Cutaneous Id Reaction After Using Cyanoacrylate for Wound Closure

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PRACTICE **POINTS**

- 2-Octyl-cyanoacrylate (2-CA) tissue adhesive has been reported to cause contact dermatitis when applied topically for surgical site closure.
- Id reactions resulting from the use of 2-CA tissue adhesive are possible, though less commonly observed.
- Id reactions caused by 2-CA tissue adhesive respond well to treatment with a combination of topical steroids and oral antihistamines. Systemic corticosteroids may be warranted in cases involving greater than 20% body surface area.

To the Editor:

In 1998, 2-octyl-cyanoacrylate (2-CA) tissue adhesive gained US Food and Drug Administration approval for topical application to easily hold closed approximated skin edges from surgical excisions and simple trauma-induced lacerations.[1] It has since been employed for a number of off-label indications, including sutureless circumcision,[2] skin graft fixation,[3] pericatheter leakage,[4] and intracorporeal use to control air leaks during lung resection.[5] Animal investigations additionally have attempted to elucidate potential future uses of 2-CA for procedures such as inguinal hernia repair,[6] bowel anastomosis,[7] incisional hernia repair with mesh,[8] and microvascular anastomosis.[9] Compared to sutures, 2-CA offers ease and rapidity of application, a water-resistant barrier, and equivalent cosmetic results, as well as eliminates the need for suture removal.[10] As 2-CA is used with increasing frequency across a variety of settings, there arises a greater need to be mindful of the potential complications of its use, such as irritant contact dermatitis (ICD), allergic contact dermatitis (ACD), and cutaneous id reaction.

A 14-year-old adolescent boy with no notable medical history and no known allergies underwent a minimally invasive Nuss procedure[11] (performed by P.L.G.) for the repair of severe pectus excavatum. Two 4-cm incisions were made—one in each lateral chest wall at the approximately eighth intercostal space—to facilitate the introduction of the Nuss bar. The surgical wounds were closed with 2 layers of running polyglactin 910 suture before 2-CA was applied topically to the incision sites. The surgery was well tolerated, and the patient's wounds healed without incident. When the patient was evaluated for Nuss bar removal 3 years later, incision sites were noted to be well healed, and he exhibited no other skin lesions. The original incision sites (bilateral chest walls) were utilized to facilitate surgical Nuss bar removal. The wounds were closed in 4 layers and 2-CA was again applied topically to the incision sites. There were no intraoperative complications; no devices, drains, or tissue implants were left in the patient at the conclusion of the procedure.

One week later, via text message and digital photographs, the patient reported intense pruritus at the bilateral chest wall incision sites, which were now surrounded by symmetric 1-cm erythematous plaques and associated sparse erythematous satellite papules (Figure 1). The patient denied any fevers, pain, swelling, or purulent discharge from the wounds. He was started on hydrocortisone cream 1% twice daily as well as oral diphenhydramine 25 mg at bedtime with initial good effect.

Three days later, the patient sent digital photographs of a morphologically similar–appearing rash that had progressed beyond the lateral chest walls to include the

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central chest and bilateral upper and lower extremities (Figure 2). He continued to deny any local or systemic signs of infection. Dermatology was consulted, and a diagnosis of ACD with cutaneous id reaction was made. The patient's medication regimen was modified to include triamcinolone acetonide cream 0.1% applied twice daily to the rash away from the wounds, clobetasol propionate ointment 0.05% applied twice daily to the rash at the wound sites, oral levocetirizine 5 mg once daily, and oral hydroxyzine 25 to 50 mg every 6 hours as needed for pruritus. Additional recommendations included the use of a fragrance-free soap and application of an over-the-counter anti-itch lotion containing menthol and camphor applied as needed. Within 24 hours of starting this modified treatment regimen, the patient began to notice an improvement in symptoms, with full resolution over the course of the ensuing 2 weeks. The patient was counseled to inform his physicians—present and future—of his allergy to 2-CA.

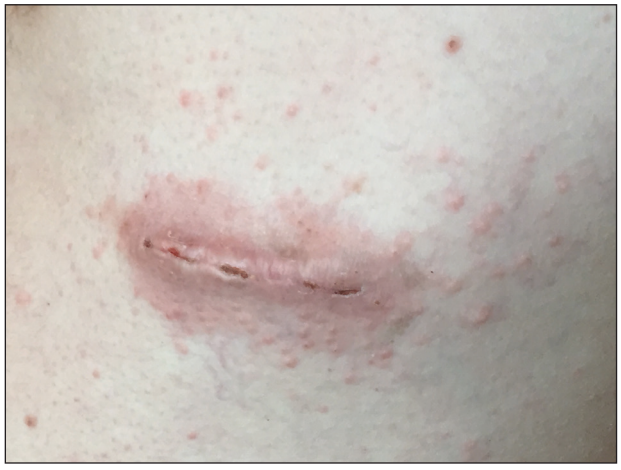

FIGURE 1. Well-demarcated erythematous plaque with sparse associated satellite papules surrounding a chest wall incision site where cyanoacrylate tissue adhesive was applied.

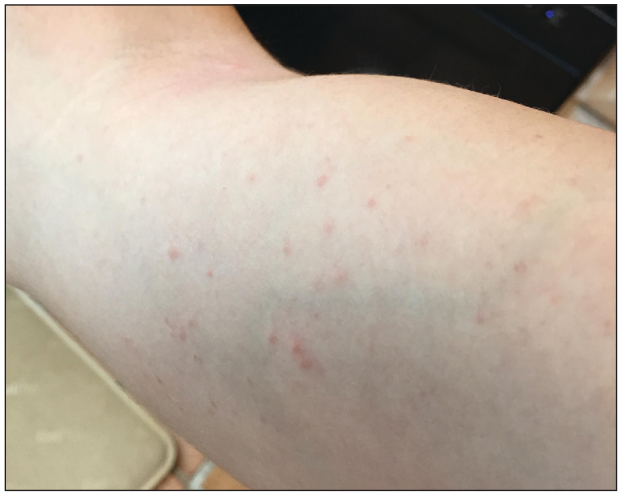

FIGURE 2. Erythematous papules on the right arm that appeared 3 days after a primary eruption at the chest wall incision sites where cyanoacrylate tissue adhesive was applied.

Contact dermatitis associated with the use of 2-CA has been described in the literature.[12-15] We report progression to an id reaction, which is characterized by the diffuse symmetric spread of a cutaneous eruption at a site distant from the primary localized dermatitis that develops within a few days of the primary lesion and exhibits the same morphologic and histopathologic findings.[16,17] In our patient, pruritic erythematous papules and plaques symmetrically distributed on the arms, legs, and chest appeared 3 days after he first reported a similar eruption at the 2-CA application sites. It is theorized that id reactions develop when the sensitization phase of a type IV hypersensitivity reaction generates a population of T cells that not only recognizes a hapten but also recognizes keratinocyte-derived epitopes.[16] A hapten is a small molecule (<500 Da) that is capable of penetrating the stratum corneum and binding skin components. A contact allergen is a hapten that has bound epidermal proteins to create a new antigenic determinant.[18] The secondary dermatitis that characterizes id reactions results from an abnormal autoimmune response. Id reactions associated with exposure to adhesive material are rare.[19]

Allergic contact dermatitis is a type IV hypersensitivity reaction that appears after initial sensitization to an allergen followed by re-exposure. Our patient presented with symmetric erythematous plaques at the surgical incision sites 1 week after 2-CA had been applied. During this interval, sensitization to the inciting allergen occurred. The allergen is taken up by antigen-presenting cells, which then migrate to lymph nodes where they encounter naïve T lymphocytes that subsequently undergo clonal expansion to produce a cohort of T cells that are capable of recognizing the allergen. If subsequent exposure to the specific allergen takes place, an elicitation phase occurs in which primed T cells are incited to release mediators of inflammation that engender the manifestations of ACD within 24 to 72 hours.[18,20] Sensitization may be promoted by skin barrier impairments such as dermatitis or a frank wound.[12,20] In most cases, the patient is unaware that sensitization has occurred, though a primary ACD within 5 to 15 days after initial exposure to the inciting allergen rarely may be observed.[18] Although our patient had 2-CA applied to his surgical wounds at 14 years of age, it was unlikely that sensitization took place at that time, as it was 1 week rather than 1 to 3 days before he experienced the cutaneous eruption associated with his second 2-CA exposure at 17 years of age.

Cyanoacrylate tissue adhesive also may cause ICD resulting from histotoxic degradation products such as formaldehyde and cyanoacetate that are capable of compromising cutaneous barrier function. Keratinocytes that have had their membranes disturbed release proinflammatory cytokines, which recruit cells of the innate

immune system as well as T lymphocytes to the site of insult to facilitate the inflammatory response. The manifestations of ICD include erythema, edema, and local necrosis that can compromise wound healing.[20] The speed at which a given cyanoacrylate adhesive degrades is proportional to the length of its carbon side chain. Those with shorter side chains—ethyl and methyl cyanoacrylate—degrade more rapidly into formaldehyde and cyanoacetate; 2-CA possesses a longer side chain and therefore degrades more slowly, which should, in theory, lessen its potential to cause ICD.[20] Because it may take 7 to 14 days before 2-CA will spontaneously peel from the application site, however, its potential to evoke ICD nevertheless exists.

Treatment of ICD entails removing the irritant while concurrently working to restore the skin's barrier with emollients. Although topical corticosteroids often are reflexively prescribed to treat rashes, some believe that their use should be avoided in cases of ICD, as their inhibitory effects on epidermal lipid synthesis may further impair the skin's barrier.[21] For cases of ACD, with or without an accompanying id reaction, topical corticosteroids are the mainstay of therapy. It is customary to start with a higher-potency topical steroid such as clobetasol and taper to lower-potency steroids as the patient's condition improves. Steroid ointments are petroleum based and are capable of causing 2-CA to separate from the skin.[10] As a result, they should be used with care when being applied to an area where 2-CA is maintaining dermal closure. Systemic corticosteroids may be warranted in cases with involvement of more than 20% of the body surface area and should start to provide relief within 12 to 24 hours.[22] Oral antihistamines and cold water compresses can be added to help address pruritus and discomfort in both ACD and ICD.

Instances of contact dermatitis caused by 2-CA are rare, and progression to an id reaction is rarer still. Physicians should be aware of the possibility of encountering a patient that manifests one or both of these complications whenever 2-CA is employed for skin closure. Physicians who employ 2-CA for skin closure should first ask patients about prior cutaneous reactions to cyanoacrylates including 2-CA and other commonly encountered acrylate-containing products including adhesive wound dressings, dental cements and prostheses, superglue, artificial nails, and adhesives for wigs and false eyelashes. Still, many patients who exhibit acrylate-induced contact dermatitis, with or without an associated id reaction, will not attest to a history of adverse reactions; they simply may not recognize acrylate as the inciting agent. Practitioners across a range of specialties outside of dermatology—surgeons, emergency physicians, and primary care providers—should be prepared to both recognize contact dermatitis and id reaction arising from the use of 2-CA and implement a basic treatment plan that will bring the patient relief without compromising wound closure.

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