Reflectance Confocal Microscopy as a Diagnostic Aid in Allergic Contact Dermatitis to Mango Sap

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PRACTICE **POINTS**

- Contact with mango tree sap can induce allergic contact dermatitis.
- Reflectance confocal microscopy (RCM) is a noninvasive imaging technique that can provide real-time in vivo visualization of affected skin in contact dermatitis.
- Predominant findings of contact dermatitis under RCM include disruption of the stratum corneum; parakeratosis; vesiculation; spongiosis; and exocytosis, vasodilation, and intercellular edema more specific to the allergic subtype.

The mango tree (*Mangifera indica*) produces nutrient-dense fruit that is consumed across the world. Interestingly, despite widespread consumption of its fruit and its categorization in the Anacardiaceae family, allergic reactions to the mango tree and its components are comparatively rare, sometimes manifesting as allergic contact dermatitis (ACD). Evaluation of ACD most commonly includes a thorough clinical assessment with diagnostic support from patch testing and histopathologic review following skin biopsy. In recent years, reflectance confocal microscopy (RCM) has shown promising potential to join the repertoire of diagnostic tools for ACD by enabling dynamic and high-resolution imaging of contact dermatitis in vivo. Herein, we present a unique case of mango sap–induced ACD imaged and diagnosed in real time via RCM.

The mango tree (*Mangifera indica*) produces nutrient-dense fruit—known colloquially as the "king of fruits"—that is widely consumed across the world. Native to southern Asia, the mango tree is a member of the Anacardiaceae family, a large family of flowering, fruit-bearing plants.[1] Many members of the Anacardiaceae family, which includes poison ivy and poison oak, are known to produce urushiol, a skin irritant associated with allergic contact dermatitis (ACD).[2] Interestingly, despite its widespread consumption and categorization in the Anacardiaceae family, allergic reactions to mango are comparatively rare; they occur as either immediate type I hypersensitivity reactions manifesting with rapid-onset symptoms such as urticaria, wheezing, and angioedema, or delayed type IV hypersensitivity reactions manifesting as ACD.[3] Although exposure to components of the mango tree has been most characteristically linked to type IV hypersensitivity reactions, there remain fewer than 40 reported cases of mango-induced ACD since it was first described in 1939.[4]

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noninvasive optical imaging technique that uses a low-energy diode laser to penetrate the layers of the skin. The resulting reflected light generates images that facilitate visualization of cutaneous structures to the depth of the papillary dermis.[11] While it is most commonly used in skin cancer diagnostics, preliminary studies also have shown an emerging role for RCM in the evaluation of eczematous and inflammatory skin disease, including contact dermatitis.[5-10] Herein, we present a unique case of mango sap–induced ACD imaged and diagnosed in real time via RCM.

Case Report

A 39-year-old woman presented to our clinic with a pruritic vesicular eruption on the right leg of 2 weeks' duration that initially had developed within 7 days of exposure to mango tree sap (Figure 1). The patient reported having experienced similar pruritic eruptions in the past following contact with mango sap while eating mangos but denied any history of reactions from ingestion of the fruit. She also reported a history of robust reactions to poison ivy; however, a timeline specifying the order of first exposure to these irritants was unknown. She denied any personal or family history of atopic conditions.

The affected skin was imaged in real time during clinic using RCM, which showed an inflammatory infiltrate represented by dark spongiotic vesicles containing bright cells (Figure 2). Additional RCM imaging at the level of the stratum spinosum showed dark spongiotic areas with bright inflammatory cells infiltrating the vesicles, which were surrounded by normal skin showing a typical epidermal honeycomb pattern (Figure 3). These findings were diagnostic of ACD secondary to exposure to mango sap. The patient was advised to apply clobetasol cream 0.05% to the affected area. Notable improvement of the rash was noted within 10 days of treatment.

FIGURE 1. Localized erythematous eczematous rash resulting from mango sap contact allergy in a 39-year-old woman.

Comment

Exposure to the mango tree and its fruit is a rare cause of ACD, with few reported cases in the literature. The majority of known instances have occurred in non–mango-cultivating countries, largely the United States, although cases also have been reported in Canada, Australia, France, Japan, and Thailand.[3,12] Mango-induced contact

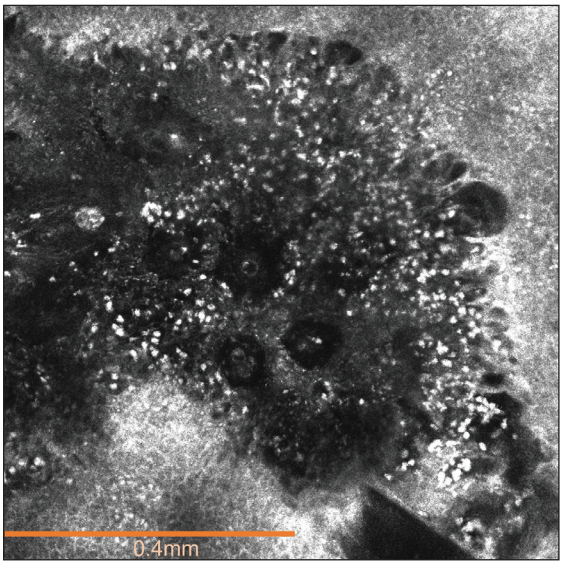

FIGURE 2. Reflectance confocal microscopy of mango sap allergic contact dermatitis demonstrating dark spongiotic vesicles containing an inflammatory infiltrate.

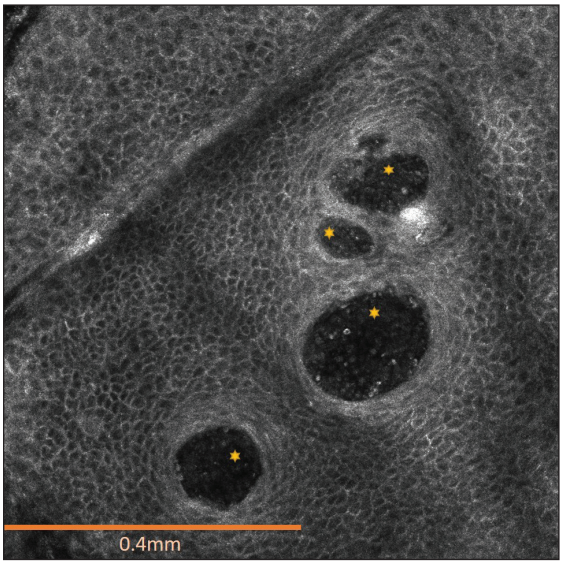

FIGURE 3. At the stratum spinosum, reflectance confocal microscopy showed dark areas (orange stars) with bright inflammatory cells infiltrating the vesicles, which were surrounded by normal skin showing a typical epidermal honeycomb pattern.

allergy follows a roughly equal distribution between males and females and most often occurs in young adults during the third and fourth decades of life.[4,12-21] Importantly, delayed-type hypersensitivity reactions to mango can manifest as either localized or systemic ACD. Localized ACD can be induced via direct contact with the mango tree and its components or ingestion of the fruit.[3,12,22] Conversely, systemic ACD is primarily stimulated by ingestion of the fruit. In our case, the patient had no history of allergy following mango ingestion, and her ACD was prompted by isolated contact with mango sap. The time from exposure to symptom onset of known instances of mango ACD varies widely, ranging from less than 24 hours to as long as 9 days.[3,12] Diagnosis of mango-induced ACD largely is guided by clinical findings. Presenting symptoms often include an eczematous, vesicular, pruritic rash on affected areas of the skin, frequently the head, neck, and extremities. Patients also commonly present with linear papulovesicular lesions and periorbital or perioral edema.

The suspected allergens responsible for mango-induced ACD are derived from resorcinol—specifically heptadecadienyl resorcinol, heptadecenyl resorcinol, and pentadecyl resorcinol, which are collectively known as mango allergens.[23] These allergens can be found within the pulp and skin of the mango fruit as well as in the bark and leaves of the mango tree, which may explain observed allergic reactions to components of both the mango fruit and tree.[12] Similar to these resorcinol derivatives, the urushiol resin found in poison ivy and poison oak is a catechol derivative.[2] Importantly, both resorcinols and catechols are isomers of the same aromatic phenol—dihydroxybenzene. Because of these similarities, it is thought that the allergens in mangos may cross-react with urushiol in poison ivy or poison oak.[23] Alongside their shared categorization in the Anacardiaceae family, it is hypothesized that this cross-reactivity underlies the sensitization that has been noted between mango and poison ivy or poison oak exposure.[12,23,24] Thus, ACD often can occur on initial contact with the mango tree or its components, as a prior exposure to poison ivy or poison oak may serve as the inciting factor for hypersensitization. The majority of reported cases in the literature also occurred in countries where exposure to poison ivy and poison oak are common, further supporting the notion that these compounds may provide a sensitizing trigger for a future mango contact allergy.[12]

A detailed clinical history combined with adjunctive diagnostic support from patch testing and histopathology of biopsied skin lesions classically are used in the diagnosis of mango-induced ACD. Due to its ability to provide quick and noninvasive in vivo imaging of cutaneous lesions, RCM's applications have expanded to include evaluation of inflammatory skin diseases such as contact dermatitis. Many features of contact dermatitis identified via RCM are common between ACD and irritant contact dermatitis (ICD) and include disruption of the stratum corneum, parakeratosis, vesiculation, spongiosis, and exocytosis.[6,10,25] Studies also have described features shown via RCM that are unique to ACD, including vasodilation and intercellular edema, compared to more distinct targetoid keratinocytes and detached corneocytes seen in ICD.[6,10,25] Studies by Astner et al[5,6] demonstrated a wide range of sensitivity from 52% to 96% and a high specificity of RCM greater than 95% for many of the aforementioned features of contact dermatitis, including disruption of the stratum corneum, parakeratosis, spongiosis, and exocytosis. Additional studies have further strengthened these findings, demonstrating sensitivity and specificity values of 83% and 92% for contact dermatitis under RCM, respectively.[26] Importantly, given the similarities and potentially large overlap of features between ACD and ICD identified via RCM as well as findings seen on physical examination and histopathology, an emphasis on clinical correlation is essential when differentiating between these 2 variants of contact dermatitis. Thus, taken in consideration with clinical contexts, RCM has shown potent diagnostic accuracy and great potential to support the evaluation of ACD alongside patch testing and histopathology.

Final Thoughts

Contact allergy to the mango tree and its components is uncommon. We report a unique case of mango sap–induced ACD evaluated and diagnosed via dynamic visualization under RCM. As a noninvasive and reproducible imaging technique with resolutions comparable to histopathologic analysis, RCM is a promising tool that can be used to support the diagnostic evaluation of ACD.

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