

Case Report

Aplasia cutis congenita: Two case reports and discussion of the literature

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Abstract

Background: Aplasia cutis congenita (ACC) is a part of a heterogeneous group of conditions characterized by the congenital absence of epidermis, dermis, and in some cases, subcutaneous tissues or bone usually involving the scalp vertex. There is an estimated incidence of 3 in 10,000 births resulting in a total number of 500 reported cases to date. The lesions may occur on every body surface although localized scalp lesions form the most frequent pattern (70%). Complete aplasia involving bone defects occurs in approximately 20% of cases. ACC can occur as an isolated defect or can be associated with a number of other congenital anomalies such as limb anomalies or embryologic malformations. In patients with large scalp and skull defects, there is increased risk of infection and bleeding along with increased mortality and therefore prompt and effective management is advised.

Case Description: We describe two cases of ACC, involving a 4 × 3 cm defect managed conservatively and a larger 10 × 5 cm defect managed surgically with the use of a temporo-occipital scalp flap. Both cases had an excellent outcome.

Conclusions: Multiple treatment regimens exist for ACC, but there is no consensus on treatment strategies. Conservative treatment has been described and advocated, but many authors have emphasized the disadvantages of this treatment modality. Decision between conservative and surgical management must be individualized according to lesion size and location.

Key Words: Aplasia cutis congenita, congenital anomalies, cranial reconstruction, scalp reconstruction

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INTRODUCTION

Aplasia cutis congenita (ACC) is a heterogenous group of disorders reported historically by Cordon in 1767, and characterized by the absence of epidermis, dermis, and occasionally subcutaneous tissues or even bone tissue, involving multiple possible body locations. The most common lesion location is the scalp (70%);^[17,41,43] however, any skin site can be affected and there is also a rare universally fatal subcategory affecting the majority of the dermis.^[51,59] In 1986, a classification system was devised by Frieden consisting of nine main ACC types based on the number, the location of the lesions, and the presence or absence of associated deformities,^[13] which is shown in Table 1.^[7]

ACC holds an estimated incidence of about 3 in 10,000 births and there has been a total of approximately 500 reported cases in the literature.^[32] The strongest risk factor reported in the literature is the antithyroid drug Methimazole,^[18,20,21,39,40,55] which according to Frieden classification, can be categorized into type 8 ACC. However, cases of ACC are extremely limited due to the very low incidence and, therefore, it is not possible to derive completely accurate epidemiological data.

Table 1: Frieden classification of ACC types

Type	Characteristics
1	ACC located on the scalp with no other anomalies whatsoever
2	ACC located on the scalp but with concomitant limb anomalies such as: Limb malformations (Adams-Oliver syndrome) Hypoplasia or aplasia of the distal phalanges Vascular malformations, fibromas, nipple and hair abnormalities
3	ACC of the scalp along with epidermal nevi, neurological and ophthalmic abnormalities: (such as seizures, mental impairment, corneal and eyelid lesions)
4	ACC accompanied by embryologic deformities: such as omphalocele, leptomeningeal angiomas, cranial stenosis, porencephaly, meningocele, spinal dysraphism, or gastroschisis
5	ACC along with fetus papyraceous, placental infarct; Extensive ACC of the trunk or limbs
6	ACC and epidermolysis bullosa involving the lower extremities
7	ACC with no epidermolysis bullosa involving the extremities
8	Teratogen associated ACC: herpes simplex and varicella-zoster virus intrauterine infections, and drugs during pregnancy such as methimazole or carbimazole
9	ACC accompanied by congenital malformations such as: Patau syndrome (Trisomy 13), Wolf-Hirschhorn (4p deletion), Setleis syndrome Johanson-Blizzard syndrome, Goltz syndrome, ADAM complex, Kabuki syndrome Delleman syndrome, Finlay-Mark syndrome, XY gonadal dysgenesis

Pathophysiology of ACC is not well studied and its exact pathogenesis is unknown.^[11,22,30,35,36] However, there are multiple factors that are probably contributing to the development of ACC according to the literature:

- Chromosomal abnormalities,^[8,31] especially BMS1^[29]; a recent study has also implicated the UBA2 gene and the SUMOylation pathway^[27]
- Trauma^[28,53]
- Amniotic irregularities^[7]
- Intrauterine complications, such as vascular accidents or infection^[7,9,13,46,50]
- Thrombosis, vascular lesions^[7,9,15]
- Teratogens: such as misoprostol, benzodiazepines, valproic acid cocaine, methotrexate, ACE inhibitors, methimasol.^[18,35,39,40,44,50]

The main pathophysiologic hypothesis about ACC is that the mechanism behind it lies in tension-induced disruption of the overlying skin occurring at 10–15 weeks of gestation when rapid brain growth occurs along with hair direction and patterning.^[31] Another less prevalent model is that premature amniotic membrane rupture and amniotic band formation might be the cause of ACC.^[7]

CASE DESCRIPTIONS

The following cases are categorized as group 1 ACC and involve patients with multiple scalp bullous lesions, with both skin and bone layer defects. We will describe both cases and discuss presentation, prognosis, and management strategies.

First case

Our first patient was a 3300 g white boy of 37 weeks of gestation. Pregnancy, labor, and delivery were without any mishaps. From the obstetrical record, we were informed that the mother was treated for hypothyroidism with T4 and also with Ritodrine (Utopar®) due to uterine contractions. No abnormal family history was reported. At birth, the boy was found to have three sizable bullae on his scalp. There was a large round-shaped occipital defect at the vertex with dimensions of 4 × 3 cm and two lesser ones at the frontal vertex with dimensions of 1 × 2 and 1 × 1 cm [Figures 1 and 2]. The defects included both scalp and skin layers and were confirmed by ultrasound and computed tomography (CT) scan examinations. The CT scan also revealed suture diastasis with thinning and hypoplasia of the fronto-parietal bones [Figure 3]. A thin membrane was covering the defect in immediate proximity to the superior sagittal sinus. During the following days, a dark dry eschar developed covering the lesion. A conservative management strategy was adapted due to relatively small size of the lesions. The wound was vigorously cleaned daily initially with betadine solution and furthermore with fucidin gauze and sterile dressings. The eschar became well demarcated shortly and the healing process

was mostly satisfying. Intravenous chemoprophylaxis with third-generation Cephalosporin (Cefotaxime®) and Teicoplanin (Targocid®) was concomitantly administered. Complete wound closure occurred at 42 days.

Second case

Our second patient was a 3660 g white boy of 42 weeks of gestation. Pregnancy, labor, and delivery were without any mishaps. The obstetrical record included history of induced delivery. The medical record revealed a family history of ACC involving the patient’s father and siblings. At birth, the patient had an extensive round-shaped hemorrhagic bullae with dimensions of 10 × 5 cm above the fronto-occipital regions of the scalp [Figures 4 and 5]. The defect included scalp and skin layers, which was confirmed by ultrasound and magnetic resonance imaging (MRI) scan examinations [Figure 6]. The MRI scan revealed a complete loss of continuity of the dermal and subcutaneous tissues [Figure 6]. Yet again, a thin membrane covered the defect in immediate proximity to the superior sagittal sinus. In contrast to the first case, in this case surgical treatment was adapted due to the increased size of the lesion, along with the proximity to the superior sagittal sinus. The defect was covered by using a single temporo-occipital scalp flap. Chemoprophylaxis was given with

intravenous injections of Ceftazidime (Solvetan®) and Teicoplanin (Targocid®). During the postoperative period, blood examinations showed increased inflammatory indexes and blood cultures were found positive for *Enterobacter cloacae*, and therefore antibiotic treatment was modified to Meropenem (Meronem®) and Vancomycin (Voncon®). Unfortunately, the infant developed septic shock influencing coagulation factors VII and IX, and thus was promptly provided with units of fresh frozen plasma. Defected areas were treated with betadine scrub and sterile gauze dressing. Following daily local treatment, the wound gradually epithelialized, and complete epithelialization was achieved at 37 days.

DISCUSSION

In the majority of cases (70%) ACC manifests as a solitary defect of the scalp, but occasionally it may present with multiple lesions such as in our first case. Although lesions



Figure 1: The largest (4x3) bullous defect of the first case



Figure 2: All 3 scalp bullous defects of the first case

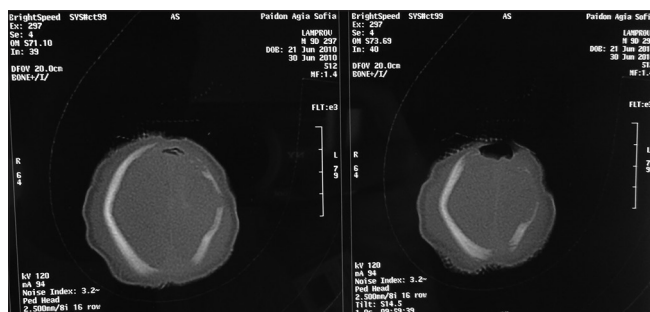


Figure 3: The CT scan, confirmed the defects which involved both bone and skin layers, and revealed suture diastasis with thinning and hypoplasia of fronto-parietal bones



Figure 4: Our second case had an extensive defect (10x5) above the fronto-occipital regions of the scalp



Figure 5: A thin membrane was covering the defect in immediate proximity to the superior sagittal sinus

are noninflammatory and well demarcated, there is great controversy concerning treatment of ACC and there has been a great scientific interest due to the extremely high mortality figures that range from 20 to 55%.^[38] High mortality/morbidity rates are a result of sagittal sinus bleeding, secondary local infection, meningitis, sagittal sinus thrombosis, or the direct result of other serious congenital defects that are associated with ACC.^[19,26,38] On examining both the presented cases, it was observed that both had lesions in very close proximity to the superior sagittal sinus; therefore, the imminent risk of infection and bleeding is apparent. Bleeding of the superior sagittal sinus is the most life-threatening complication of ACC with 36% mortality.^[19] This fatal complication occurs between 1 and 3 months of age, has been shown to be more frequent with lesions involving a larger portion of the superior sagittal sinus, and is probably the cause of superior sagittal sinus exposure and insufficient protection.^[19] It is important to prevent such fatal complications through prompt and effective ACC management.

The management of scalp ACC is controversial. Treatment may be either conservative or operative, and there is no consensus or guidelines on treatment strategy. Choosing between conservative and operative modalities is challenging and should be individualized.^[47] Lesion size is the only universally accepted criterion with larger lesions favoring the surgical approach.^[6] Additionally, lesion location plays an important role, with lesions above critical areas, especially with sagittal sinus compromise favoring a surgical approach due to increased bleeding and infection risk.^[50]

Conservative management consists of regular wound cleansing and application of dressings along with the use of systemic antibiotics.^[18] This includes physiological saline, continuous saline drips, betadine solution, bacitracin ointment, and silver sulfadiazine dressings,^[37]

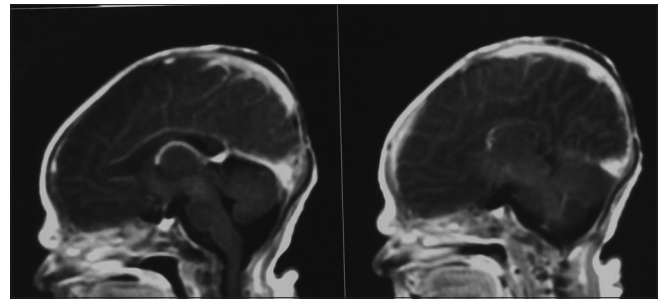


Figure 6: MRI confirmed that the defect included scalp and skin layers and revealed complete loss of continuity of the dermal and subcutaneous tissues

which are utilized in order to preserve moisture, prevent desiccation, and allow spontaneous epithelialization to occur.^[48,56,58] There are multiple reports of specialized adherent wound dressings that are thought to offer increased wound healing rates,^[3,4,23] as well as recent reports of novel dressing materials such as fatty gauzes.^[49] However, none of the more specialized dressing materials have proven to be significantly superior, and therefore, it is accepted to treat ACC with standard traditional wound care.^[30] Although conservative treatment has traditionally been the default strategy for normal and small-sized lesions, lately there have been reports of extensive ACC lesions managed through the conservative route with excellent healing results,^[14,37] and this shows a tendency of recent literature in favor of the conservative approach. In addition, there have been reports of even more specialized conservative treatment techniques such as the use of autologous cultured fibroblasts and keratinocytes^[10] or the application of fibroblast growth factors that accelerate wound healing, a modality which might represent the future of ACC treatment drastically decreasing the number of surgically managed cases.^[33]

Surgical management, on the contrary, includes various procedures. Standard surgical care includes primary wound closure, skin grafting (autologous or allografts),^[5,26,57] local scalp flaps with or without tissue expansion,^[37,54] free flaps,^[26] muscle flaps,^[52] full-thickness or split-thickness skin grafts,^[1,45] and cranial vault reconstruction using bone grafts.^[16,37] Specialized surgical techniques such as utilizing bipedicle opposing local flaps,^[12,32] rotational flaps,^[24,31,42,50] or L-shaped flaps^[2] have been used with satisfying results. However, wound repair through a single, large scalp flap seems adequate and effective for the majority of ACC lesions,^[38] offering adequate wound closure and protection of the sensitive underlying structures. Closure of the associated skull defect is usually achieved through the use of artificial bone grafts, which should be designed according to current bone defect size, although the use of autologous bone grafts has been described.^[16,34] Bone defects, according to the literature, can self-regenerate with an impressive speed,^[57] however, many authors advise to repair skin defects and

skull defects concomitantly for optimal results,^[34] or in a delayed cranioplasty operation. In conclusion, the exact surgical technique must be tailored according to each individual patient and lesion, as well as the surgeons personal preference and expertise.^[6] Surgery for ACC is accompanied by the usual complications of every surgical operation, and consists mainly of intraoperative hemorrhage and postoperative infections. These complications are rare, but can be effectively managed. Since ACC mortality is particularly high especially for larger lesions due to similar complications involving both life-threatening hemorrhage and infection, postoperative complications should not be considered as a discouraging factor when managing a patient with an extended ACC lesion.^[31]

CONCLUSION

In conclusion, we strongly believe that a conservative approach minimizes complications, avoids unwanted operative sequelae, and takes full advantage of the innate rapid regeneration ability of the newborn.^[17] Therefore, whenever the conservative approach seems feasible, it is strongly advised to initially adapt it and save the surgical approach in cases of treatment failure.^[41] In the near future, even more technologies are about to emerge to facilitate wound healing and wound closure, such as fibroblast growth factors and cultured skin, possibly even rendering surgical management obsolete. Throughout the literature, there are reports of extremely large defects treated conservatively with impressive results,^[14] however, there are no reports of surgical management for lesions of size $<30 \text{ cm}^2$.^[25] Present publications generally illustrate that conservative management is preferable, and surgical management is generally considered, but not always utilized, for lesions of size $>30 \text{ cm}^2$.

In our specific cases, we utilized a conservative approach in Case 1, which involved a smaller defect ($1 \times 2 \text{ cm}$), whereas for the larger defect of Case 2 ($10 \times 5 \text{ cm}$), a surgical approach with the application of a single scalp flap was utilized. Results were satisfying in both cases, with complete wound closure. Taking into account both our own experience and the literature, we strongly believe that utilizing a size threshold for deciding between conservative or surgical approach along with meticulous sterile dressings and wound care is the optimal management strategy for ACC. The optimal size threshold and specific treatment guidelines remain yet to be determined. The literature complete lacks any precise guidelines or suggestions on the subject and further research is required. Therefore, it must be noted that due to the lack of treatment algorithms and guidelines on ACC management and the need for individualized treatment decisions, it is important for such cases to be

managed in centers specialized in pediatric neurosurgery with sufficient experience and expertise.

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Conflicts of interest

There are no conflicts of interest.

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