

More than 500 cases have been reported since it was first described, but because of significant underreporting of this generally benign disorder, the precise frequency is unknown (9).

Table 1. Frieden's classification of aplasia cutis congenita

Group	Associations
I	Scalp ACC without multiple abnormalities
II	Scalp ACC with limb abnormalities, hypospastic or absent distal phalanges, syndactyly, club foot, others
III	Scalp ACC with epidermal and sebaceous nevi
IV	ACC overlying embryologic malformations such as gastroshisis, omphalocele, meningomyelocele, and others
V	ACC with fetus papyraceus or placental infarction
VI	ACC associated with epidermolysis bullosa (extremities and torso)
VII	ACC limited to extremities without epidermolysis bullosa
VIII	ACC due to teratogens such as methimazole (scalp), varicella and herpes simplex infections (any area)
IX	ACC associated with syndromes of malformations such as Goltz Syndrome, trisomy 13, ectodermal dysplasia, and others

CASE REPORT

We describe the case of a newborn boy who presented with bilateral symmetrical skin lesions on the trunk, noted at birth. He was an outcome of triple pregnancy with two other papyraceus fetuses. The boy was born at term, and there was no family history of congenital anomalies.

The skin lesions presented symmetrically on both sides of the trunk and were well demarcated. There were six lesions: two over the sides of the thorax, two on the abdominal region, and two on the back part of the trunk. The appearance of the lesions varied. Two thoracic lesions were triangular, were not deep, and measured 5×3.5 cm in size. Symmetrical lesions on the abdominal wall revealed atrophic parchment-like scars 2 cm in diameter (Figure 1). The lesions on the back were semicircular, deeper, and measured 5×3.5 cm in size (Figure 2). There was no sign of inflammation.

There were no other systemic or organ abnormalities at clinical examination. Radiological examination and ultrasonography of the abdomen revealed no abnormalities. Routine laboratory tests and skull X-ray were normal. The newborn boy had no obvious neurological defects.

Ultrasonography and routine laboratory tests during pregnancy were within normal limits except for the triple pregnancy. Serologic examination for virus varicella zoster infection was negative.

Histologic examination revealed flattened epidermis in many newly formed capillaries in the dermis. Inflammatory infiltrate was found in the surrounding sparce stroma. Adnexal structures such as pilosebaceous structuresa and eccrine glands were absent. Collagen bundles were arranged in various directions, with proliferation of fibroblasts (Figure 3).

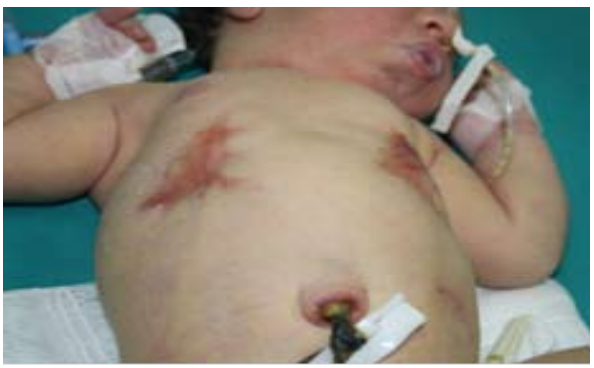

Figure 1. Aplasia cutis congenita at time of birth – symmetrical large involvement of the trunk (black arrow: parchment like scar).

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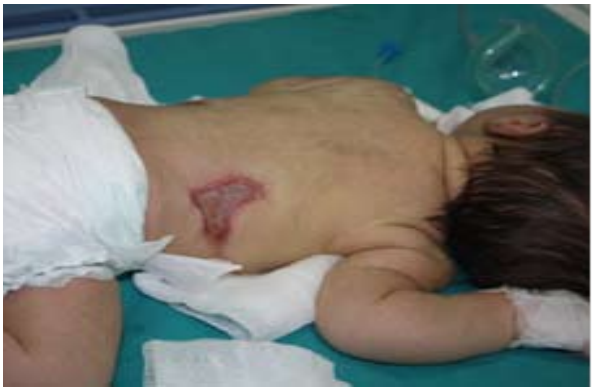

Figure 2. Aplasia cutis congenita at time of birth – symmetrical large involvement of the back (black arrow: second lesion).

The newborn was treated with local therapy that included gentle cleansing and application of bland ointment in order to prevent desiccation of the lesion. Antibiotics were not necessary because there were no signs of infection. Erosions progressively healed spontaneously over six weeks. During hospitalization, the infant remained in good condition in the neonatal care unit.

DISCUSSION

ACC is an uncommon disorder of multivariate etiology presenting at birth. Many hypotheses have arisen in the attempt to explain this rare disorder, and many authors speculated about the cause of ACC (ranging from the amniotic adherence to the fetal skin to intrauterine trauma**),** but there was no evidence to prove any of these (10-12). The most common presentation is a solitary lesion on the scalp, and almost 86 percent of cases belong to this group. The majority of the articles describe lesions in this localization. Scalp lesions can be found in association with limb reduction defects and in association with epidermal and organoid nevi. Lesions may overlie overt or occult embryologic malformations. The condition may be associated with epidermolysis bullosa, specific teratogens, or intrauterine infections, or it may occur in the presence of chromosomal abnormalities, ectodermal dysplasias, or other syndromes of malformation (13). According to Frieden, ACC is classified into nine clinical groupings (Table 1) (14-16). Although ACC involves the scalp most frequently as single defect, more complex presentation may warrant further examination. This case provides such an example, as 10% of all non-scalp variants of ACC are associated with fetus papyraceous (17). There have been no reports of scalp lesions in an infant with ACC and fetus papyraceus. This particular infant had symmetrical involvement of the trunk as a consequence of the decay of two other fetuses simultaneously in the triple pregnancy, placing it into group V of Frieden's classification (1). Truncal aplasia cutis with fetus papyraceous has also been reported (5,9,18-21). These findings confirm that the etiology of ACC is variable in general and seems to be multifactorial (21). Important aspects of examination include family history, history of similar syndromes, as well as good genetic counseling. Course of pregnancy, trauma, medications, and infections are data that must be taken into account. During delivery discovery of fetus papyraceus the single umbilical artery or abnormal placenta must be examined. In order to rule out epidermolysis bullosa and viral infections (varicella and herpes simplex), biopsy and serology is recommended. The infant with ACC must also be carefully examined for other ectodermal abnormalities such as nail hypoplasia as well as a cleft lip and palate. In cases of suspicious chromosomal abnormalities or stigma trisomy 13 and deletion of 4p, karyotype analysis must be performed. Fortunately, the majority of infants with ACC are uncomplicated cases (22).

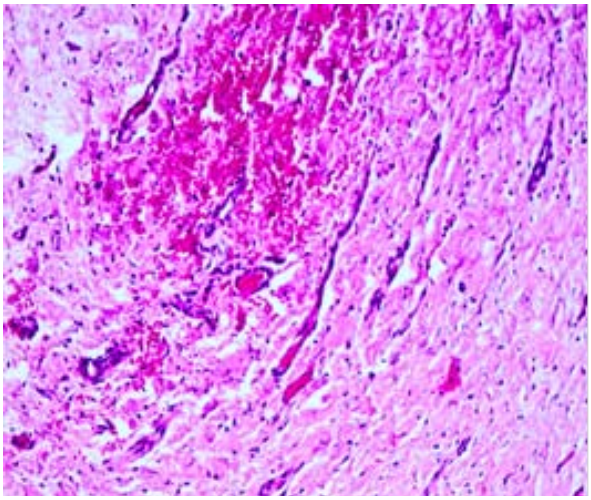

Figure 3. Biopsy specimen from the edge of the truncal lesion showed flattened epidermis with a lot of newly formed capillaries in the dermis. Sparse inflammatory infiltrate and absence of adnexal structures in the surrounding stroma (Hemalaun and Eosin ×40).

Histological details are available in very few reports. The histological features of the skin vary according to the depth of the aplasia and its duration. At birth, ulcerated lesions may present with a complete absence of skin. After healing, the epidermis appears flattened with proliferation of fibroblasts within connective tissue stroma and absent of adnexal structures. Total absence of epidermal appendages remains a characteristic feature. The histological features of our newborn's lesion were in agreement with literature data (5).

Our infant is a severe example of ACC associated with two fetus papyraceous. This disorder occurs sporadically with no familial history. The cause of the symmetrical type of aplasia cutis is a vascular disruption inducing abnormal dermoepidermal development or cutaneous lesions through ischemic and thrombotic events. The intrauterine death of one of the fetuses should cause the release of the thrombosis-promoting material from the dead fetus. These substances can cause placental infarction, disseminated intravascular coagulation, and cutaneous lesions (23). Our infant did not have any other organ abnormalities. It is suggested that the death of the twin in earlier gestation could lead to more extension and increase of the truncal form of this lesion in his surviving twin. However, in other cases no relationship was found between the extension and localization of the disorder in the viable twins.

Topical treatment options help spontaneous wound epithelization within a few weeks after delivery. Infections must be cured with topical antibiotics in order to prevent them from affecting deeper dermal structures; this is especially important for deeper scalp lesions. Surgical treatment is necessary if conservative expectative treatment causes complications.

CONCLUSION

In conclusion, ACC is a rare condition, and further studies are needed on the relationship between ACC and developmental defects. Different clinical presentations may be observed in infants with ACC born from twin or triple pregnancies associated with the early death of one or two fetuses, and we have to think about that in the context of modern reproductive medicine. Conservative topical treatment is recommended and surgical treatment only if topical treatment causes complications.

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