Extremely Low Birth Weight Infant Born with Extensive Abdominal Cutis Aplasia

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Aplasia cutis congenita (ACC) is a condition characterized by congenital absence of the skin that may involve all layers of the skin, adnexal structures and underlying bone. The pathogenesis is currently unknown but several theories have been suggested, including hypotension, thrombosis, trauma, infection, and exposure to teratogens. Most cases are sporadic, but cases with family association have been described. There are currently at least 500 cases reported in the literature and about 85% of these include solitary lesions of the scalp, although any other area of the body may be involved. For clinical practice, Frieden’s classification – which is based on the distribution of the lesion(s), associated anomalies, infections or syndromes – is currently used [1]. Type-V ACC in Friedman’s classification is associated with the loss of a monochorionic twin during the late first to early second trimester, otherwise known as fetus papyraceus (FP). At least 44 cases of ACC and FP have been reported and recently summarized in two reviews [2,3] detailing the distinctive bilateral symmetrical lesions over the trunk, buttocks and/or extremities. Almost all the cases describe full- or near-term neonates.

We report here a case of type V ACC in a premature extremely low birth weight infant and highlight some of the unique features of the clinical course and treatment considerations, leading to abdominal skin recovery and his discharge from the neonatal intensive care unit (NICU) without major morbidity.

PATIENT DESCRIPTION

Intrauterine insemination resulted in a monochorionic di-amniotic twin pregnancy in a 26 year old primipara healthy mother. After 12 weeks of gestation spontaneous intrauterine demise of one of the twins was diagnosed. At 28 weeks gestation she was hospitalized due to suspected intrauterine growth retardation and underwent cesarean section at 29+0 weeks gestation for non-reassuring fetal heart rate monitoring. A male infant weighing 720 g was born. Placental pathology revealed a 3.5 g fetus mummified in one placenta, and a focus of extensive avascular villi, suggestive of fetal thrombotic vasculopathy, in the other placenta. Apgar scores of the surviving infant were 6 and 8 at 1 and 5 minutes, respectively. In the delivery room he required respiratory support with continuous positive airway pressure and was transferred to the neonatal intensive care unit (NICU). Physical examination revealed bilateral skin absence of the abdomen from below the thorax to the groins demarcated in a butterfly shape [Figure 1A and B]. The tissue over the abdomen was transparent and most probably increased abdominal pressure that precipitated the development of large bilateral inguinal hernia sacs containing a large amount of intestine [Figure 1E and G]. In order to prevent even higher...
abdominal pressure due to constipation, he was treated with lactulose to soften feces. At 4.5 months he underwent successful bilateral inguinal hernia repair with reduction of small intestine, cecum and appendix from the hernia sacs. This was followed by a second laparotomy due to intussusception and bowel obstruction that resulted in partial small bowel resection. Pathology workup revealed necrotic small intestine. During his hospitalization he was treated once for sepsis due to *Klebsiella pneumoniae* after the abdominal surgery.

Nutritional management included administration of hyper-alimentation immediately after birth with maximal protein (4 g/kg/day) and lipid (4 g/kg/day) intake, resulting in a gradual increase in his enteral nutrition. He reached full enteral nutrition at the age of 11 days, which enabled the removal of all intravenous lines that might increase the risk of infection in such an infant.

The infant’s head ultrasound imaging following birth, during hospitalization and before discharge was normal, as was his neurologic assessment before discharge. Ophthalmic follow-up revealed retinopathy of prematurity at stage 1-2 in both eyes, requiring no intervention. He was discharged at the age of 5 months with no need for medications, weighing 3.37 kg at the corrected age of 49+2 weeks (below the 3rd percentile). At his last follow-up visit at the age of 11 months his developmental milestones were satisfying for his 8 months corrected age.

### Comment

Most cases of aplasia cutis congenita with fetus papyraceus can be treated with simple non-adherent dressings and topical preparations. The prognosis is usually excellent with wound epithelialization and resolution [2,3]. In severe cases, surgical intervention may be needed; however, no major complications have been reported in term or near-term babies. ACC with FP has been reported previously in low birth weight newborns; one required a few days of ventilatory support and in both cases the
skin healed spontaneously [4,5]. To the best of our knowledge this report describes the smallest newborn with ACC and the first with extremely low birth weight. The main therapeutic challenges in this case included fluid management to overcome the risk of dehydration and electrolyte abnormalities in such a small infant, respiratory issues for his prematurity and the unique structure of his chest and abdomen, prevention of infections for the large area with absence of skin surface barrier, local treatment to enhance skin growth, optimal nutrition management to achieve overall optimal growth, and the reduced abdominal wall space, leading to volume depletion and hypotension resulting in ischemia of the skin in presumed vascular border zones. In this particular case, evidence of thrombosis was found in the surviving twin placenta, which could be related to passage of thrombogenic material to the viable twin. There was no other evidence in this case supporting a different etiology such as teratogenic exposure, infection or trauma.

In this era of modern reproductive medicine, with increasing incidence of multiple gestation pregnancies, the importance of fetus papyraceous is probably underappreciated and may be diagnosed in very or extremely low birth weight infants. This case demonstrates that under current advanced neonatal management and multidisciplinary care, successful treatment of extremely low birth weight infants with ACC is possible.

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**References**


**Pharmacological chaperone for α-crystallin partially restores transparency in cataract models**

Cataracts reduce vision in 50% of individuals over 70 years of age and are a common form of blindness worldwide. Cataracts are caused when damage to the major lens crystallin proteins causes their misfolding and aggregation into insoluble amyloids. Using a thermal stability assay, Makley et al. identified a class of molecules that bind α-crystallins (cryAA and cryAB) and reversed their aggregation in vitro. The most promising compound improved lens transparency in the R48C cryAA and R120G cryAB mouse models of hereditary cataract. It also partially restored protein solubility in the lenses of aged mice in vivo and in human lenses ex vivo. These findings suggest an approach to treating cataracts by stabilizing α-crystallins.

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**The genetic evolution of melanoma from precursor lesions**

The pathogenic mutations in melanoma have been largely catalogued; however, the order of their occurrence is not known. Shain and co-authors sequenced 293 cancer-relevant genes in 150 areas of 37 primary melanomas and their adjacent precursor lesions. The histopathologic spectrum of these areas included unequivocally benign lesions, intermediate lesions, and intraepidermal or invasive melanomas. Precursor lesions were initiated by mutations of genes known to activate the mitogen-activated protein kinase pathway. Unequivocally benign lesions harbored BRAF V600E mutations exclusively, whereas those categorized as intermediate were enriched for NRAS mutations and additional driver mutations. A total of 77% of areas of intermediate lesions and melanomas in situ harbored TERT-promoter mutations, a finding that indicates that these mutations are selected at an unexpectedly early stage of the neoplastic progression. Biallelic inactivation of CDKN2A emerged exclusively in invasive melanomas. PTEN and TP53 mutations were found only in advanced primary melanomas. The point-mutation burden increased from benign through intermediate lesions to melanoma, with a strong signature of the effects of ultraviolet radiation detectable at all evolutionary stages. Copy-number alterations became prevalent only in invasive melanomas. Tumor heterogeneity became apparent in the form of genetically distinct subpopulations as melanomas progressed.

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