



Bullous *aplasia cutis congenita* – a report of two cases and brief review of the literature

Bulozna kongenitalna aplazija kože – prikaz dva bolesnika i kratak pregled literature

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Abstract

Introduction. *Aplasia cutis congenita* (ACC) is a rare condition characterized by the focal absence of skin, and sometimes other underlying structures at birth. It may occur as an isolated defect or associated with other anomalies and defects. Bullous ACC (BACC) is a clinical subtype of the condition with few cases reported in the literature. It presents as a bullous lesion at birth which gradually transforms into an atrophic scar covered by a thin epithelial membrane. It is considered as cutaneous sign of possible neural tube dysraphism. Some cases present with a dark hair around the lesion (the hair collar sign), which can be even more indicative of neural tube defect. However, cases of BACC reported till today are inconclusive regarding this connection. **Case report.** We report a two cases of BACC of the scalp, in one patient associated with hair collar sign without neural tube defects and the other with hemangioma and we give a brief review of the selected literature. **Conclusion.** Bullous or membranous *aplasia cutis congenita* is benign condition, but may represent as a cutaneous marker of occult neural tube defect. Recognising the condition is important in order to rule out associated anomalies.

Key words:

congenital abnormalities; ectodermal dysplasia; scalp; hypertrichosis; hemangioma.

Apstrakt

Uvod. Kongenitalna aplazija kože je retko oboljenje, koje predstavlja lokalizovan nedostatak kože, a nekada i dublje smeštenih tkiva, prisutan na rođenju. Javlja se kao izolovani poremećaj ili udružen sa drugim anomalijama. Bulozna *aplasia cutis congenita* – ACC (BACC) je klinički podtip kongenitalne aplazije kože o kome ima malo objavljenih slučajeva. Manifestuje se buloznim lezijama prisutnim na rođenju, koje postepeno epitelizuju, uz razvoj atrofičnih, ožiljačnih promena. Smatra se kožnim znakom mogućeg disrafizma nervne cevi. Kod nekih bolesnika se oko lezija može videti pramen kose koji je pigmentovaniji od okolne dlake (znak „ogrlice od dlake”) i može još više upućivati na defekt u razvoju nervne cevi. Međutim, u slučajevima koji su do sada objavljeni, ova povezanost nije sa sigurnošću utvrđena. **Prikaz bolesnika.** Prikazujemo dva slučaja BACC kapilicijuma, jedan udružen sa znakom „ogrlice od dlake” bez defekta nervne cevi i drugi sa hemangiomom, uz kratak pregled izabrane literature. **Zaključak.** Bulozna ili mebranozna kongenitalna aplazija kože je benigno stanje koje može predstavljati kožni znak blagog oblika defekta nervne cevi. Prepoznavanje ovog poremećaja je važno kako bi se dijagnostikovalе moguće udružene anomalije.

Ključne reči:

anomalije; ektodermalna displazija; scalp; hipertrichoza; hemangiom.

Introduction

Aplasia cutis congenita (ACC) is a rare condition characterized by the localized absence of the skin, accompanied sometimes with absence of other underlying structures. It

may be isolated defect, or can be associated with accompanied anomalies of the skin or nervous system as well as genetic diseases or syndromes^{1,2}. Bullous ACC (BACC) is a subtype of ACC. It is present at birth in the form of one or several blisters, or with round areas of eroded skin if blisters

already ruptured during delivery. It is rarely seen by dermatologist in its initial bullous form since it appears at birth. Usually the child with BACC is referred to dermatologists with a flat scar once the bullae have already reabsorbed. In this stage, the condition is known as a membranous *aplasia cutis congenita* (MACC). BACC is considered as one of the cutaneous signs of occult neural tube dysraphism. A ring of dark long hairs encircling a congenital skin lesion is referred as hair collar sign. It represents even more convincing neural tube defect marker, considering that it is often, but not always, associated with encephaloceles, meningoceles, and heterotopic brain tissue³. Certainly, this association imposes mandatory search for possible comorbidities, and its early recognition is important. Diagnosis is based on clinical findings, and histopathological confirmation is rarely needed².

We present two cases of BACC of the scalp. One case was accompanied by hair collar sign, and the other by hemangioma on the lower back.

Case report

Case 1

A 14-days-old male infant presented to our dermatology department with bullous lesions localized on right parietal scalp. The six bullous lesions were oval, lined one after another, ranging from 5–15 mm in size of longest diameter, filled with clear content. Around described skin area, a collar of dense black hairs, which were thicker than surrounding hair, were present (Figure 1). These skin lesions were noticed at birth. There were no underlying skull defects.



Fig.1 – Bullous lesion with a rim of hairs on the right parietal scalp of the neonate (the Case 1).

The infant was born from a non-consanguineous marriage, at term, by spontaneous delivery. There was no history of maternal chicken pox or herpes simplex infection during pregnancy. During pregnancy, his mother was taking beta-blocker (metoprolol) due to gestational hypertension, advised by her obstetrician. Otherwise, the pregnancy was uneventful. The infant was eutrophic, healthy, with neither major nor minor malformations revealed on several physical examinations. Laboratory findings regarding infections, including testing of titer of immunoglobulin M on toxoplasmosis, rubella, cytomegalovirus, and herpes infections, were within normal ranges. Lesion swab was sent for culture and sensitivity, but no pathogens were isolated. Karyotype was normal male. The sonographic exams of brain, abdominal organs and

lumbar and sacral region as well as the ophthalmological exam were unremarkable.

The diagnosis of BACC was set, and local therapy, including gentle cleansing followed by gentamicin ointment, was recommended. The bullous lesions drained spontaneously and a flat atrophic scar was formed during the first few months of life. The infant was followed-up by a dermatologist as well as a neonatologist. At the age of 9 month, all the lesions were of the approximately same size and shape as at birth, but with the residual atrophic scarring instead of bullae. Hair collar sign was still visible. Motor and mental development of the infant was normal.

Case 2

A 7-month-old girl was presented with a four round, slightly erythematous atrophic areas of alopecia, varying in size from 5 to 17 mm in diameter, partially covered with a thin crustose membrane. The lesions were localized at the scalp, near the vertex (Figure 2A).



Fig. 2 – Clinical manifestations of bullous *aplasia cutis congenita* (BACC) in the 2nd presented patient (the Case 2).

A) A round, membranous bald macule, with crustose membrane near the vertex of the scalp; B) Membranous bald macule near the vertex of the scalp and hemangioma on the lower middle part of the back.

Underlying bone was not affected. At the lower middle part of the back, above vertebra, infantile hemangioma was present. It was in a form of irregular rectangle, less than 1 mm above surrounding skin, 35 x 12 mm in size (Figure 2B). At the left gluteus, near the intergluteal cleft, oval pigmented nevus of about 5 mm in diameter was present. The lesions on the scalp were present at birth. They were described as two oval lesions of about 10 mm in size and two of about 3–4 mm. The lesions imposed as areas of bare dermis, with red and moist surface and slightly raised edges. On one of the bigger lesions bulla was still present and the others seemed as if the bullae had already ruptured. Infantile hemangioma appeared at the age of about 2 weeks, and was smaller at first, but enlarged slowly.

The infant was born as the first child from non-consanguineous marriage. Pregnancy as well as the delivery was completely uneventful. At birth, the baby was eutrophic, healthy, with no visible major and minor congenital anomalies. The laboratory findings regarding infections and sonographic exam of the brain and abdominal organs were unremarkable.

Right after birth, on the scalp lesions just mild local antiseptic was applied. At the age of 2 weeks crusts formed and persisted for several months.

At the age of 7 months, when the infant was referred to us for the first time, the crust was still present; we recommended gentamicin ointment for BACC and the local therapy with timolol-maleate 0.5% gel for hemangioma. Two months later scalp lesions were in the form of oval bald areas of atrophic skin, slightly pinkish, with no crust. Hemangioma was of the same size and shape, but almost flat and with initial signs of regression in the middle. The local therapy was regularly applied. Nevus was unchanged.

Discussion

ACC is a heterogeneous group of disorders characterized by the absence of skin in a localized or widespread area at birth. It is a rare condition, with the estimated incidence of 3 in 10,000 births^{1,2}. ACC manifests as a solitary defect of the scalp in 70% of cases, but sometimes it may occur as multiple lesions, or can be found on trunk or extremities. ACC is most often a benign isolated defect, but it can be associated with other physical anomalies or malformation syndromes. It can be accompanied with absence of underlying structures such as bone or dura (20–30% of patients). There are described cases of association with hydrocephaly, linear epidermal nevus, hemangiomas, and multiple defects^{1–5}. BACC or MACC is a clinical subtype of this condition, with extremely few cases reported in the literature, either because of underreporting or due to a rare occurrence^{1,4–7}. The lesions are cystic or bullous at birth which transform over time into an atrophic, flat scar covered by a thin epithelium. Some authors equate the terms “bullous” and “membranous” in the description of this subtype of lesion^{1,3}.

In 1960, O'Brien and Drake⁴ reported 5 patients with BACC on the scalp, of which in one female infant 0.5 cm hemangioma of the left upper arm was also present. In 1993,

Fryburg and Greer⁵ reported an infant with BACC above the back hairline accompanied by extensive unilateral linear epidermal nevus and 2 small hemangiomas on the upper portion of the back. In both cases of BACC accompanied by hemangiomas no other congenital anomalies were found, the same as in our Case 2.

Sometimes BACC is accompanied by a collarette of dark, coarse hair around the skin defect, so called hair collar sign^{3,8,9}. Only few cases of BACC with the hair collar sign have been previously reported^{3,7}. In 1995, Drolet et al.³ reported 6 patients with MACC. Two of the patients had single lesions, the rest had multiple lesions. In all cases a hair collar sign was present. Imaging studies failed to identify intracranial anomalies. Of the 6 reported patients, the bone defects and the associated findings (port-wine stain, meningeal arteriovenous fistula and corneal change) were diagnosed in 3. These patients were not reported to have any other major abnormal physical findings. In 2005, Fujita et al.⁷ reported two cases of MACC surrounded by a rim of hairs, one case associated with dense dermal melanocytosis and the other with *naevus flammeus*, but no other anomalies or defects. The present Case 1 of BACC and hair collar sign was without neural tube defects and associated malformations, as well.

Drolet et al.³ proposed that MACC is a form fruste of a neural tube defect. The patients had a hair collar sign that is regarded as a relatively specific marker for cranial neural tube closure defects. In 2003, Colon-Fontanez et al.¹ presented a new case of BACC and summarize the clinical and histologic findings of the 16 cases reported previously. Some, but not all of the cases were presented with a hair collar sign, too. The histological appearance was similar in all patients evaluated, a distinct pattern containing fibrovascular stromas, edematous stroma, or both. The identical histologic findings can be found in encephaloceles and meningoceles. Finally, the membranous posterior cranial closure sites in the neural tube defects resemble the findings in MACC. This supports a hypothesis that BACC may represent the forme fruste of a neural tube closure defect^{1,10}.

The etiology of ACC is unknown. It is probably a combination of genetic factors, maternal medications, compromised vasculature to the skin, infection, and intrauterine trauma^{2,11,12}. The configuration, distribution, and clinical appearance of BACC would suggest incomplete closure of embryonic fusion lines, rather than vascular interruption or trauma to the skin¹³. Most reports of BCC are sporadic, however because some forms of ACC are inherited, genetic counseling of the family regarding the risk of recurrence is recommended². In all patients with ACC, a complete obstetric and family history should be obtained. History should include a review of maternal medications (eg, methimazole, carbimazole, misoprostol, valproic acid) and infections such as varicella or herpes simplex viruses during the pregnancy^{2,12,14}. Metta et al.¹⁵ reported BACC in an infant with HIV association. ACC was described in infants exposed *in utero* to antithyroid drugs and valproic acid, but it was not related to metoprolol^{12,14}. BACC and metoprolol intake during pregnancy in our Case 1 may be a random association and similar observations are needed to suggest causality.

The differential diagnosis of bullae present at birth should include infections and hereditary disorders with increased skin fragility¹⁶. Key toward the BACC diagnosis is existence of lesions at the very birth, on a limited, localized area of the skin, good general health of the newborn and excluding laboratory findings. But possibility of accompanied congenital anomalies must be ruled out.

The course of BACC depends to some degree on the size of the defect. The lesion almost always heals spontaneously, assuming that underlying structures are not affected. If the defect is small, which is most often the case, recovery is uneventful, with gradual epithelialization and formation of a hairless, atrophic scar over several weeks. Management remains controversial, guided by location, size, and depth of the defect. Because of frequent coloniza-

tion and possible superinfection of existing bullae and erosions, conservative treatment is chosen (silver sulfadiazine, antibiotic ointments or petrolatum) in most of the cases. Larger defects that extend into the dura or cover large skin area, need early surgery^{17,18}.

Conclusion

BACC is an extremely rare or much underreported type of ACC, of still unclear etiology. It can rarely manifest as multiple bullous lesions on the scalp, as in our patients. Many reports of BACC have no other associated anomalies as in our presented cases. But literature data of accompanied anomalies and syndromes imposes the obligation to rule out such a possibility in every single case of BACC.

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