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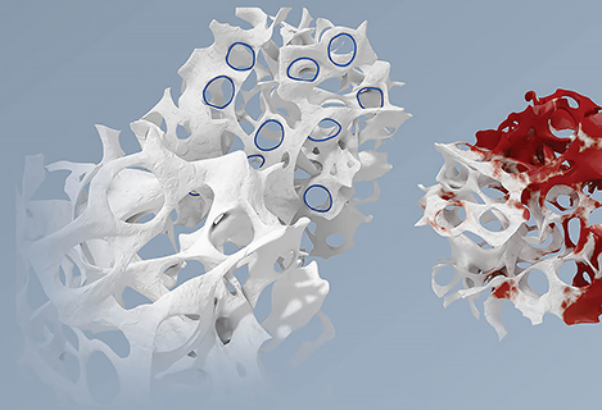
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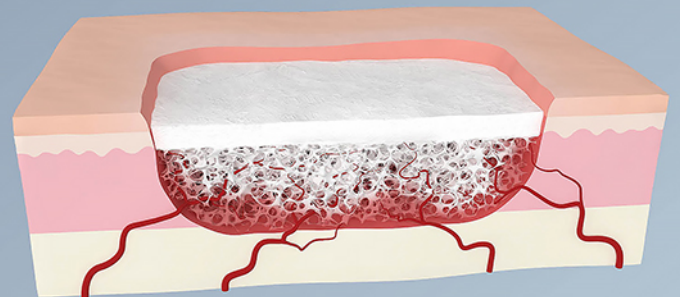
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LETTER TO THE EDITOR

Skin necrosis after filler-associated vascular compromise: successful treatment with topical epidermal growth factor

Dear Editors,

Vascular compromise that leads to skin necrosis is one of the most concerning complications of filler injection. It is usually caused by direct vascular injury, perivascular compression by excessive filler volume or intravascular obstruction because of the filler material itself. Filler-induced necrotic wounds are difficult to treat and are likely to leave a permanent scar. Affected patients might experience depression as a result of the opposite outcome of what was expected after cosmetic soft tissue augmentation. In this study, we report the effects of topical epidermal growth factor (EGF) solution on wound healing in a case of filler-induced facial skin necrosis.

A 42-year-old female presented with a diffuse dusky red painful patch on the right nasolabial fold, cheek and nasal dorsum (Figure 1). She had received a hyaluronic acid (HA) filler injection in both nasolabial folds the day before presentation. Hyaluronidase was injected immediately into the lesional site to resolve and disperse the HA filler materials. Sublingual nitroglycerin and low-dose aspirin were also prescribed to increase lesional blood flow and to prevent further clot formation, respectively. A wet dressing was applied twice daily until no newly developed pustules were observed at day 5. Then, we applied topical recombinant human epithelial growth factor solution (EASYEF 0.005%, Daewoong Pharmaceutical Co., Ltd., Seoul, Korea) to the occlusive wet dressing applied to the necrotic ulcer once daily for 2 weeks. The wound showed gradual reepithelisation and was completely resolved after 4 weeks, leaving no residual scarring (Figure 2).

EGF has been administered to enhance the healing process in various kinds of wounds. EGF is known to promote

chemotaxis, cytoprotection and mitogenesis during tissue repair (1). EGF plays a role as a direct mitogen for endothelial cells and dermal fibroblasts, which in turn accelerate reepithelisation and increase proliferation and tensile strength of the dermis. Studies with partial thickness burn wounds treated with topical EGF have revealed that the topical application of growth factors significantly reduces healing time compared to standard wound care alone (2). These healing events, especially for acute wounds like in this case, are an integrated result of the following: (i) stimulation of cellular migration towards the injured area; (ii) granulation tissue outgrowth, including extracellular matrix accumulation and angiogenesis; (iii) wound contraction by activating myofibroblasts; and (iv) resurfacing by stimulating migration and proliferation of epithelial cells (3,4).

The topical application of EGF solution is well tolerated by most patients, and the drug is able to bypass the primary metabolism or digestion through the gastrointestinal tract, avoiding unwanted potential systemic effects. However, the efficacy of EGF products may be limited by their transdermal delivery. Because of the large molecular size and hydrophilic nature of EGF, its transdermal permeation and further distribution into the stem cell layer can be critically inhibited (5). Therefore, further studies are necessary to maximise the therapeutic potential of this topical wound-healing drug.

There are no previously reported cases of applying topical growth factor agents to a filler-induced necrotic wound. The present results suggest that topical EGF therapy could be an effective add-on treatment to standard wound care for filler-associated necrosis, although high-quality, large-scale trials are needed to confirm the conclusion.



Figure 1 Dusky red painful patch and pustules on the right nasolabial fold, cheek and nasal dorsum of the patient at presentation.



Figure 2 After 4 weeks, the wound showed complete resolution, with no residual scar.

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