Aplasia cutis congenita: a conservative approach of a case with large, extensive skin, and underlying skull defect

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Introduction

Aplasia cutis congenita (ACC) is a rare disorder characterized by a focal absence of epidermis, dermis, and in some cases subcutaneous tissues – including bone and dura mater [1–3].

Cordon first described this disorder in the extremities in 1767, and Campbell described it in the scalp in 1826 [2, 4]. Most presentations (80–90%) involve the vertex of the scalp, although any part of the body may be affected [3–6]. The estimated rate of incidences is three in 10,000 births, with a female/male ratio of approximately 7:5 [3]. It is reported that only 15–20% of the cases of scalp ACC are associated with an underlying bone defect [4, 7].

The exact pathophysiology underlying ACC remains unclear; although genetics certainly plays a part in the etiology of this condition, other factors including vascular accidents and developmental abnormalities may be responsible in some cases [4]. Other factors that are possibly implicated include intrauterine trauma, local amniotic adhesions, and exposure to varicella and herpes simplex or to teratogenic agents, such as antithyroid drugs, valproic acid, marijuana, heroin, alcohol, and cocaine [3, 5–7].

Aplasia cutis congenita is primarily diagnosed on a clinical basis. In 1986, Frieden proposed a classification system for ACC that included nine groups based on the lesion characteristics, associated abnormalities, and type of inheritance (Table 1) [4, 8]. The disorder is usually seen on the scalp, often as solitary lesion without other anomalies. Scalp lesions may be associated with limb reduction defects and in association with epidermal and organoid naevi. Lesions may overlie overt or occult embryological malformations. A form of ACC occurs in association with the placental infarcts or the in utero death of a twin fetus. The condition may be associated with epidermolysis bullosa, specific teratogens, or intrauterine infections, ectodermal dysplasias, chromosomal abnormalities (trisomy 13, the 4p (-) syndrome), or other malformation syndromes like Adams-Oliver syndrome [4].

Both conservative and surgical methods have been proposed to treat this condition [1], but the large scalp defects present a management dilemma [2]. The mortality associated with ACC is related to the depth and the size of the defect. If a bony defect is present, rates of complication increase, and the associated mortality has been estimated to be as high as 25–55%. Complications of large ACC with bony defect include sagittal sinus hemorrhage or thrombosis, site infection, or meningitis. Death is
usually from sagittal sinus hemorrhage caused either by eschar drying and separation following a conservative approach or surgical manipulation [3–5, 7].

Case Report

The patient was born at 40 weeks gestation to a 25-year-old mother after an uneventful first pregnancy. No record of maternal morbidities or intake of suspected substances during the pregnancy were reported. There was no family history of skin problems or genetic abnormalities. Both parents are young and unrelated.

During the course of the delivery, a bone defect in the skull was found, leading to a secondary cesarean section. The patient’s Apgar scores were 4/8/10, and her birth weight was 2960 g. At birth, a physical examination revealed a full-thickness defect of epidermis, dermis, subcutaneous tissue, and bone. The defect measured $9 \times 10$ cm; it was located at the midline and extended to both parietal regions of the cranial vertex, exposing the dura mater. Overlying the defect were large, superficial, grossly dilated veins (Fig. 1). There was no cerebrospinal fluid leakage.

The patient was otherwise healthy with no other cutaneous lesions, including persistent cutaneous marmorata or abnormalities of limbs or digits. Physical and neurological examinations were within normal limits. All metabolic and hematological laboratory panels were normal. A skull radiograph confirmed the bone defect. Echocardiogram, cerebral, and abdominal ultrasound were normal. Subsequent magnetic resonance imaging showed no brain morphological abnormalities. Our patient is included in group 1 of Frieden’s classification.

Initially, to keep the wound moist and aseptic, the defect was dressed with saline-soaked gauze; however, it retracted during healing. Dressing was changed to polyurethane foam to avoid the possible complication of infection and hemorrhage. On day eight the patient was discharged. However, she was readmitted 2 days later because of bleeding. During this second hospital stay she had four more episodes of bleeding, requiring two red-blood cell transfusions. Also had a course of antibiotics (fluclouoxacinil and amikacin for 7 days). The scalp swab showed the growth of *Klebsiella pneumonia* and blood cultures were negative.

Because of the frequent hemorrhages, it was decided that the patient should undergo an acellular dermal matrix graft. Moreover, the clinical evolution after these events was favorable, with proper healing and no new

| Group | Definition | Inheritance |
|-------|------------|-------------|
| 1     | Scalp ACC without multiple anomalies | Autosomal dominant or sporadic |
| 2     | Scalp ACC with associated limb abnormalities (limb reduction abnormalities; syndactyly; club-foot; nail absence or dystrophy; skin tags on toes) | Autosomal dominant |
| 3     | Scalp ACC with associated epidermal and organoid nevi | Sporadic |
| 4     | ACC overlying embryologic malformations such as meningo(myelo)celes, gastroschisis, and omphalocoele | Depends on the underlying condition |
| 5     | ACC with associated fetal papyraceous or placental infarcts | Sporadic |
| 6     | ACC associated with epidermolysis bullosa (EB) | Depends on EB type: It may be autosomal dominant or recessive |
| 7     | ACC localized to extremities without blistering | Autosomal dominant or recessive |
| 8     | ACC caused by specific teratogens (methimazole, valproic acid and herpes simplex infection) | Not inherited |
| 9     | ACC associated with malformation syndromes (Trisomy 13; 4p- syndrome; many ectodermal dysplasias; Johanson-Blizzard syndrome; focal dermal hypoplasia; amniotic band disruption complex; XY gonadal dysgenesis) | Various, depending on the specific syndrome |

Figure 1. At birth. Absence of the epidermis, dermis and subcutaneous tissue, with bone defect ($9 \times 10$ cm), exposing the dura mater.
episodes of bleeding or other complications. After a multidisciplinary meeting – involving neonatology, dermatology, and plastic surgery – the therapeutic strategy was revised, and after weighing the pros and cons of each approach, it was decided to continue with conservative treatment, changing the dress three times a week. Patient was discharged on day 40 and obtained complete epithelialization at 5 months (Fig. 2). No complications were encountered during follow-up.

It has been indicated that the dura mater has the osteogenic potential to initiate and sustain bony closure of the defect [9]. Three-dimensional computed tomography (CT) was performed at 10 months old to evaluate the bone defect (Fig. 3). She maintained parietal defects measuring 4 cm in diameter on the left and 1.5 cm on the right.

At the present age of 18 months, the patient is doing well overall and meeting developmental milestones. However, alopecia persists. She continues to undergo multidisciplinary follow-up in the pediatrics, dermatology, plastic surgery, and neurosurgery outpatient departments. Reconstruction cranioplasties are advised, when the patient is 3 or 4 years old [4].

Discussion

We report on a newborn presenting with an extensive area of ACC and a large underlying bone defect. The goal of the treatment was to achieve complete closure of the defect and avoid important risks, such as meningitis, hemorrhage, and trauma to the brain, which lead to a mortality rate between 25 and 55% [4, 5, 7].

The course of ACC depends to some degree on the size of the lesion. However, there is currently no consensus on the management of this condition, particularly when a bone defect is present [3–5]. Treatments for the more characteristic small lesions tend to be conservative, consisting of local wound care that allows for granulation and definitive healing with alopecic scars [3, 5, 7]. Larger defects of the skin and underlying bone, such as our index patient presented, are particularly challenging. Such cases present the dilemma of choosing between an early operative intervention or following a conservative approach.

The surgical treatment options include skin grafts, rotation flaps, free flaps, and tissue expansion [3, 7, 10]. The advantage of early surgical intervention is the reduced risk of meningitis, sinus thrombosis, or hemorrhage. However, in addition to the elevated perioperative risk of hemorrhage and infection in infants, any graft – especially one used to cover large defects – entails a high risk of partial or total graft failure. Furthermore, the graft may not expand to accommodate the growing brain [3, 10]. Additionally, serious difficulties may arise from the secondary reconstruction of the bone defect, leading to massive bleeding from the underlying brain and sagittal sinus after the skin graft is removed. Moreover, surgical intervention may lead to delayed healing and scarring; with consequent wound contraction [3].

Mortality from infections or hemorrhages of the sagittal sinus is equally associated with both conservative treatment and surgical repair [3, 5]. This fact along with the extreme rarity of this condition and the small number of reported cases make it difficult to evaluate the best therapeutic approach [4].
Conservative management has been advocated by several authors. The rationale for this approach is avoiding surgery and its associated risks [1, 4]. The conservative treatment is simple, easy to carry out, and allows granulation and complete healing. Also, there are clinical reports and experimental studies suggesting that the dura mater is capable of inducing new bone formation. However, some serious complications such as hemorrhage, infections, sagittal sinus thrombosis, and even hydrocephalus have been reported [4, 10].

We report this case to demonstrate that even for the largest skin and bone defects, an initial conservative approach may allow for complete wound closure without the need for early surgical intervention. The final result was satisfactory.

Our conclusion is that each case must be evaluated individually. For smaller lesions it is consensual that we should opt for conservative treatment; the most extensive defects imply more difficulty in choosing the treatment, given the pros and cons of each method and the limited numbers published in the literature. There are significant and life-threatening risks to conservative treatment as well as operative treatment. It is the risk of complications, success rate of the potential surgical options, and the patient’s overall prognosis that must be considered.

Conflict of Interests

The authors declare that they have no conflict of interests regarding the publication of this article.

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