



Review article

Allergic contact dermatitis to Dermabond™: A case and review of the literature

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ABSTRACT

The differential diagnosis for post-operative wound dehiscence is vast, including incisional infections, hematoma, and inadequate surgical closure. Allergic contact dermatitis (ACD) is an under-recognized and frequently missed cause of post-operative wound complications. Improved access to healthcare and high prevalence of surgical and procedural care mean patients are exposed to an increasingly vast spectrum of potential contact allergens. Early identification, diagnosis, and treatment of ACD will improve patient outcomes and prevent future exposures and wound complications. We present a case of severe ACD to Dermabond™, review previously reported cases of ACD to Dermabond™, and discuss other potential causes of perioperative ACD to raise awareness of this rare but important cause of wound complications.

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1. Introduction

Allergic contact dermatitis (ACD) is a type IV hypersensitivity reaction that occurs in patients previously sensitized to an allergen. In the surgical setting, it often presents as a pruritic, erythematous, and sometimes crusted or vesicular eruption around the surgical site beginning one-to-two weeks post-operatively; it can mimic cellulitis and cause wound dehiscence.

Dermabond™ (Ethicon, Inc., Somerville, NJ), or 2-octyl-cyanoacrylate, is a topical skin adhesive commonly used in the closure of surgical incisions. It is considered a weak allergen and thus, despite its extensive use, ACD to Dermabond™ has only rarely been documented [1–10]. Herein, we present a case of severe ACD in a pediatric patient to Dermabond™ following a congenital nevus excision. To our knowledge, this is only the third reported case of contact allergy to Dermabond™ within the pediatric population. The purpose of this report is to inform clinicians of this potential allergen as a cause of post-operative surgical wound complications and to outline relevant allergens one may consider in suspected post-operative ACD.

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Fig. 1. Photos of the perioperative site depicting wound dehiscence with a concomitant pruritic, erythematous, and exudative rash approximately 1-month post-operatively (1a). The wound epithelialized and rash fully resolved by 3-months post-op, following treatment with desoximetasonone cream and a 10-day course of amoxicillin for bacterial superinfection (1b).

2. Case

Our patient is a 7-year-old female with a past medical history of atopic dermatitis and allergic rhinitis, who underwent surgical excision of a medium-sized congenital nevus of her left lower leg. The surgical site was pre-operatively cleansed with isopropyl alcohol and chlorhexidine and sterilely prepped. The nevus was excised, and post-excision wound closure was performed using two absorbable sutures (poliglecaprone 25 and fast absorbing gut) as well as Dermabond™. The postoperative course was subsequently complicated by wound dehiscence with a concomitant pruritic, erythematous and exudative rash involving the perioperative site (Fig. 1a). A subsequent autoeczematous reaction ensued with widespread pruritic eczematous plaques (Fig. 2a). The patient was seen by Pediatric Dermatology and treated with desoximetasonone cream and a 10-day course of amoxicillin due to concern for bacterial superinfection. This led to complete resolution of the rash (Figs. 1 b and 2 b). The wound, however, did not heal in a cosmetically elegant fashion and 7 months later, the patient underwent surgical scar revision. The surgical site was again cleansed, prepped and closed using the same materials as the previous procedure. The patient subsequently experienced a similar post-operative course with a vesicular eczematous rash of the surgical site resulting in further wound dehiscence (Fig. 3) and another auto-eczematous flare of her trunk, arms and face.

ACD was suspected and she was referred to our clinic for patch testing (the gold standard for diagnosing ACD). In addition to the

North American Contact Dermatitis Group (NACDG) standard 70-allergen series (which includes chlorhexidine), she was tested to our corticosteroid, preservative, and vehicle panels as well as poliglecaprone 25 sutures, fast absorbing gut suture, desoximetasonone cream, and Ethicon Dermabond™ Advanced Skin Adhesive (tested semi-open). Reactions were read on day 3 and day 7. Final reactions showed strong/very strong reactions to Dermabond™, formaldehyde, quaternium-15, bacitracin, hydroquinone and the patient's shampoo; mild reactions to DMDM hydantoin and fragrance mix; and relevant weak reactions to imidazolidinyl urea and an over the counter antibiotic ointment containing bacitracin. (Of note, strong and mild reactions are interpreted as true allergy; weak (doubtful) reactions may be true allergy as guided by the clinical scenario.) We considered all of these reactions to be relevant.

3. Discussion

3.1. Pathophysiology

ACD is a delayed cell-mediated hypersensitivity reaction, that is characterized by two phases: initial sensitization (patient is first exposed to the allergen, which sensitizes the immune system) and elicitation (allergic response triggered upon re-exposure) [11]. The duration of these phases varies somewhat depending on the patient's history. Primary sensitization with rash can occur and is characterized by clinical signs of ACD 7 to 10 days following initial

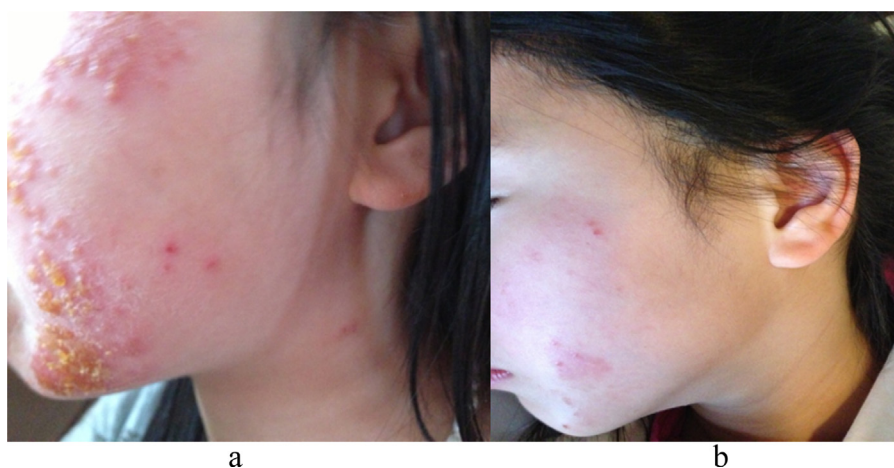


Fig. 2. Autoeczematous reaction with facial pruritic eczematous plaques accompanied the rash involving the perioperative site (2a), which resolved following treatment with desoximetasonone cream (2b).



Fig. 3. Surgical wound dehiscence with the surrounding pruritic, vesicular, and erythematous plaque of dermatitis following surgical scar revision (3a). Site healed (3b).

allergen exposure. Once sensitized, elicitation upon re-exposure usually manifests as a dermatitis rash within 12–48 hours.

3.2. Acrylates and allergic contact dermatitis

Acrylates are monomers that become bound together through a process of polymerization in the formation of plastics. These monomers are strong irritants and allergens; however, the act of polymerization renders them non-reactive. Cyanoacrylates are a specific family of acrylate polymers with durable and fast-acting adhesive properties; they are commonly found in glues, plastics, paints, and inks. Cyanoacrylates are also frequent ingredients in many topical skin adhesives, including 2-octyl-cyanoacrylate (Dermabond™), 2-butyl cyanoacrylate (e.g. Histoacryl™, Liquiband™), and 2-ethyl cyanoacrylate (e.g. Epiglu™). 2-Ethyl cyanoacrylate has been reported to cause ACD from nail cosmetics [12]. Cyanoacrylates like Dermabond™ rarely cross-react with other acrylates and methacrylates, but may cross-react with each other [3,6,8].

3.3. Previously reported cases

Including our patient, there have been 21 cases of ACD to Dermabond™ reported in the literature. Table 1 outlines salient demographic and clinical features of the reported cases. Notably, a majority of cases were adult females. Patients commonly presented with a pruritic, erythematous and dermatitic peri-incisional rash, whereas a minority of patients demonstrated vesicles or bullae on examination. Interestingly, six cases had no known prior history of exposure to cyanoacrylates. The majority of documented cases appropriately underwent patch testing.

Despite widespread use of Dermabond™ in the postoperative, emergency medicine, and clinical settings, it has a relatively low rate of sensitization with only rare reports of contact allergy documented in the literature [1–10]. There are several possible explanations for the low allergenic potential of Dermabond™. First, its cyano groups readily polymerize upon contact with keratin, rendering the product fairly inert.¹⁰ Second, it has been hypothesized that keratinocytes envelope Dermabond™ haptens,

Table 1
Reports of Allergic Contact Dermatitis to Dermabond.

Case	Sex	Age (years)	Anatomical site of dermatitis	Operation or procedure	Approximate time to presentation (days)	Known previous exposure	Patch Testing Performed?
1 ¹	F	35	Breast	Excision of breast mass	8	Yes	No
2 ¹	F	39	Breast	Excision of breast mass	NR	Yes	No
3 ¹	F	61	Breast	Mastectomy	5	Yes	No
4 ²	F	33	Lower back, right buttock	Surgical implantation of spinal cord stimulator	7	No	Yes
5 ²	F	65	Abdomen	Nissen fundoplication	7	Yes	Yes
6 ²	F	35	Abdomen	Laparoscopic left hepatectomy	7	Yes	Yes
7 ²	F	44	Abdomen	Laparoscopic cholecystectomy	7	Yes	Yes
8 ³	F	50	Hip, trunk, limbs, face	Hip replacement	21	No	Yes
9 ³	F	41	Lower limbs	Radio-frequency treatment for varicose veins	2	Yes	Yes
10 ⁴	NR	49	Trunk, limbs	Extirpation of 35 lipomas	3	NR	Yes
11 ⁵	NR	NR	Knee	Total knee arthroplasty	NR	NR	Yes
12 ⁵	NR	NR	Knee	Total knee arthroplasty	NR	NR	Yes
13 ⁶	F	66	Knee, thigh	Patello-femoral joint replacement	28	No	Yes
14 ⁷	F	47	Breast	Bilateral breast reduction	6	NR	No
15 ⁷	F	55	Abdomen	Scar revision after abdominoplasty	7	NR	Yes
16 ⁸	NR	12	Knee	Three operations to correct genu valgum	7*	No	Yes
17 ⁸	NR	14	NR	Two operations for bone lengthening to correct achondroplasia	7*	No	Yes
18 ⁸	NR	16	Feet	Two operations for pes planus	7*	No	Yes
19 ⁹	F	36	Breast	Bilateral replacement of silicone breast implants, bilateral mastopexies	4	Yes	No
20 ¹⁰	F	32	Lower abdomen	Abdominoplasty	7	NR	Yes
21	F	7	Leg	Surgical excision of congenital nevus	14	Yes	Yes

NR = Not reported.

* Pruritus affecting the peri-incisional site approximately 2–3 days after the first operation, then papulovesicular eruption 1–2 weeks post-op.

Table 2

Perioperative Causes of Allergic Contact Dermatitis.

PREOPERATIVE	PERIOPERATIVE	POSTOPERATIVE
Antiseptics Alcohols (isopropyl alcohol) [15–19] Chlorines (chlorhexidine gluconate, hexachlorophene) [20–26] Iodophors (povidone-iodine) [27–29] Benzalkonium chloride [30–33]	Gloves [43–49] Latex Nitrile (rubber accelerators and stabilizers)	Topical Skin Adhesives [61–63] Tincture of benzoin Mastisol (Ferndale Laboratories Inc., Ferndale, MI) Dermabond™
Local Anesthetics (topical & injectable) [34–40] Amides (e.g. benzocaine, tetracaine, procaine) Esters (e.g. lidocaine, prilocaine, dibucaine)	Metals [50–52] Surgical instruments (stainless steel, chromium, nickel) Surgical staples Implants (rare)	Dressings [64,65] Colophony (rosin)
Surgical Marking Pens [41,42]	Sutures [53–56] Suture fibers Non-absorbable (e.g. polypropylene, nylon, polyamide, silk) Absorbable (e.g. catgut, chromicized catgut) Suture-related chemicals Sterilizing chemicals (e.g. triclosan, ethylene oxide) Suture dyes	Topical Antibiotics [66–69] Aminoglycosides (e.g. neomycin, tobramycin) Bacitracin Polymyxin B
	Acrylates [57,58] Cyanoacrylates (e.g. topical skin adhesives, liquid bandages, bone and dental cement)	Topical Steroids [70–73] Tixocortol pivalate Triamcinolone Hydrocortisone Clobetasol propionate Desoximetasone
	Formaldehyde [59,60] Permanent press fabrics Dermabond™ (hydrolyzed to formaldehyde) Sterilizing chemicals Biopsy specimen preservation	Vehicles(base of products) [74–76] Propylene glycol Sorbitan sesquioleate Lanolin

* Latex gloves are a rare cause of delayed hypersensitivity, instead they typically cause type-1 immediate reactions.

making elicitation of the immune system difficult [7]. However, once in contact with skin, polymerized cyanoacrylates are hydrolyzed to formaldehyde, a known sensitizing material [4].

In our case, it is interesting to note that the patient did not react to acrylates other than the Dermabond™ itself, but she did have reactions to two strengths of formaldehyde, as well as three formaldehyde releasers (quaternium-15, imidazolidinyl urea, DMDM hydantoin), suggesting that the breakdown of Dermabond™ to formaldehyde was the sensitizing trigger. As such, our patient was counseled on avoidance of her allergens, including both formaldehyde and formaldehyde-releasing chemicals in products.

3.4. Perioperative causes of allergic contact dermatitis

In addition to the common causes of wound dehiscence (infection, excessive wound tension, inadequate undermining of the wound during surgery), surgeons and wound clinicians alike should consider perioperative ACD as a cause of wound closure failure [13]. Although not specific, pruritus, erythema, vesicle or blister formation of the affected area that eventually rupture and scale are symptoms and signs favoring a diagnosis of ACD. The standard treatment of ACD includes strict avoidance of the allergen(s) and when appropriate, short-term use of topical steroids and antihistamines to manage symptoms.

Determining the cause of postoperative contact dermatitis can be daunting, as patients are exposed to numerous potential allergens during the perioperative period (Table 2) and a single product may contain multiple allergens [3]. If contact allergy is suspected in the postoperative period, referral to a dermatologist who specializes in skin patch testing is warranted. Once referred, a thorough history and comprehensive patch testing should be

performed, as many important surgically relevant allergens (e.g. acrylates) are not included on the TRUE Test panel® (Thin-Layer Rapid Used Epicutaneous Patch Test; Smart Practice, Phoenix, AZ).

The NACDG standard series contains 70 allergens, many of which are present in other international baseline series. The NACDG standard panel broadly screens for many surgery-related causes of contact allergy including formaldehyde, formaldehyde releasers (quaternium-15, bromo-nitropropane-diol, diazolidinyl urea, DMDM hydantoin, imidazolidinyl urea and tris hydroxymethyl nitromethane), topical antimicrobials (neomycin, bacitracin, chlorhexidine digluconate, benzalkonium chloride, tea tree oil), adhesives (colophony, ethyl acrylate, methyl methacrylate), anesthetics (benzocaine, lidocaine, dibucaine), and metals used in surgical tools and implants (nickel, cobalt chloride) [13]. Testing to additional acrylates, corticosteroids, product vehicles, preservatives, suture materials, skin adhesives, dressings, gloves, and antiseptics should be considered on a case-by-case basis.

3.5. Conclusion

Worldwide, the prevalence of contact allergy is increasing [14]. Clinicians and surgeons should be aware of the potential allergens that patients are exposed to throughout the perioperative period. Accurate identification of the causative allergen(s) through patch testing helps not only to confirm the diagnosis, but also allows for education of both the patient and provider regarding causative allergens so future wound complications from ACD can be avoided.

Conflicts of interest

None declared.

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