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“BULOZNA KONGENITALNA APLAZIJA KOŽE- PRIKAZ DVA BOLESNIKA I KRATAK PREGLED IZABRANE LITERATURE“


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“BULLOUS APLASIA CUTIS CONGENITA – A REPORT OF TWO CASES AND BRIEF REVIEW OF THE SELECTED LITERATURE“

“Bulozna kongenitalna aplazija kože- prikaz dva bolesnika i kratak pregled izabrane literature“

Type of article: case report

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Running title: Bullous Aplasia Cutis Congenita

Kratak naslov: Bulozna kongenitalna aplazija kože
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 aplasia cutis congenita (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 two cases of BACC of the scalp, one case associated with hair collar sign without neural tube defects and the other with hemangioma, and give a brief review of the selected literature. Conclusion: Bullous or membranous aplasia cutis congenita is a 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. Keywords: aplasia cutis, neural tube defect, localized hypertrichosis

Sažetak

Uvod: Kongenitalna aplazija kože (ACC) je retko oboljenje, koje predstavlja lokalizovan nedostatak kože, a nekada i dublje smeštenih tkiva, prisutan na rođenju. Javlja se kao izolovan poremećaj ili udružen sa drugim anomalijama. Bulozna kongenitalna aplazija kože (BACC) je klinički podtip sa malim brojem 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 je oko lezija BACC 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 dijagnostikovale moguće udružene anomalije.

**Ključne reči:** aplazija kože, defekt nervne cevi, lokalizovana hipertrihoza

**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. Bullous aplasia cutis congenita (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, as it appears at birth. Usually the child with BACC refers at dermatologists with a flat scar once the bullae have already reabsorbed. In this stage, the condition is known as membranous aplasia cutis (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 tissue. Certainly, this association imposes mandatory search for possible comorbidities, and its early recognition is important. Diagnosis is based on clinical findings, and pathohistological confirmation is rarely needed.

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 (Fig. 1). These skin lesions were noticed at birth. There were no underlying skull defects. 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 TORCH infections, were within normal ranges. Lesion swab was sent for culture and sensitivity, but no pathogens were isolated. Karyotype was normal male. Sonographic exams of brain, abdominal organs and lumbar and sacral region, as well as ophthalmological exam were unremarkable. The diagnosis of BACC was set, and local therapy including gentle cleansing followed by gentamicin ointment was recommended. Bullous lesions drained spontaneously and flat atrophic scar was formed during the first few months of life. The infant was followed-up by dermatologist as well as 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 scaring instead of bullae. Hair color 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 thin crustose membrane. The lesions were localized at the scalp, near the vertex (Fig. 2). 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 (Fig. 3). 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
10mm in size and two of about 3-4 mm. The lesions imposed as areas of bare dermis, with red and moist surface, and with slightly raised edges. On one of the bigger lesions bulla was still present, and the others seemed as if the bullae have 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. 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 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 heterogenous 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. 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. 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. 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 Drake 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 \(^4\). In 1993, Fryburg and Greer 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 \(^5\). 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. 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 reported 6 patients, in 3 bone defects and associated findings (portwine stain, meningeal arteriovenous fistula and corneal change) were diagnosed. These patients were not reported to have any other major abnormal physical findings \(^3\). In 2005, Fujita at al. 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 \(^7\). The present Case 1 of BACC and hair collar sign was without neural tube defects and associated malformations, as well.

Drolet et al. have 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 \(^3\). In 2003 Fontanez et al. presented a new case BACC, and summarize the clinical and histologic findings of the 16 cases previously reported. Some, but not all of the cases were presented with a hair collar sign, too. Histological appearance has been similar in all patients evaluated, a distinct pattern containing fibrovascular stromas, edematous stroma, or both. Identical histologic findings can be found in encephaloceles and meningoceles. Finally, membranous posterior cranial closure sites in 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 skin. 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 recommended. 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. Metta et al. reported the of BACC in an infant with HIV association. ACC has been described in infants exposed in utero to antithyroid drugs and valproic acid, but has not been related to metoprolol. BACC and metoprolol intake during pregnancy in our Case 1 may be a random association, and similar observations are needed to suggest causality.

Differential diagnosis of bullae present at birth should include infections and hereditary disorders with increased skin fragility. Key toward BACC diagnosis are presens 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 colonization 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.

In conclusion, BACC is an extremely rare or much under-reported type of ACCC, of still unclear etiology. Rarely can it manifest as multiple bullous lesions on the scalp, as in our patients. It is hypothesized to be a form fruste of a neural tube dysraphism. Some cases present with a dark hair collar sign, which is considered to be even more indicative of an underlying neural tube defect. Many reports of BACC have no other associated anomalies, as well 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.
REFERENCES:


Fig.1 Bullous lesion with a rim of hairs on the right parietal scalp of the neonate
Fig. 2 A round, membranous bald macule, with crustose membrane on the vertex
Fig. 3 Membranous bald macule on the near the vertex and haemangioma on the lower middle part of the back

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