

# Treatment of an ulcerated hemangioma with dehydrated human amnion/chorion membrane allograft



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**Key words:** pediatrics and neonatology; therapy and treatment; ulcers of the skin; vascular malformations and hemangioma; wound healing.

## CASE REPORT

We report the case of a 10-month-old girl with a large segmental “beard-distributed” infantile hemangioma (IH) with recalcitrant ulceration, successfully treated with dehydrated Human Amnion/Chorion Membrane allograft (dHACM, EpiFix; MiMedx Group, Marietta, GA). The patient initially presented at 10 days of life with respiratory distress and was noted to have a segmental IH of the lower face and neck. Endoscopy confirmed involvement of the upper airway. Findings from a PHACE (posterior fossa malformations, hemangiomas, arterial anomalies, cardiac defects, eye abnormalities, sternal cleft, and supraumbilical raphe) workup were normal. She was started on 0.5 mg/kg/d of propranolol, which was increased to 2 mg/kg/d over 48 hours. She was discharged home on a dose of 2 mg/kg/d, and the hemangioma proliferation appeared halted. However, despite continued therapy, she developed devastating ulceration and tissue destruction of the bilateral ears and lower lip 1 week after discharge. Her subsequent course was marked by severe, painful and recalcitrant ulceration.

Multiple treatments were initiated to heal her ulcers, including propranolol (1-3 mg/kg/d), prednisone (1 mg/kg/d) in conjunction with low-dose propranolol (1 mg/kg/d), and trials of topical silvane, over-the-counter zinc oxide, compounded zinc oxide 25% paste, becaplermin, collagen matrix dressing covered with Nu-derm (hydrocolloid

### Abbreviations used:

dHACM:	dehydrated human amnion/chorion membrane allograft
IH:	infantile hemangioma
PDGF:	platelet-derived growth factor

dressing), and Leptospermum honey. Her ulcers were frequently superinfected, and she was treated with systemic antibiotics for positive culture results. The patient also underwent 2 trials of VBEAM laser therapy (4 pulses each) 1 week apart at 8 months of age with laser settings of fluence of 8.5 J/cm<sup>2</sup>, pulse duration of 1.5 msec, and spot size of 7 mm.

Despite interventions, she continued to have a large recalcitrant ulcer on the lower chin for 5 months (Fig 1), and a decision was made to begin EpiFix to the ulcerated portion of the hemangioma. Micronized EpiFix was placed into the wound bed on her chin at 1-week intervals for 3 weeks starting at age 8 months and covered with Xeroform gauze and duoderm. She was concurrently treated with propranolol, 2.5 mg/kg/d, and was tapering off prednisone over that time. Two weeks after her third grafting, the ulcer had healed completely (Fig 2).

## DISCUSSION

Secondary ulceration is the most common complication of IHs, with frequency between 10% and

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This case was presented at the World Congress of Pediatric Dermatology meeting in 2017 as part of a series of patients with severe ulceration of infantile hemangiomas. Treatment with EpiFix was not discussed. A summary of this work has been submitted in the form of an abstract to the International Society for the Study of Vascular Anomalies (ISSVA) Conference in 2018.

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**Fig 1.** Before treatment.

30%.<sup>1</sup> Adverse outcomes associated with ulceration include pain, irritability, poor feeding and sleeping, infection, scarring, and deformity of adjacent structures.<sup>1</sup> There is no uniformly effective modality for the treatment of ulcerated IHs.<sup>2</sup> Multiple treatments are often used simultaneously and include propranolol, timolol, barrier creams, antibiotics, and pulsed-dye laser.<sup>1</sup> Although our patient underwent 2 VBEAM procedures, treatments were limited to small test spots to assess tolerability. The authors, therefore, do not feel that these procedures would be considered therapeutic.

EpiFix is a nonviable cellular amniotic membrane allograft that contains several growth factors, cytokines, and extracellular matrix proteins present in amniotic tissue. In addition to containing platelet-derived growth factor (PDGF), more than 50 growth factors, cytokines, and chemokines have been identified in dHACM tissues.<sup>3</sup> EpiFix contains quantifiable levels of PDGF promoting cell proliferation in connective tissue, epidermal growth factor promoting proliferation of epithelial cells, transforming growth factor promoting normal wound healing, and fibroblast growth factor promoting cellular proliferation.<sup>4</sup> It is thought to enhance healing, modulate inflammation, upregulate angiogenesis, and



**Fig 2.** After treatment.

reduce scar tissue formation. EpiFix has been found to promote revascularization and tissue healing within poorly vascularized, nonhealing wounds and is effective in the treatment of diabetic foot ulcers and venous ulcers.<sup>3,5</sup> Although the precise mechanism of hemangioma ulceration is not well understood, it is hypothesized that rapid expansion of the tumor causes it to outgrow its blood supply.<sup>6</sup> We postulate that the growth factors supplied directly to the wound bed by EpiFix promoted the healing of our patients' ulcer by upregulating angiogenesis and creating an environment conducive to tissue repair.

Of note, becaplermin gel (Regranex) is a PDGF therapy that is approved by the US Food and Drug Administration for diabetic neuropathic ulcers and has been used to effectively treat ulcerated IHs.<sup>7</sup> However, an increased rate of mortality secondary to malignancy was observed in patients treated with 3 or more tubes of Regranex gel in a postmarketing retrospective cohort study, and its safety in pediatric patients younger than 16 years has not been established.<sup>7</sup>

It is not entirely clear through which mechanism EpiFix promoted healing of the ulcer without also causing further proliferation of the hemangioma. It has been suggested that the granulation tissue promoted by Regranex arises through a different angiogenic pathway than the hemangioma itself, which could hold true for EpiFix as well.<sup>8</sup>

Early treatment of ulcerated IHs is vital in minimizing ulcer progression, infection, and scarring. Our case illustrates that dHACM may be a useful alternative in the treatment of IHs with recalcitrant ulceration.

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