Pustular eruption on the palms and soles associated with zinc allergy and perspiration

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INTRODUCTION

Persistent pustular eruption localized to the palms and soles may occur in relation to palmoplantar pustulosis, smoking, bacterial infections, metal allergy, and tumor necrosis factor-alfa inhibitors.[1,2] It presents with crops of sterile pustules on an erythemato-squamous background, sometimes accompanied by nonpalmoplantar skin lesions or peripheral/axial arthritis.[1] In certain cases, bacterial infections, including tonsillitis and dental infections, and dental metal allergy to nickel, mercury, and gold may be involved in the pathogenesis of pustular formation.[2] However, it is unknown how metal allergy is related to neutrophilic inflammatory reactions localized to the palmoplantar area. We report a case of pustular eruption on the palms and soles associated with zinc allergy, where sweat containing zinc likely contributed to the development of skin lesions.

CASE REPORT

A 61-year-old Japanese woman presented with 1- to 2-mm pustules with slight pain on the palms and soles. Vesicles, crusts, and scaly erythema were observed during the course of pustules (Fig 1, *A* and *B*). She had been taking a calorie- and nutrient-adjusted liquid diet containing zinc via a gastrostomy tube due to a physical disability. The tracheal cannula and gastrostomy tube were made exclusively of plastic without metals due to a history of unspecified metal allergy. Microscopic examination of pus and scale samples, collected from the affected area and stained with the Parker Quink blue black/potassium hydroxide technique, showed no bacterial and fungal components. Her tonsils were not inflamed, and there was an absence of other oral lesions. Topical 0.05% betamethasone butyrate propionate ointment did not lead to any improvement. Three months later, sternoclavicular joint pain appeared. The pustules further spread to the lower portion of her legs as perspiration increased during her rehabilitation exercises during the summer (Fig 1, *C*).

Metal allergy was investigated by patch testing since she had a total of 10 teeth crowned with metal prostheses and a history of metal allergy. A patch test was performed using a standard metal series (Torii Pharmaceutical Co, Ltd) (Supplementary Data, available via Mendeley at https://data.mendeley.com/datasets/bsx57dysk9/2). Zinc chloride provoked erythema and small pustules at the testing site 48 hours later, although no other metals prompted notable skin reactions (Fig 2, *A*). Later, the patch-induced pustules turned into yellowish crusts and then desquamated, being similar to the clinical course of pustules in the original lesion on the palms and soles. This result suggested a possible association between zinc allergy and pustule development. Her serum zinc level was 49 μg/dL (normal range, 65-110 μg/dL).

Exercise-induced aggravation of her pustules during the summer implied that her eruptions were also sweating-related. To explore the association of her symptoms with perspiration, her arm was wrapped with double-folded polyurethane film to suppress sweat excretion from the sweat pores. Forty-eight hours later, vesicles appeared under the

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Fig 1. A, Pustules, vesicles, and crusts with erythema on the right sole. **B,** A macrophotograph of panel (**A**). **C,** Pustules spread to the lower portion of the legs as her perspiration increased during her exercises in summer.

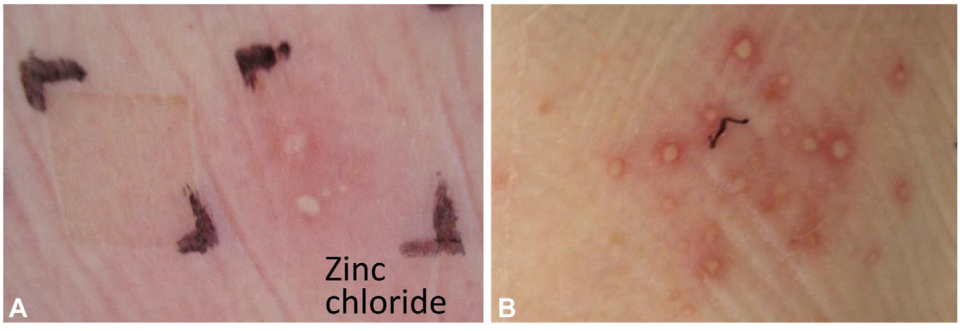

Fig 2. A, Pustule formation at the patch-testing site with zinc chloride (48 hours later). **B,** Pustule and crust formation 6 days after wrapping the patient's arm with polyurethane film.

film followed by the formation of pustules and yellowish crusts (Fig 2, *B*). A skin biopsy specimen obtained from a pustule induced by the film occlusion shared histologic findings with that from the original lesion on the sole of the right foot (Fig 3). In both specimens, subcorneal pustules were filled with neutrophils in the absence of the associated spongiosis in the acanthotic epidermis (Fig 3, *A* and *D*), and neutrophilic microabscesses were found at the periphery of the pustules (Fig 3, *B* and *E*). No bacterial and fungal colonies were observed. Notably, dermal sweat ducts were surrounded and

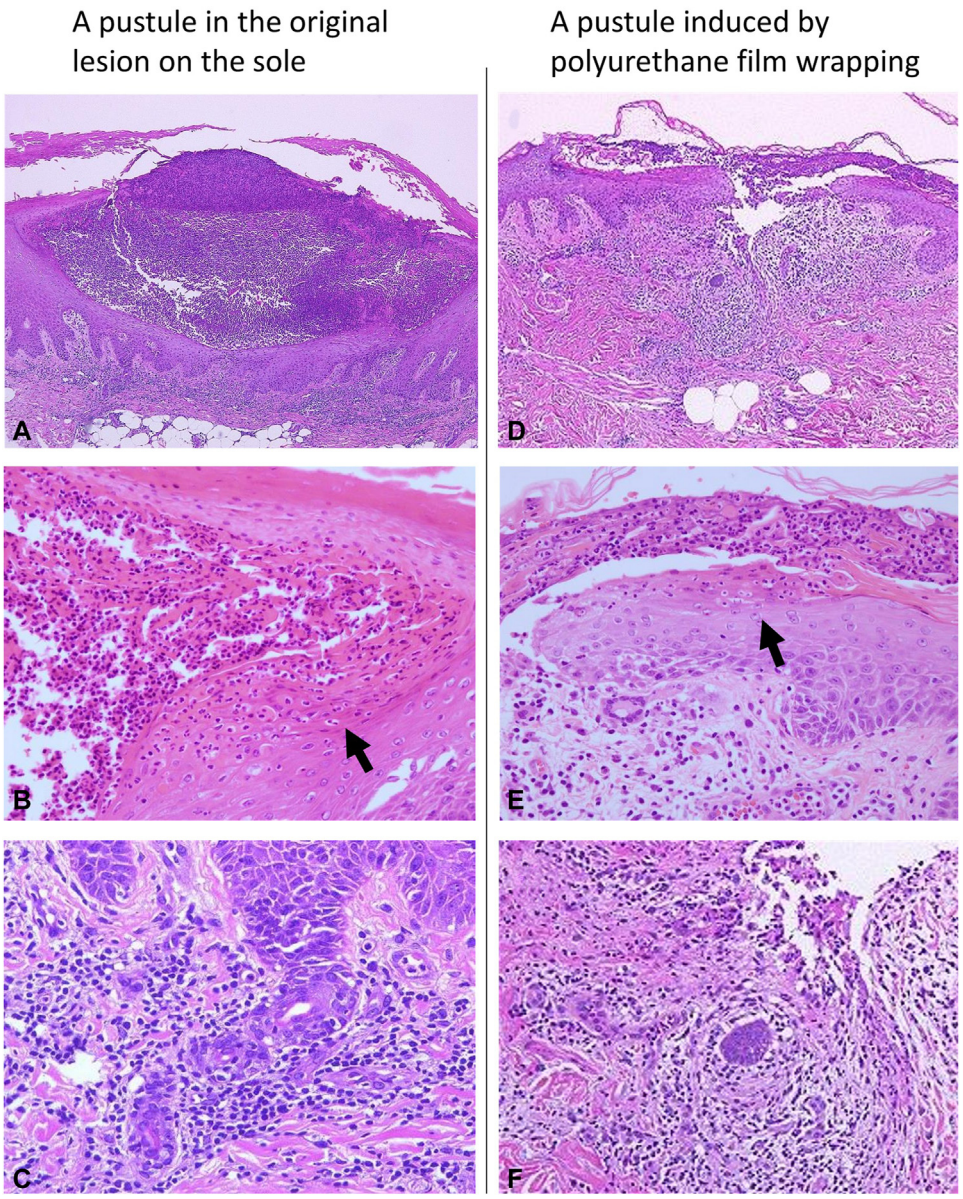

Fig 3. A, A biopsy specimen from the pustule in the sole showed a subcorneal pustule filled with neutrophils and epidermal acanthosis. **B,** Neutrophilic microabscesses (*arrow*) formed on the edge of a pustule in the right sole. **C,** Lymphocytic infiltration was noted in and around the sweat duct in the specimen from the sole. **D,** In a specimen of the pustule induced by film occlusion on the arm, a subcorneal neutrophilic pustule like in panel (**A**) was observed. **E,** Neutrophilic microabscesses (*arrow*) formed in a pustule induced by polyurethane film. **F,** A sweat duct was infiltrated by lymphocytes as seen in panel (**C**).

infiltrated by lymphocytes, implying an association with sweating (Fig 3, *C* and *F*).

X-ray fluorescence spectroscope analysis for metals revealed that 2 of her 10 tooth crowns contained zinc. Removal of the zinc-containing crowns and simultaneous treatment for 1 decayed dental root achieved partial relief of pustules 2 months after the treatment. Finally, reduction of perspiration after completion of her rehabilitation exercise program resulted in complete remission of her symptoms 3 years after the removal of dental zinc. A few years after remission, a positive reaction to zinc chloride was still reproducible by patch testing.

As the patient died and was therefore incapable of giving consent, their next of kin gave consent for the patient's photographs and medical information to be published in print and online and with the

understanding that this information might be publicly available.

DISCUSSION

In this case, the development of pustular eruption on the palm and soles was associated with both zinc allergy and sweating. Like common metal allergens, Yanagi et al[3] reported that zinc allergy was involved in the development of pustules on the palms and soles. In our case, the association of zinc allergy with pustular eruption was supported by reproducible pustule formation in response to patch testing with zinc chloride. Removal of dental metals in some patients with metal allergy has been reported to improve palmoplantar pustules, but its effectiveness is still controversial.[4] Our case showed only a partial response after removing dental zinc; however, reduction of perspiration resulted in complete remission of her pustule lesions, suggesting the involvement of not only zinc allergy but also perspiration.

The contribution of the sweat gland apparatus to pustule formation on the palms and soles has been described in the literature. Murakami et al[5] reported that acrosyringium is the origin of vesicle formation followed by pustulosis. In our case, skin surface occlusion using polyurethane film induced pustules that mimicked the original pustular lesion on the palms and soles. Histologic examination revealed lymphocytic infiltration in and around the dermal sweat ducts. Given that human sweat contains a higher concentration of zinc than serum,[6] and that this may leak into the dermis as observed in several skin diseases,[7,8] it is feasible that the film occlusion promoted sweat leakage with a high concentration of zinc into the dermis from the sweat ducts. Subsequently, the concentrated zinc-containing sweat might allow an allergic reaction around the sweat ducts that leads to cytokine induction, and finally provoke intraepidermal pustules and inflammation under the epidermis. In fact, zinc reportedly increases cytokine secretion more efficiently than other related divalent cations, such as cobalt, nickel, and mercury.[9] Peripheral blood mononuclear cells from patients with zinc allergy stimulated with zinc sulfate also produce significantly higher dose of inflammatory cytokines than healthy controls.[10] Moreover, in our case, the thick corneal layer and increased perspiration in the palm and sole may play a crucial role in retention and leakage of sweat in the dermis, and acral predominance of distribution.

Collectively, this case implies that sweating may contribute to the development of pustular eruption on the palms and soles in a patient with zinc allergy.

X-ray fluorescence spectroscope analysis was carried out at the Center of Oral Clinical Examination at Hiroshima University Hospital.

Conflicts of interest

None disclosed.

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