

Erythema Multiforme like Allergic Contact Dermatitis Associated with *Nigella sativa* oil

Christina I Tejada^{1*}, Frederick Bartholomew², Stephen Vance² and Ali Dana³

¹Columbia Vagelos College of Physicians and Surgeons, New York, USA

²Department of Dermatology, Columbia University Medical Center, New York, USA

³James J. Peters Veterans Affairs Medical Center, New York, USA

Introduction

Allergic contact dermatitis (ACD) is a common skin disease that affects approximately 20% of the population and is characterized as a delayed type IV hypersensitivity reaction to external agents [1]. Erythema multiforme-like (EM) allergic contact dermatitis is a deeply erythematous, dermal, and possibly aggressive vesicular or bullous variant of ACD that is rare but well-documented. Its clinical presentation is variable and can range from localized to disseminated rash [2]. Here we report a case of erythema multiforme-like ACD induced by the topical application of *Nigella sativa* black cummin seed oil.

Case report

A 48-year-old African American male with a past medical history of hypertension, human immunodeficiency virus 1 (HIV-1), atopic dermatitis and folliculitis presented with five days of a pruritic, painful rash. He initially presented to his primary care physician with a pruritic rash circumferentially around his neck and in his groin. The patient was started on a five-day prednisone 40 mg taper for his rash which was initially attributed to contact with poison ivy. Four days later he presented to the emergency department for worsening pruritic and erythematous rash of the neck and groin in addition to swelling of the foreskin. Dermatology consultation was requested and examination revealed coalescing dusky erythematous atypical targetoid plaques as well as vesicles and bullae on the head, face, neck, abdomen, scrotum, and bilateral lower extremities (Figures 1-3). His skin was Nikolsky and Asboe-Hansen sign positive, and the eruption involved 20% of the patient's total body surface area. His penile shaft was edematous with inability to retract the foreskin. He had no mucosal involvement (the urethral mucosa could not be assessed), although his eyes had a faint yellow discharge without sensation of burning and grittiness. He denied history of herpes simplex virus, recent cold sores, fevers or difficulty swallowing. His medications included efavirenz/emtricitabine/tenofovir and hydrochlorothiazide, none of which had been recently started.

The patient was afebrile with normal vital signs. Laboratory test results (complete cell count, basic biochemical analyses, prothrombin time, international normalized ratio, urinalysis, mycoplasma titers, immunoglobulin A, nasal/skin/blood cultures) were normal with an eosinophil count of 5.0%. A serum HSV 1 IgG was positive. Erythrocyte sedimentation rate and c-reactive protein were elevated to 20 and 161.8, respectively. Two 4mm punch skin

biopsies were obtained from the left upper chest. Histopathology of the chest revealed complete epidermal-dermal separation with a devitalized epidermis containing numerous apoptotic keratinocytes (Figure 4). The dermis contained a moderately dense perivascular and band-like superficial to mid-dermal lymphocytic infiltrate with superficial melanophages (Figure 5). Direct immunofluorescence was negative.

Upon further history, the patient had applied topical *Nigella sativa* oil (NSO) to his face, neck, and groin for 4 days prior to the initial eruption as the oil was marketed as a skin care product. There were no symptoms present before the oil was used. The patient also recalled that other family members have had mild irritate reactions to topical NSO, although they were not formally evaluated by a physician. The patient's eruption resolved with coral prednisone taper of 80mg for 2 days, 60 mg for 1 day, 40 mg for 2 days, 20 mg for 3 days, 10mg for 1 week and 5 mg for 1 week and avoidance of NSO. The patient declined patch testing with NSO.

The timing of onset, resolution of the rash with NSO cessation, and absence of other potential etiologies suggests NSO as the inciting cause of the patient's bullous eruption. Although we cannot disprove poison ivy, the involvement of the area in which NSO was directly applied suggests a contact dermatitis to this product.



Figure 1. Separation of the papillary dermis from the basal layer on the neck.



Figure 2. Plaques and bullae on the trunk.



Figure 3. Plaques and bullae on the face.

Discussion and conclusion

Nigella sativa oil (NSO), also known as black cumin seed oil, is extracted from the plant *Nigella sativa* and is traditionally used in Africa and Asia for its therapeutic properties [3,4]. *Nigella sativa*'s active ingredients include thymoquinone, p-cymene, carvacrol, thymo-hydroquinone and thymoquinone. These ingredients have been reported to have a wide range of pharmacologic effects, including anti-carcinogenic, anti-inflammatory, anti-hypertensive, anti-asthmatic, antioxidant, hypoglycemic, antiulcer and anti-parasitic [5]. The oil extract has been topically used to treat improve acne vulgaris and vitiligo in Iraq and Iran [6,7].

Allergic contact dermatitis is a T cell-mediated immune response that causes direct cytotoxicity against keratinocytes. In addition to local reactions, secondary dissemination may occur with the manifestation of erythema multiforme-like, purpuric and vasculitis-like eruptions [8]. The precise mechanism of EM-like reaction secondary to ACD is unknown but is thought to be delayed-type hypersensitivity [9]. Clinical presentations of EM-like ACD include targetoid lesions, purpura, vesicles, and annular or urticarial plaques; histologic findings are highly variable, with features typically reported as spongiotic dermatitis and perivascular infiltrate. (9) However, typical histologic findings may be obscured

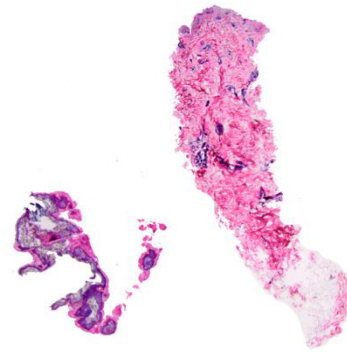


Figure 4. Epidermal-dermal separation with a devitalized epidermis containing numerous apoptotic keratinocytes.

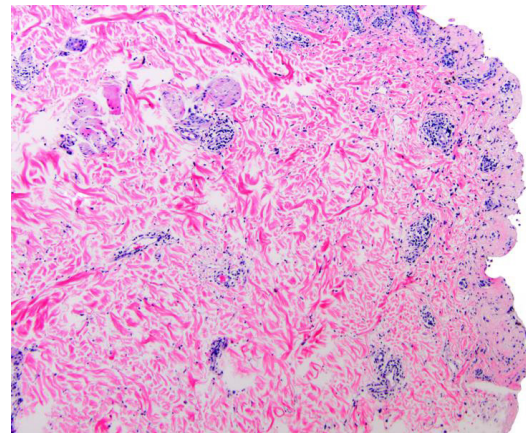


Figure 5. Dermis showing moderately dense perivascular and band-like superficial to mid-dermal lymphocytic infiltrate with superficial melanophages

in bullous allergic contact dermatitis. In severe cases of bullous ACD, lesions can develop frank necrosis, with ulceration of the epidermis and the development of notable epidermal hyperplasia [10].

Documented cases have shown that EM-like ACD is more commonly caused by plants, exotic woods, topical medications, and cosmetics [8]. EM-like ACD has also been linked to topical use of turmeric essential oil [9]. The first published case of an allergic reaction to *Nigella sativa* oil was in 1997 with subsequent reports in 2002, 2011, and 2012 [11].

A case report of EM-like ACD from 2016 describes a 50-year-old man who presented to clinic with an itchy rash on the bilateral knees that spread to the neck, trunk and arm. He had applied topical turmeric oil for 14 days to his right knee for osteoarthritic pain. He had no preceding illness or medication changes. The primary site of application, his right knee, had a sharply demarcated violaceous plaque with overlying scale and desquamation. The neck, trunk and arms had erythematous targetoid papules and plaques. Mucous membranes were unaffected. Pathology showed orthokeratosis, spongiosis, interface dermatitis, and Civatte bodies with perivascular and interstitial eosinophils. The patient

improved with IV methylprednisolone and prednisone taper. The authors diagnosed this case as EM-like ACD to turmeric oil [12].

While EM-like ACD is rare, the clinical findings of our case may be consistent with EM-like ACD to NSO. This is supported by the historical onset days after application of NSO, absence of typical EM-related prodromal syndrome, and presence of focal eczematous dermatitis at the site of application preceding the targetoid eruption. Although the patient's histopathology was consistent with true EM or SJS/TEN spectrum disease, it is likely that necrosis due to severe ACD obscured any histologic features of spongiosis. Further, the patient denied ingesting the oil and SJS/TEN due to topical medications is rare [13]. Thus, we believe this case represents a rarely reported EM-like ACD due to NSO.

References

1. Tan CH, Rasool S, Johnston GA. Contact dermatitis: allergic and irritant. *Clin Dermatol*. 2014; 32: 116-124.
2. Barrientos N, Abajo P, de Vega MM, Dominguez J. Erythema multiforme-like eruption following allergic contact dermatitis in response to para-phenylenediamine in a temporary henna tattoo. *Int J Dermatol*. 2014; 53: e348-e50.
3. Bonhomme A, Poreaux C, Jouen F, Schmutz JI, Gillet P, et al. Bullous drug eruption to *Nigella sativa* oil: Consideration of the use of a herbal medicine – clinical report and review of the literature. *J Eur Acad Dermatol Venereol*. 2017; 31: e217-e9.
4. Zedlitz S, Kaufmann R, Boehncke W-H. Allergic contact dermatitis from black cumin (*Nigella sativa*) oil-containing ointment. *Contact Dermatitis*. 2002; 46: 188.
5. Ali BH, Blunden G. Pharmacological and toxicological properties of *Nigella sativa*. *Phytother Res*. 2003; 17: 299-305.
6. Ghorbanibirgani A, Khalili A, Rokhafrooz D. Comparing *Nigella sativa* Oil and Fish Oil in Treatment of Vitiligo. *Iran Red Crescent Med J*. 2014; 16: e4515.
7. Eid AM, Elmarzugi NA, Abu Ayyash LM, Sawafta MN, Daana HI. A Review on the Cosmeceutical and External Applications of *Nigella sativa*. *J Trop Med*. 2017: 7092514.
8. Hong SJ, Chang CH. Erythema multiforme-like generalized allergic contact dermatitis caused by *Alpinia galanga*. *Contact Dermatitis*. 2006; 54: 118-120.
9. Smart DR, Powell DL. Erythema multiforme-like allergic contact reaction to topical triamcinolone. *Dermatitis*. 2014; 25: 89-90.
10. Grimbaldston MA, Nakae S, Kalesnikoff J, Tsai M, Galli SJ. Mast cell-derived interleukin 10 limits skin pathology in contact dermatitis and chronic irradiation with ultraviolet B. *Nat Immunol*. 2007; 8: 1095-1104.
11. Steinmann A, Schätzle M, Agathos M, Brett R. Allergic contact dermatitis from black cumin (*Nigella sativa*) oil after topical use. *Contact Dermatitis*. 1997; 36: 268-269.
12. Huber J, deShazo R, Powell D, Duffy K, Hull C. Erythema Multiforme-Like Allergic Contact Dermatitis to Turmeric Essential Oil. *Dermatitis*. 2016; 27: 385-386.
13. Sachs B, Fischer-Barth W, Erdmann S, Merk HF, Seebeck J. Anaphylaxis and toxic epidermal necrolysis or Stevens–Johnson syndrome after nonmucosal topical drug application: fact or fiction? *Allergy*. 2007: 877-883.

***Correspondence:** Christina I. Tejada, Columbia Vagelos College of Physicians and Surgeons, New York, USA, Tel: 727-365-9976; E-mail: cit2106@columbia.edu

Rec: Mar 08, 2019; Acc: Mar 22, 2019; Pub: Mar 26, 2019

J Clin Case Rep Rev. 2019;2(2):34
DOI: [gsl.jccrr.2019.000034](https://doi.org/10.21960/jccrr.2019.000034)

Copyright © 2019 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY).