



Published by
Department of Dermatology and
Venereology, Universitas Udayana

Clinical features of allergic contact dermatitis to sandals: a case series



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Submitted: 2023-04-05

Accepted: 2023-04-13

Published: 2023-12-31

ABSTRACT

Background: Allergic contact dermatitis (ACD) is a skin inflammation caused by a type 4 delayed-type hypersensitivity reaction. One of the most common types of ACD is shoe dermatitis, characterized by pruritic or painful bilateral and symmetrical erythema, papules, vesicles, scaling, crusting, lichenification, or fissures at the site of footwear contact.

Case series: We present seven patients with allergic contact dermatitis caused by rubber flip-flop sandals who presented with acute to chronic eczema and leukoderma. Patients range in age from 4 to 65 years old, with symptoms lasting from 5 months to 2 years. Two of the seven patients had a history of atopy.

Conclusion: Flip-flop sandals are the most common offending footwear in Indonesian ACD patients because they are appropriate and comfortable in hot and humid climates like Indonesia. Rubber and rubber chemicals, preservatives, shoe adhesives, and leather materials are the most common offending allergens.

Keywords: ACD, flip-flop sandals, rubber, shoe dermatitis.

Cite This Article: Gotama S, Hapsari Y, Kusuma DR, Clinical features of allergic contact dermatitis to sandals: a case series. *Bali Dermatology Venereology and Aesthetic Journal*. 2023;6(2):20-25. DOI: 10.51559/b596s971

INTRODUCTION

Allergic contact dermatitis (ACD) is an inflammatory skin condition caused by type 4 delayed-type hypersensitivity reaction. It is caused by interacting irritating or antigen chemical agents with the skin, followed by a T-cell-mediated reaction.^{1,2} Allergic contact dermatitis caused by footwear is termed shoe dermatitis or footwear dermatitis.³

Allergic contact dermatitis is a common condition that affects approximately 15-20% of adults in the general population.^{1,4,5} Allergic contact dermatitis is responsible for 20% of contact dermatitis, and allergens vary greatly depending on location, personal habits and interests, and the types of preservatives legally permitted.⁶ In Dr. Mohammad Hosein General Hospital Palembang, the prevalence of ACD was 13.42% in 2008.⁷ The prevalence of footwear ACD in patch-tested individuals for foot dermatitis is between 3-24.2%.^{3,8} An epidemic-allergological study by Chowduri and Ghosh in India showed that footwear dermatitis comprises 24.22% of contact dermatitis cases.⁹ Footwear ACD affects both sexes and any age group, including children.⁸

The prevalence of shoe allergic contact dermatitis (ACD) is approximately 1.5% to 24.2% of all patch-tested positive patients.¹⁰ ACD of the feet is characterized by bilateral and symmetrical erythema, vesicles, papules, oozing, scaling, or crusting on the skin in contact with the footwear. Lichenification, fissuring, and scaling are more prevalent in chronic ACD. Blistering, oozing, and crusting can also occur in chronic ACD with further exposure to the hapten. Hypopigmented lesions (leukoderma) may also be found and are commonly associated with hydroquinone.¹¹ The most commonly reported symptoms are pruritus, burning, and pain. Any part of the foot can be affected, but the dorsum of the foot is the most commonly affected due to its larger surface area, thin stratum corneum, and constant contact with the upper portion of the footwear.^{6,10,12-14}

Major risk factors for footwear dermatitis are heat, friction, occlusion, hyperhidrosis, and atopy.^{12,15,16} The prevalence of footwear ACD is highest in warm-climate countries such as Indonesia, where heat and humidity cause sweating, increased pressure, and skin occlusion.^{12,14} In a study of 64 patients suspected of

having shoe dermatitis in Indonesia, Febriana et al. discovered that rubber slippers or sandals are the most common footwear (50.7%) causing footwear ACD.¹⁴

There are over 3,700 substances that can trigger ACD.^{17,18} The prevalence of a particular antigen in causing ACD depends on its sensitizing potential and the frequency and duration of exposure.¹⁸ Globally, the most common sensitizers of footwear ACD are rubber and rubber chemicals such as mercaptobenzothiazole, thiuram mix, and black rubber mix.^{9,14,19} A study of 46 shoe dermatitis patients in Indonesia found that the most common sensitizers are rubber allergens, preservatives, shoe adhesives, and leather materials.¹⁴ This corresponds well with Indonesians' preference for rubber slippers or sandals.

The only effective treatment for footwear ACD is preventing contact with the sensitizers.^{10,12,20} Therefore, characterizing footwear ACD, especially one caused by sandals, is important to provide an effective treatment plan for ACD patients. The objective of our case series is to highlight the characteristics of shoe dermatitis caused by rubber flip-flops often worn by Indonesians.

CASE REPORT

Patient characteristics

There were 7 patients from 2019 to 2021 attending Mataram University Hospital's Dermatology Outpatient Clinic were suspected of having allergic contact dermatitis to flip-flop sandals (Figure 1). Four of 7 patients (57%) were females, and the remaining 3 were males (43%). All patients complained of pruritus and erythema, followed by lichenification, blisters, and leukoderma in some other patients. In all cases, the lesion was located on the dorsal foot, and flip-flops sandals can be easily identified as the causative agent because the morphological lesions resembled this agent. Two patients had a history of atopy and a history of family atopy. The age of the patients varied from the youngest at 4 to the oldest at 65 years old. The duration of the symptoms varied from 2 months to 5 years (Table 1). The manifestations of ACD caused by flip-flops sandals in our patients are shown in Figure 1. All of our cases presented with pruritus and erythema except Case 7 who only reported pruritus without erythema. Case 1 also showed blisters and hyperpigmented crusts in the shape of the rubber flip-flops sandals that they used. Case 2, 4 and 5 had lichenification on the dorsum aspect of both feet. Case 3 was the only case that showed leukoderma in the shape of the rubber strap of her sandal. In addition to pruritus and erythema, case 6 complained of blisters and skin erosion. Case 7 was the only patient who showed skin atrophy and desquamation.

DISCUSSION

Allergic contact dermatitis (ACD) is a cell-mediated, type IV hypersensitivity reaction caused by repeated and direct skin exposure to contact allergens.^{1,2,5,17} Allergic contact dermatitis caused by footwear (shoe dermatitis) may present as acute, subacute, intermittent, or chronic disease and appear superimposed on endogenous eczema or other skin diseases.^{3,12} Three criteria must be met to generate an A: a genetic predisposition, an intact immune system, and low molecular weight substances that can penetrate the skin.^{17,21} Most allergens are haptens, simple chemicals that require proteins to be a

Table 1. Characteristics of patients diagnosed with ACD to flip-flop sandals

Case	Age	Gender	Sign & Symptoms	Location of lesion	Duration of symptoms	History of atopy	History of family atopy
1	18	Female	Pruritus, erythema, blister, hyperpigmented crust	Medial anterolateral dorsum pedis resembling flip-flops and dorsal part of digiti pedis	Swallow [®] flip flop sandals, fashion flip-flop sandals	4 months	No
2	60	Male	Pruritus, erythema, fissure lichenification	Medial anterolateral dorsum pedis resembling flip-flops	Swallow [®] flip flop sandals	1 year	No
3	47	Female	Pruritus, erythema blister, leukoderma	Medial anterolateral dorsum pedis resembling flip-flops and dorsal part of digiti pedis	Swallow [®] flip flop sandals	5 years	Yes
4	65	Female	Pruritus, erythema, lichenification	Medial anterolateral dorsum pedis resembling flip-flops, dorsal part of digiti pedis and anterior part of the ankle	Swallow [®] flip flop sandals	2 years	No
5	56	Male	Pruritus, erythema, lichenification	Medial anterolateral dorsum pedis resembling flip-flops, dorsal part of digiti pedis and anterior part of the ankle	Swallow [®] flip flop sandals	5 years	No
6	4	Male	Pruritus, erythema, blister, erosion	Medial and anterior dorsum pedis, dorsal part digiti pedis I, II	Fashion flip-flop sandals	2 months	Yes
7	54	Female	Pruritus, skin atrophy desquamation	Medial anterolateral dorsum pedis resembling flip-flops, dorsal part of digiti pedis	Swallow [®] flip flop sandals	2 years	No



Figure 1. The manifestations of ACD in our patients. All of the cases showed skin lesions on the dorsal parts of their feet that were in contact with the rubber straps of their sandals (A-G). Case 1 showed blisters and hyperpigmented crusts (A); Case 2 showed fissure lichenifications (B); Case 3 showed blisters and leukoderma (C); Case 4 and 5 both showed lichenification that extended beyond the dorsal part of the feet (D, E); Case 6 showed blisters and erosions (F); and Case 7 showed skin atrophy and desquamation (G).

complete antigen before sensitization.¹⁷ ACD is a two-stage process that starts with T-cell sensitization to low-molecular-weight allergens (haptens), aided by dermal dendritic cells (Langerhans cells) in the proximal draining lymph node. During the sensitization phase, effector T-cells (CD8+ cytotoxic T-cells) are produced. Subsequent contact with the specific hapten results from the elicitation phase through activating the previously induced T-cell population. These T-cells are recruited in the skin and activated by skin cells that present the hapten on MHC class I and II molecules. The activated T cells produce type 1 cytokines (IFN- γ , IL-2, IL-17). These cytokines are cytotoxic and can destroy various skin cells, including keratinocytes. Apoptosis of skin cells causes inflammation, which leads to eczema lesions 72 hours after re-exposure to the offending hapten. This hypersensitivity response is primarily mediated by TH1 cells, but TH2, TH17, and TH22 cells may also be involved.^{6,13}

Furthermore, the absence of dermatitis

when patients wear substitute footwear and patch test reactions to one or more allergens found in the footwear are both indicators of footwear ACD.^{5,12,14} The onset of shoe dermatitis is often sudden, with a history of a reaction to a new pair of footwear.¹² All of our patients presented with pruritus. Intense pruritus, pain, or burning sensation are the most common complaints of patients with footwear ACD.^{12,21,22} At the sites of allergen contact, clinical manifestations include erythema, vesicles or blisters, papules, scaling, oozing and crusting. Lichenification and hyperpigmentation with cracks and fissures may develop in chronic cases.^{1,10,12,22} Three of our patients (Cases 2, 4, and 5) had chronic manifestations of footwear ACD, which manifested as lichenifications. These patients have had ACD for 1 to 5 years. The lesions of footwear ACD usually have distinct lines and borders that outline the shape of the footwear or sandals.²² This characteristic is evident in 6 out of 7 patients (Cases 1, 2, 3, 4, 5, and 7) whose lesions were in the

shape of their flip-flop sandals. Another important diagnostic parameter in footwear ACD is the presence of normal skin that is not in contact with the footwear between eczematous areas.²⁰

Atopic dermatitis (AD) has been linked to an increased probability of ACD. Individuals with AD have skin-barrier disruptions, which increases the absorption of irritants and contact allergens two-fold. Irritants cause further skin barrier breakdown, increased transcutaneous penetration of contact allergens, and an increased risk of contact sensitization and presentation. The skin barrier disruption is thought to be caused by inflammatory cytokines released during AD. During the acute and chronic phases of AD, Th2 cells stimulate the release of IL-4, IL-5, IL-13, and IL-31, whereas Th1 cells contribute during the chronic phase. Two of these cytokines, IL-4 and IL-5, are known to disrupt the skin barrier. This establishes a link between inflammation and skin barrier disruption, even in patients who have never had defects. Furthermore,

during the acute phase, studies have found increased IL-17 (secreted by Th17) and IL-22 (secreted by Th22). Bacterial colonization, common in AD, has also been linked to increased contact sensitization by creating an inflammatory environment. These mechanisms show that AD and ACD might share immune pathways, especially those involving Th1, Th2, Th9 and/or Th17. Despite these mechanisms, studies show varying results regarding the relationships between atopy and ACD.^{16,23} In our study, only 2 patients (28.6%) had a history of atopy. A low prevalence of atopy in footwear ACD patients was also found in a study of 276 patients in India, in which only 24.64% of patients had a history of atopy. The relationship between atopy and ACD has not been well-established, and studies have shown varying results.¹⁶

The prevalence of footwear ACD is highest in warm-climate countries such as Indonesia, where heat and humidity cause sweating, increased pressure, and skin occlusion.^{12,14} In a study of 64 patients suspected of having shoe dermatitis in Indonesia, Febriana et al. discovered that rubber slippers or sandals are the most common footwear (50.7%) causing footwear ACD.¹⁴

Four out of seven patients (57.1%) presented in our study were females. This is similar to the results of various other studies. A study by Chowduri and Ghosh (2007) in 155 shoe dermatitis patients in India found that 61.93% of their patients were females.⁹ Similarly, an Indonesian study conducted in 2015 also found that 68.8% of shoe dermatitis patients were females.¹⁴ These studies show that women are more frequently affected by footwear ACD as they often wear more varieties of footwear, exposing them to more haptens. Women are also generally more concerned about their health and seek medical assistance more often.^{16,19} Furthermore, women have higher levels of immunoglobulin (IgM and IgG) than men, hence stronger cell-mediated immune responses.²⁴ Indonesian housewives are more susceptible to footwear ACD because they are constantly exposed to water, household detergents, and cleaning agents while performing household chores barefoot or in sandals. These agents may impair epidermal function, allowing

allergens to penetrate deeper into the skin.^{9,14}

One of our patients is a child aged 4 years old. Although ACD is more common in productive age groups, children can also be diagnosed with ACD.^{12,25} The prevalence of ACD in the pediatric population has been estimated to be between 14.5%-70%. The highest sensitization rate is found in children between 0-3 years old. Pediatric ACD most commonly affects the skin of the legs, feet, hands, and face caused by metals, footwear, topical medications, and cosmetics. Children have a higher risk of ACD due to their thinner stratum corneum, incomplete epidermis layers, and higher skin surface area to body weight ratio, all of which cause increased absorption of substances in contact with the skin.²⁶ Although ACD is more common in productive age groups, children can also be diagnosed with ACD.^{12,25} Allergic contact dermatitis is a close differential diagnosis for juvenile plantar dermatosis (JPD) and often aggravates the pre-existing JPD that mainly affects children aged 3-14 years. Juvenile plantar dermatosis is characterized by shiny, dry, fissured dermatitis of the plantar surface of the forefoot.²⁵ Atopic children and those suffering from juvenile plantar dermatosis (JPD) may become sensitized to footwear chemicals.¹² Patch testing should be performed on children with sole dermatitis to rule out ACD caused by rubber additives, adhesives, and/or chromates (found in leather shoes).²¹ A study by Perumbil et al. analyzed the role of footwear allergy in JPD and found that 52.5% of the subjects used plastic footwear, 25% used leather footwear, and 12.5% used rubber footwear, with most patients presented with erythema and fissuring. The study found that footwear causes flare-ups of JPD in 20% of the patients.²⁵

Rubber comes in both natural and synthetic forms, and sandals may contain a combination of the two.¹⁰ In Indonesia, the straps of flip flops or sandals are frequently made of natural rubber latex, while the insoles are made of neoprene rubber covered with fabric.¹⁴ Lazzarini et al. found that rubber was the most common component of footwear that tested positive in ACD patients (55.2%), with positive results for carba mix,

thiuram mix, PPD mix, 1,3-diphenyl guanidine, para-phenylenediamine, and 4,4-dithiomorpholine. In sandals, rubber can be found in soles and elastics.¹⁹ When rubber chemicals are considered a group, they are the most common allergen in footwear. According to North American Contact Dermatitis Group Study in 2001-2004, the most common allergens found in footwear are carba mix, thiuram mix, mercapto benzothiazole, mercapto mix, mixed dialkyl ureas, and rubber mix. Thioureas are chemical accelerators used to manufacture neoprene and foam rubber, frequently associated with footwear ACD.^{10,12,14,15} Black or gray rubber contains para-phenylenediamine, a common cause of occupational dermatitis.^{9,10,16} Black rubber mix was the most common allergen found in a study of 276 patients with footwear dermatitis by Thyvalappil et al.¹⁶ ACD is also associated with the aromatic diamine 4,4'-diaminodiphenylmethane (DDM), which is commonly used in the production of rubber, plastics, diisocyanates, dyes, and adhesive. DDM is particularly associated with Asian-made footwear.¹⁰

The rubber antioxidant and depigmenting agent hydroquinone monobenzylether may also cause sensitization.¹⁰ Hydroquinone monobenzylether used in footwear has a depigmentary mechanism that leads to leucodermic lesions manifesting as confetti-like or hypopigmented macules.^{14,27} Hydroquinone causes depigmentation by inhibiting the tyrosinase enzyme, DNA replication, and RNA transcrip, directly cytotoxic effect on melanocytes, and causing melanosome degradation. Several studies have reported the occurrence of leucodermic skin lesions following the application of hydroquinone monobenzylether or monomethyl ether.^{11,27} Leucoderma was observed in one of our patients (Case 3) who had suffered from ACD for 5 years, implying that her flip-flop sandals may have contained hydroquinone monobenzylether. However, patch testing is required to confirm this hypothesis. Cyclohexylthiophthalimide has also been found through patch testing as a common rubber allergen.¹⁰ In a Study by Freeman, rubber was the most common cause of allergic shoe

dermatitis (43.1%), followed by potassium dichromate (23.6%), 4-tert-butylphenol formaldehyde resin (PTBFR) (20%), and colophonium (9%).²⁸ Similarly, a study of 64 shoe dermatitis patients in Yogyakarta discovered that rubber allergens, specifically 2-mercaptobenzothiazole and 1,3-diphenyl guanidine, were the most common sensitizers of allergic shoe dermatitis. Most rubber-allergic patients had hyperkeratotic skin lesions frequently associated with rubber.¹⁴

Footwear ACD has also been linked to adhesive sensitivity, although the frequency remains undetermined.¹⁰ Adhesives are important footwear components to attach various shoe or sandals components.¹⁵ An adhesive most often used in footwear production is p-tertiary-butyl-phenol formaldehyde resin (PTBFR) often added in rubber glues and a component of neoprene adhesive used to attach shoe linings and insoles.^{10,15,16} PTBFR accounts for approximately 10-20% of footwear allergies.¹⁵ Colophony, a sap from pine or spruce trees added to natural rubber latex cement, is another common adhesive in footwear. A resin acid known as abietic acid is a key component of colophony. ACD sensitizers are produced during the oxidation of abietic acid.^{3,10,20} Dodecylmercaptan and epoxy resins are two other known allergens in footwear adhesives. Polymerization of diglycidyl ether of bisphenol A (DGEBA) or polymerization of diglycidyl ether of bisphenol F (DGEBF) results in the production of epoxy resins, both of which are associated with ACD of the foot. Foot dermatitis after wearing plastic flip-flops due to the presence of bisphenol A (1% petrolatum) was reported in a study.¹⁰

All of our patients presented with bilateral, symmetrical lesions on the dorsum of the feet and none on the soles. Our findings are consistent with those of other studies. A study by Febriana et al. found that foot eczema most frequently occurred on the dorsum of the feet in 47.6% of patients in Yogyakarta.¹⁴ Similarly, Lazzarini et al. found that the most common location was the dorsum of the feet and toes, as these areas are in closer and longer contact with the shoes, have larger surface areas and have thinner stratum corneum.^{12,14,19} The most frequent location of ACD of the feet is the

dorsum pedis with interdigital sparing and the sole.^{10,12,14,19} The interdigital spaces are often the sites of microbial or fungal infections.¹² Most of the patients observed had skin lesions on the dorsum of their feet where the sandal/slipper strap came into contact with them.¹⁴ ACD of the foot often appears as bilateral and symmetrical dermatitis, although in some cases, patchy and unilateral lesions may be found.^{12,29} These differences might be due to different percutaneous penetration in various anatomical regions.¹² Footwear ACD might also expand beyond the original exposure site through inadvertent contact or auto sensitization.^{12,17} This is demonstrated in Cases 4 and 5, where the lesions extend cranially beyond the dorsum of the feet.

The most important part of footwear ACD treatment is determining the sensitizers and subsequently avoiding them by substituting patients' footwear with ones that do not contain materials that trigger the ACD.^{10,12,20} Patients should be advised to wear hypoallergenic substitute footwear, such as ordering custom footwear that does not contain sensitizers. Injection-molded plastic shoes, wooden shoes, or vinyl shoes may be an alternative for patients allergic to rubber.¹² Patients may reduce contact by using barriers such as barrier socks.¹⁰ Patients may also be educated to avoid re-dyed footwear because they have a higher probability of causing dye leakage.^{14,20} Patients allergic to colophony or 4-tert-butylphenol formaldehyde resin should be advised to wear footwear without or with stitched rather than glued linings.^{12,14}

There are several limitations to our study. Patch-test results were not used to diagnose ACD to flip-flop sandals in our patients. We decided against performing the patch test because all of the patients had clinical manifestations related to using rubber flip-flops. In addition, patch testing kits were difficult to come by in rural areas like ours.

CONCLUSION

We present 7 cases of ACD to flip-flop sandals that manifested as pruritic acute or chronic lesions on the dorsum of the feet after wearing flip-flop sandals. Although patch testing was not performed, the signs

and symptoms developed by all of our patients indicated a strong link between ACD and flip-flop sandals. However, patch testing is still necessary to determine the exact components of the sandals that cause allergic reactions in each patient to provide the most effective management.

ETHICS IN PUBLICATION

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have consented for their images and other clinical information to be reported in the journal. The patient understands that their name and initials will not be published.

CONFLICT OF INTEREST

No conflict of interest.

FUNDING

None.

AUTHOR CONTRIBUTIONS

Authors and co-author are responsible for taking care of, following up with the patients, manuscript preparation, and publication.

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