

Anaphylaxis Associated With Topical Application of 5-Aminolevulinic Acid

5-Aminolevulinic acid (ALA) is a topically applied medication used in the treatment of actinic keratoses (AKs) by photodynamic therapy (PDT). Photodynamic therapy using ALA is often the preferred treatment for AK because of its efficacy, safety, and tolerability.¹ However, a severe anaphylactic reaction to ALA was observed in the case described in this article. The therapeutic parameters of PDT using ALA, including the preillumination incubation time, light source, and photoactivation time, have been extensively studied and optimized over the past 2 decades that this technique has been used for the treatment of cutaneous actinic damage.² Nonetheless, as with any medical intervention, side effects, some of which can be life threatening, must always remain a consideration. We describe the first published instance of an anaphylaxis reaction caused by the topical application of ALA.

An 85-year-old man with a medical history of non-melanoma skin cancer, blistering sunburns, eczema, hypercholesterolemia, and type 2 diabetes, with no known drug allergies, presented to the clinic for treatment of AKs on the scalp, face, ears, and nose. He was treated with blue-light PDT, which included a topical application of ALA.

Soon after leaving the clinic, the patient began to develop a new rash along with severe itching and difficulty breathing. The patient returned to the clinic, where he disclosed that he had taken 2 diphenhydramine 25 mg tablets after noticing the rash and trouble breathing. He also reported having been given hylan G-F 20 injections to his knee earlier the same day, by his orthopedic surgeon, with no associated reaction. The patient reports having received hylan G-F 20 injections to his knee several times before and after this event, without experiencing other episodes of anaphylaxis. To date, no cases of anaphylaxis from hylan G-F 20 injections have been published.

On physical examination, angioedema and erythematous evanescent edematous plaques were distributed on the head, neck, and trunk, which were consistent with acute urticaria (Figure 1A, B). The patient was immediately transported to the emergency department in an ambulance, where he was given supplemental oxygen by mask. His vitals remained stable. Paramedics gave nebulizer treatment, epinephrine, and steroids

intravenously. Once in the hospital, the patient was awake, alert, and breathing on his own but was admitted for observation. The acute anaphylactic reaction resolved after treatment.

Discussion

AK is one of the most common dermatologic conditions in the United States, with an estimated 40 million cases per year. There are several available therapies for treating AK,^{3,4} among which PDT with ALA is often preferred because it is well tolerated and provides the best cosmetic results.⁵

The mechanism of action of ALA is well understood. In keratinocytes, it is converted to protoporphyrin IX (PpIX) through enzymes of the heme pathway. Protoporphyrin IX is a potent photosensitizer that can be activated by exposure to blue or red light. Once activated, PpIX generates active oxygen species that damage the cell membranes and kill the targeted AK cells. Topically applied ALA is not photoactive and must first be converted to PpIX by proliferating cells to elicit the therapeutic effect. During clinical trials, burning, itching, temporary erythema, and temporary edema were noted during the administration of PDT, but only in the targeted areas.¹

Because of the severity of the symptoms, which included breathing difficulties, as well as the widespread nature of the urticaria and the fact that symptoms ceased after cessation of the PDT treatment, we believe that this was an episode of anaphylaxis. The patient was advised to avoid similar treatments in the future, and ALA was added to his allergy list. Practitioners should be aware of the possibility of developing an anaphylactic reaction after PDT treatment with ALA, and patients should be counseled on the actions they should take if such symptoms develop.

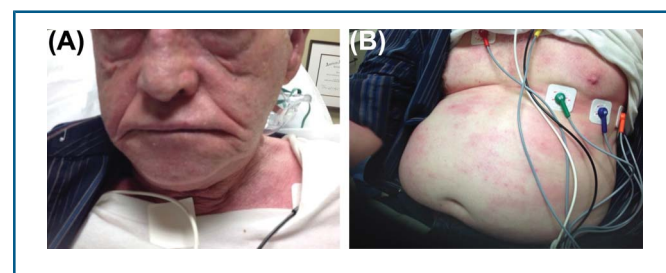


Figure 1. (A) Angioedema of the face. (B) Urticaria of the abdomen.

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