

Amnion membrane allografts in a critically ill infant with Netherton syndrome–like phenotype



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Key words: amnion membranes; ichthyosiform erythroderma; Netherton syndrome; skin care; wound care.

INTRODUCTION

Netherton syndrome (NS) is a triad of nonbullous congenital ichthyosiform erythroderma, typical hair dysplasia, and severe atopic features.¹ The incidence is 1 in 50,000 births, with 18% of all congenital erythrodermas attributed to NS. The skin is noted to be abnormal at birth or within the first month of life. Complications include thermoregulatory problems, electrolyte imbalances, hypernatremic dehydration, recurrent or severe infections, and failure to thrive. Skin hygiene represents a challenge in critically ill and unstable patients. This report describes a novel approach to skin management in NS.

CASE REPORT

A male infant was born at 35 weeks and 1 day gestation with erythroderma and respiratory insufficiency requiring respiratory support. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. A skin examination at birth revealed sparse hair on the scalp and erythroderma with areas of desquamation on all limbs, although there were no erosions or ulcerations. This presentation was later thought to be consistent with NS based on the clinical appearance, findings of trichorrhexis invaginata, and genetic testing that revealed a chromosome 5 deletion resulting in monosomy for *SPINK5*.¹ The second copy of *SPINK5* was normal, raising the possibility of a Netherton-like syndrome. Cardiology workup revealed pulmonary valve and left pulmonary artery (LPA) stenosis.

The patient had failure to thrive and multiple infections, including Cytomegalovirus resulting in hearing loss, Respiratory Syncytial Virus, coagulase-negative *Staphylococcus* bacteremia, *Pseudomonas* pneumonia, and multiple urinary tract infections over the first few months of life. He underwent an attempted balloon valvuloplasty and LPA dilation at 3 months of age followed by a pulmonary valvotomy and LPA angioplasty at 5 months. The postoperative period was complicated by worsening pulmonary hypertension and severe bronchopulmonary dysplasia with cardiopulmonary instability and ventilator dependence. Minimal manipulation of the patient, including skin cleansing and application of topical steroids under occlusion, triggered bronchospasm. Within a 20-day period, the patient survived 5 cardiorespiratory arrests. The inability to perform regular skin care and dressing changes led to the use of an amnion membrane allograft (AMA) to keep his skin moist and protected without requiring daily wound care.

AMA application and skin management

AMA is obtained from donated placental tissue at the University of Utah.² The allografts are collected and processed at delivery as either dry or wet allografts and are then released for clinical use.³ AMA was applied to the patient's cleansed and dried skin on the scalp, anterior and posterior trunk, and all extremities. Next, petrolatum-impregnated nonstick silver hydrogel gauze dressing

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Conflicts of interest: None disclosed.

Reprints not available from the author(s).

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JAAD Case Reports 2019;5:395-7.

2352-5126

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<https://doi.org/10.1016/j.jidcr.2019.02.011>



Fig 1. **A**, Erythrodermic newborn. **B**, Several months later, on the day of amnion membrane allograft placement, erythroderma had not significantly improved. **C**, Marked improvement of the patient's erythroderma was noted 5 days after the amnion membrane transplant.

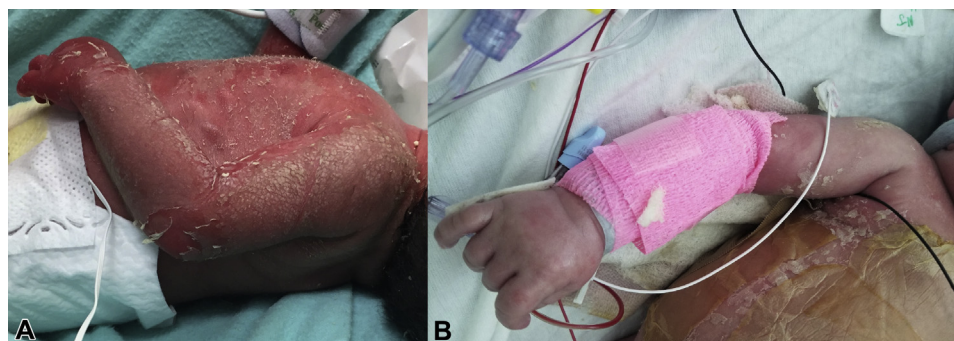


Fig 2. **A**, Upper extremities in the newborn period and **(B)** 5 days post—amnion membrane allograft placement. A dramatic improvement in the erythema and scaling of the patient's skin was obtained without the need for daily wound care.

was applied over the AMA followed by a single layer of Kerlix gauze and elastic bandages. The dressing was initially kept in place for 5 days (to prevent AMA shear) with subsequent dressing changes every 2 days. On day 5, nonadherent AMA was replaced with a new AMA. Additional skin management included the regular application of petrolatum ointment on all uncovered areas. Any areas of localized trauma were treated with continued liberal petrolatum application and avoidance of application of devices and sensors. Application of any other topical agent was limited because percutaneous absorption is dramatically increased in these patients.

Post-AMA application observations

The patient completed a cycle of AMA application for 18 days with decreased erythema and reduction

in new ulcerations where the AMA was applied (Figs 1 and 2). In contrast, areas that were not amenable to AMA application showed persistent erythema and device-related ulcers. AMA acted as a skin barrier by restoring the integrity of the skin surface. Despite the improvement in his dermatologic condition, persistent pulmonary disease eventually led to his death.

DISCUSSION

NS is a rare autosomal recessive disorder that is characterized by a triad of congenital ichthyosiform erythroderma or ichthyosis linearis circumflexa, hair shaft abnormalities, and atopic diathesis with elevated serum levels of immunoglobulin E. This results from an abnormality in the protease lymphoepithelial Kazal type inhibitor protein, which

leads to dysregulation of epidermal proteases and severe skin barrier defects. Like burn patients, these patients lose proteins and electrolytes through their skin and have an increased risk for infections and metabolic dyscrasias. There is no cure or satisfactory treatment currently available for NS. Daily skin care is necessary to maintain skin barrier function and prevent infection. Therapeutic options include topical glucocorticoids and retinoids, oral retinoids, and narrowband ultraviolet B light phototherapy.^{4,5} Topical tacrolimus has been shown to be efficacious and may be used safely with careful laboratory monitoring.⁶ The use of topical medications is limited by the potential for systemic absorption and toxicity in the setting of a defective skin barrier.

Since the 1900s, AMAs have supported patients with burn injuries and other soft tissue defects. AMA is an immune-privileged product and exhibits little to no side effects, making it an ideal biologic dressing. Theoretically, AMA cells also support the wound through the addition of growth hormones and cell signaling substrates from the graft.⁷ AMA may play a key role in patients with fragile skin, such as the patient discussed herein. Skin fragility is not a typical feature of NS; however, this infant had severe skin fragility, especially at areas of shear related to critical care equipment and monitors. AMA was a valid alternative to daily skin care in the presented case to skin manipulation and subsequent inflammation. Successful use of AMA has also been reported for other pediatric skin conditions, including chronic nonhealing ulcers of recessive dystrophic epidermolysis bullosa^{8,9} and ulcerated infantile

hemangioma.¹⁰ AMA should be considered a valuable tool when dealing with similar patients as the case presented.

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