

Aplasia cutis congenita: Insights from a 14-year study of a rare condition

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ABSTRACT

Background: Aplasia cutis congenita (ACC), also referred to as congenital cutaneous aplasia (CCA), is a rare congenital disorder characterized by the absence of skin layers, typically affecting the scalp, but also potentially involving the trunk and extremities. This study aimed to investigate the epidemiological, clinical, and therapeutic aspects of ACC, a rare condition that presents in various forms. It emphasizes the importance of recognizing ACC across specialties, including dermatology, gynecology, pediatrics, and general practice, with an emphasis on effective physician–parent collaboration for optimal management. **Materials and Methods:** A retrospective study was conducted on sixteen patients diagnosed with ACC over a fourteen-year period. Data on demographic characteristics, clinical presentation, treatment methods, and outcomes were collected. The study also explored the effects of consanguinity, prenatal care quality, and syndromic associations, with particular focus on Bart’s syndrome. **Results:** Of the sixteen patients, 75% were treated conservatively, while 25% required surgical intervention. Complete healing was achieved in 31% of the cases, and 43% experienced persistent complications. Septic shock was the primary cause of mortality in 19% of the cases. A significant correlation was found between consanguinity, inadequate prenatal care, and more severe forms of ACC. **Conclusion:** This study highlighted the need for early diagnosis, genetic counseling, and improved prenatal care, particularly in regions with high rates of consanguinity. Furthermore, it underscores the significance of parental education and collaboration during treatment. A multidisciplinary approach is essential for managing ACC, especially in syndromic cases. Further research is necessary to explore genetic and environmental factors that influence ACC and to refine treatment strategies.

Key words: Aplasia Cutis Congenita, Bart’s Syndrome, Congenital Abnormalities, Genetic Counseling, Skin Diseases, Wound Healing

INTRODUCTION

Aplasia cutis congenita is a rare congenital defect characterized by the lack of the epidermis, dermis, and, in some cases, subcutaneous tissue. This condition may be localized or widespread. Initially described by Cordon in 1767 [1], ACC predominantly affects the scalp, yet it may also occur on the face, trunk, and limbs [2-4]. Although the exact incidence is not well documented, ACC is considered an uncommon disorder that is often overlooked and not fully understood.

Clinically, ACC presents in a range of forms, from mild, scar-like lesions to more severe ulcerations, which may be accompanied by systemic abnormalities [5,6]. In 1986, Frieden proposed a classification system for ACC, organizing it into nine categories based on the location of the lesions, associated anomalies, and patterns of inheritance [1]. This classification has provided significant insights into the condition. However, there remain significant knowledge gaps concerning its causes and the most effective treatment strategies. While isolated ACC cases are usually non-threatening,

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syndromic forms of the disorder, such as those associated with Bart's syndrome (dominant dystrophic epidermolysis bullosa), present considerable diagnostic and management difficulties. These syndromic forms are often accompanied by additional malformations and increase the risk of severe complications, including infections and systemic issues [7-9].

In some countries, where cultural practices and healthcare limitations may contribute to the challenges in managing ACC, factors such as consanguinity, limited prenatal care, and inadequate access to specialized care further complicate the situation [10]. Moreover, the absence of local epidemiological data hinders the formulation of targeted prevention and management strategies.

This study, conducted at a tertiary dermatology center, aimed to examine the epidemiological, clinical, and evolutionary aspects of ACC. By evaluating sixteen cases over a span of fourteen years, the goal was to enhance understanding of this rare condition and improve management strategies in similar healthcare settings.

MATERIALS AND METHODS

This retrospective, descriptive study was conducted at the dermatology department of our hospital from 2010 to 2024. The hospital is a tertiary care center serving as a regional referral hub for pediatric dermatology. A total of 11,723 consultations were performed during the study period.

The study comprised sixteen pediatric patients diagnosed with congenital cutaneous aplasia (CCA), accounting for approx. 0.14% of all pediatric dermatology consultations. Patients were included if they had a confirmed diagnosis of ACC through clinical examination, with additional diagnostic investigations conducted when needed. The exclusion criteria involved incomplete medical records or a diagnosis other than ACC.

Data Collection

Data was extracted from patient records using a structured form designed to capture key information on the following variables:

- Epidemiological data: age at presentation, sex, and the family history of CCA or other dermatological conditions.

- Clinical features: detailed description of lesion location, size, morphology, and any associated anomalies, including systemic malformations.
- Obstetric history: maternal medical history, pregnancy follow-up, and any relevant antenatal findings.
- Management and outcome: details of therapeutic interventions, complications, and the follow-up outcome.

Data Analysis

Descriptive analysis was performed using Microsoft Excel, with categorical variables (e.g., sex, lesion types) were expressed as frequencies and percentages, while continuous variables (e.g., lesion size, age at presentation) were summarized as means and ranges.

Ethical Considerations

Ethical approval was granted by the institutional review board of the hospital. Due to the retrospective nature of the study, informed consent was not required. Patient confidentiality and anonymity were strictly maintained, and identifiers were removed from all records. Images containing identifiable features were anonymized or masked when necessary.

RESULTS

Epidemiological Data

Sixteen pediatric cases of congenital cutaneous aplasia (CCA) were identified, accounting for 0.14% of all pediatric dermatology consultations. The age of the patients at presentation ranged from birth (day 1) to 18 months, with a male-to-female ratio of 10:6 (sex ratio of 0.6).

- Family history and consanguinity: approx. 33% of the patients reported a history of consanguinity, indicating a possible genetic link. Additionally, 13% had a recorded family history of congenital cutaneous aplasia (CCA), which included cases of Bart's syndrome—a form of dominant dystrophic epidermolysis bullosa. Interestingly, there were two twins with CCA who had a sibling who had passed away due to Bart's syndrome.
- Obstetric history: two mothers reported infections during pregnancy, and one was treated with benzodiazepines during the first trimester. Additionally, 66% of pregnancies were poorly monitored or unmonitored, highlighting potential gaps in prenatal care.

Clinical Characteristics

The clinical presentation varied, with lesions mainly occurring on the limbs (50%) (Fig. 1), flanks, and abdomen (12%) (Fig. 2). Scalp involvement was seen in two cases, one with a large irregular plaque exposing the dura mater (Fig. 3) and the other with a small lesion associated with cranial deformity (Fig. 4).

- Lesion size and morphology: lesions varied in size from 1 cm to 15 cm. The majority were large and displayed diverse characteristics, including translucent plaques with visible vascular networks, as well as cicatricial, ulcerated, or fibrinous plaques.
- Blistering and mucosal involvement: blistering was observed in 26% of cases (Fig. 5) often at sites of friction. Mucosal involvement, including

blisters and erosions, was noted in some patients, particularly in the oral mucosa.

- Systemic malformations: 30% of patients had associated systemic malformations, including bilateral clubfeet, radial club hands, cleft lip, and craniosynostosis. One patient with vertex aplasia also had a bony defect.

Management and Outcomes

The treatment approach was largely symptomatic, with a combination of conservative and surgical management.

- Conservative treatment (75% of cases) included petrolatum-based dressings, analgesics for pain management, and antibiotics to prevent or treat infections. These interventions were



Figure 1: Aplasia cutis congenita of the limbs, with some lesions presenting as bullous formations.



Figure 2: ACC of the abdomen.



Figure 3: Large, irregular ACC plaque exposing the dura mater.



Figure 4: Small ACC lesion associated with cranial deformity.



Figure 5: Blistering and mucosal involvement in ACC.

effective for small to moderate lesions without complications.

- Surgical treatment (25% of cases) involved skin grafting or directed wound healing using local flaps

for larger lesions or those with severe tissue loss (Fig. 6).

- Healing and follow-up:
 - Complete healing (31%): Achieved in patients with minor lesions and no associated malformations.
 - Persistent complications (43%): included incomplete healing and chronic infections, requiring long-term follow-up.
 - Fatal outcome (19%): two patients, both with Bart's syndrome, died from septic shock. In both cases, follow-up care was insufficient as their parents, who had previously lost a child to Bart's syndrome, refused further treatment after the initial discharge. These parents also declined psychological support and left the hospital without medical consent.

Follow-Up

The follow-up care varied depending on the severity of the condition:

- Bart's syndrome cases: These patients underwent daily follow-up during their hospital stay at the neonatal department, which included daily dressing changes and wound care. After discharge, follow-up continued at the pediatric department, with visits becoming weekly, then monthly, and later spaced further apart as the patients' conditions stabilized.
- Other patients: For patients with milder lesions, follow-up care was handled by informed parents, with visits weekly initially, then monthly as the patient healed.

Risk Factors and Observations

Key risk factors for CCA included:

- Consanguinity (33% of cases): Reinforcing the potential genetic origin and emphasizing the importance of genetic counseling.
- Prenatal care (66% poorly monitored): Indicates the need for enhanced prenatal care and the early identification of high-risk pregnancies.
- Teratogenic exposures: Some maternal medications, particularly benzodiazepines during early pregnancy, could potentially contribute to the onset of CCA.
- Syndromic associations: Many patients had associated syndromes, including Bart's syndrome, which could contribute to the severity of the condition.

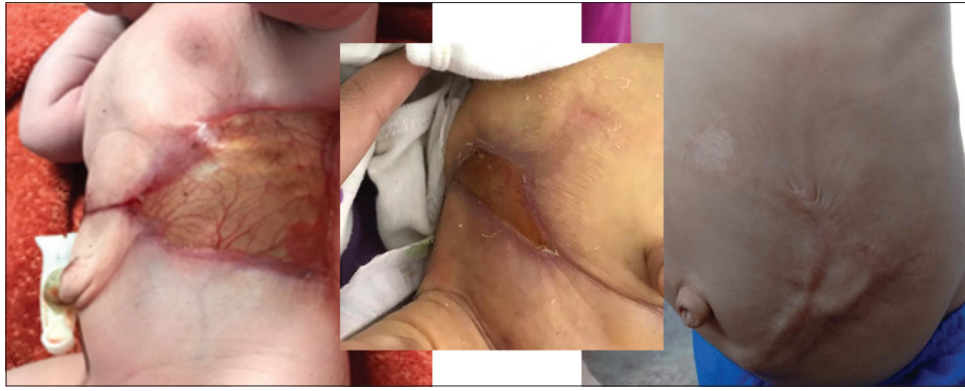


Figure 6: Aplasia cutis congenita treated with a surgical graft and guided wound healing.

DISCUSSION

Aplasia cutis congenita (ACC) is an uncommon condition characterized by the absence of skin at birth, which may also present alongside other systemic abnormalities. While the precise cause of ACC is not fully understood, several potential factors have been suggested, such as genetic mutations, intrauterine trauma, viral infections, and maternal influences. Recent studies, particularly by Marneros (2024) [11], have highlighted the significant role of genetic mutations in the development of ACC. Specifically, mutations in *KCTD1* and *KCTD15* disrupt normal skin formation by impacting cranial neural crest cells and keratinocytes. These findings emphasize genetic components in some cases and support the need for genetic counseling. This is especially true in families with a documented history of ACC or related genetic skin conditions.

In our study, we observed a 33% rate of consanguinity, which suggests a potential genetic predisposition in affected families. This highlights the importance of early genetic counseling in populations with a history of ACC or other genetic skin conditions, ensuring better-informed family planning and management decisions.

The study also examined sixteen ACC cases, revealing key insights into its clinical features, prevalence, and treatment approaches. The high rate of consanguinity in our cohort supported the notion of a genetic link in ACC. This finding aligned with previous studies highlighting the hereditary nature of certain ACC forms, such as those seen in syndromic conditions such as Bart's syndrome.

The clinical presentation of ACC in our cohort was diverse, with lesions mostly found on the upper and lower limbs (50%). The relatively low incidence of scalp

aplasia (12%) in our study was noteworthy, as scalp aplasia is commonly regarded as a key feature of ACC, especially when accompanied by the characteristic hair collar sign.

In contrast to other studies where scalp aplasia is more frequent, the relatively low incidence in our cohort may have reflected geographic or genetic differences [12,13]. In newborns presenting with scalp aplasia, a thorough clinical examination should be conducted as this condition may be linked to other significant malformations, including cranial defects. Previous studies have recommended neuroimaging (e.g., CT or MRI) for cases of scalp aplasia to evaluate potential underlying dysgraphia defects. Although central nervous system dysraphism is uncommon in patients with isolated head ACC, routine imaging may not be required for all individuals. However, certain clinical signs, may suggest a higher risk of associated defects and warrant further evaluation, such as the hair collar sign. Early detection and imaging remain essential to prevent complications and inform appropriate management [14].

Our study also found that insufficient prenatal care (66% of cases) was a significant issue, which emphasizes the need for improved prenatal monitoring, especially in high-risk pregnancies [15,16]. While previous studies have not definitively established a direct connection between prenatal care and the incidence of ACC, early identification of at-risk pregnancies could potentially reduce the impact of intrauterine factors associated with ACC [17,18].

A key practical implication of our findings is the importance of parental education in the management of ACC. In our cohort, patients whose parents were well-educated on proper wound care, dressing techniques,

and follow-up schedules had better outcomes [19]. This supports the idea that parental involvement plays a key role in managing the condition. For instance, in cases of Bart's syndrome and other syndromic forms, pain management, wound care, and prevention of infections are critical. Our study reinforces the need for early and thorough parental education, which should be incorporated into the management plan for all ACC cases. This is consistent with recommendations from other studies that highlight the significance of parental involvement in wound care and ongoing follow-up [20].

Moreover, multidisciplinary collaboration between healthcare providers and parents is essential for successful ACC management. This includes close monitoring of patients during the neonatal period, as ACC lesions may be prone to infection, especially in syndromic cases. Pain management and infection prevention are critical, as superinfections may have severe consequences, including fatal. This insight into the role of collaborative care is in line with findings from other research that recommends a holistic approach to ACC treatment.

In comparing our study to other literature, several observations are noteworthy. The lower incidence of scalp aplasia in our cohort contrasted with studies that report higher rates of scalp involvement. This discrepancy may have reflected the geographic or genetic differences in patient populations. Similarly, our cohort's higher rate of consanguinity (33%) compared to other studies (typically lower) suggested that genetic factors may be more prominent in certain populations [12,13]. These findings underline the need for systematic genetic counseling in areas with high rates of consanguinity, especially in families with a known history of ACC.

The high rate of syndromic associations in our cohort (30%) was consistent with existing literature, where syndromic forms like Bart's syndrome and Adams–Oliver syndrome are observed in ACC patients. As reported in other studies, patients with ACC and underlying syndromes often present with more complex clinical courses, requiring multidisciplinary management. This underscores the importance of early and thorough clinical evaluations, especially in neonates, to detect potential systemic malformations that may complicate treatment.

Future Research

Future research on ACC should focus on understanding the genetic basis of the condition, particularly in syndromic forms such as Bart's syndrome and Adams–Oliver syndrome. Prospective studies are also needed to examine the long-term effects of different treatment approaches (doi.org), along with the influence of early prenatal care and genetic counseling in preventing the development of ACC. Neuroimaging in cases of scalp aplasia must be further investigated to better define its role in early diagnosis and management. Finally, expanding the multidisciplinary approach to include geneticists, dermatologists, pediatricians, and surgeons is crucial to improving patient outcomes.

CONCLUSION

Congenital cutaneous aplasia (CCA) is a rare malformation, often presenting as an isolated anomaly yet sometimes being part of a more complex condition. This study offered valuable insights into its epidemiology, clinical characteristics, and management, aligning with existing literature, while highlighting unique aspects such as the high prevalence of consanguinity and the relatively low incidence of scalp aplasia amongst our patients, which merit further investigation. Given the association of CCA with syndromic conditions, a multidisciplinary approach is essential for the diagnosis and treatment of Bart's syndrome, incorporating genetic counseling and early intervention to prevent complications.

Even if the diagnosis of CCA is typically straightforward, its management remains complex, requiring collaboration between healthcare providers and families. Managing pain and taking preventive measures against superinfections are critical, as these complications may lead to severe, even fatal consequences.

Research should focus on understanding the genetic and environmental factors contributing to births with congenital cutaneous aplasia and improving management strategies, particularly in syndromic cases, to enhance patient outcomes.

Statement of Human and Animal Rights

All the procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 2008 revision of the Declaration of Helsinki of 1975.

Statement of Informed Consent

Informed consent for participation in this study was obtained from all patients.

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