Case report

Acidic oral environment's potential contribution to palladium-induced systemic contact dermatitis: Case report

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Acidic oral environments may trigger systemic contact dermatitis via ionization of metals, including palladium. A patch test revealed a late delayed positive response to palladium, emphasizing the need for nuanced diagnostic approaches for allergy management. (J Allergy Clin Immunol Global 2024;3:100333.)

Key words: *Systemic contact dermatitis, palladium, patch test, acidic environment, case report*

Systemically administered allergens induce systemic contact dermatitis (SCD), characterized by a spectrum of skin and mucosal reactions.[1] These reactions can be triggered by various allergens, including medications, foods, and dental metals, and identifying the precise cause can be challenging.[2] We report the case of a patient who experienced palmar eruption and oral discomfort several hours to more than a day after consuming acidic substances. Despite negative allergy test results for various food antigens, a patch test revealed a delayed positive response to palladium. Subsequent removal of the patient's metal dental implants led to symptom alleviation. Additionally, mass spectrometry analysis under various pH conditions, including tomato juice consumed by the patient, suggests that palladium ionization in acidic oral environments might contribute to the development of SCD.

Abbreviation used
SCD: Systemic contact dermatitis

A 45-year-old woman with a medical history of asthma, allergic rhinitis, and conjunctivitis presented with a palmar rash and oral discomfort. For 5 years leading up to her initial consultation, she had experienced a chronic sensation of swelling in the oral cavity. Her oral discomfort was exacerbated 3 to 4 hours after consuming tomatoes and tomato juice, which led to the development of vesicles on her palms lasting 3 to 5 days after consumption. Oranges and lemons caused similar symptoms. Given the suspicion of food allergies, the patient was referred to our allergy center. During her first consultation, she exhibited small, pinhead-size vesicles dispersed across her palms and fingertips (Fig 1, *A* and *B*) without evident oral mucosal lesions. The results of pollen- and food antigen–specific IgE tests, as well as prick tests for tomatoes, tomato juice, and ketchup, were all negative except for the test for cedar pollen (0.52 UA/mL). Despite the absence of definitive findings, the timing of symptom onset was consistent with food intake and the fact that the patient had undergone dental metal implantation more than 10 years ago prompted a dermatology consultation. Suspecting SCD due to metal allergy, we performed a metal-series patch test. Seven days after application, the test site exhibited only discoloration, with no signs of erythema, vesicles, or papules (Fig 1, *C*). However, erythema and palpable infiltration, along with itchiness, appeared 2 to 3 weeks later. On day 35 after application, responses corresponding to the application site of palladium chloride were identified (Fig 1, *D*). In view of the patient's allergy to palladium, multiple dental metals in her oral cavity were removed, leading to symptom amelioration. Consequently, the patient was diagnosed with SCD due to dental metal containing palladium. No recurrence of her eruptions or oral discomfort was observed, even with acidic food consumption, in the following 2 years.

Systemic reactions, such as hand dermatitis or generalized eczematous reactions, may arise from exposure to dental metals, including palladium.[3] These are typically mediated by

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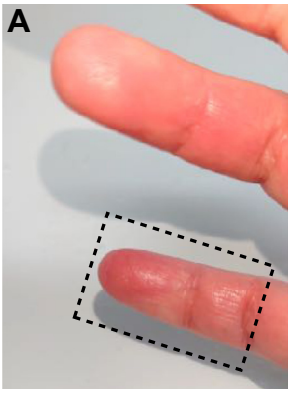
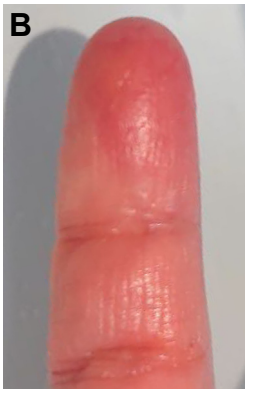
2015 **Onset**

Five years history of oral discomfort and vesicles on palms after consumption of acidic foods

2020 **First visit**



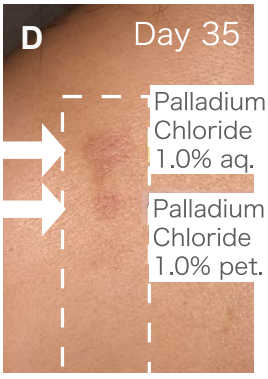


Diagnostic tests

Antigen-specific IgE	Pollen: cedar + Food: negative
Prick tests	Tomato juice, tomatoes, and ketchup: negative

2021 **Metal patch tests**

Delayed positive reaction against palladium



2022 **Removal of dental metals**

Amelioration

Oral discomfort and palmar eruptions resolved without recurrence after consumption of acidic foods

FIG 1. Case report timeline with clinical and patch test findings. **A** and **B**, Presentation of small, pinhead-sized vesicles scattered across the patient's palms and fingertips. **C,** Metal patch test site showing only discoloration at the site of palladium chloride application (*white arrows*) on day 7 after application. **D,** Erythema and palpable infiltration evident on day 35, indicating a delayed hypersensitivity reaction against palladium.

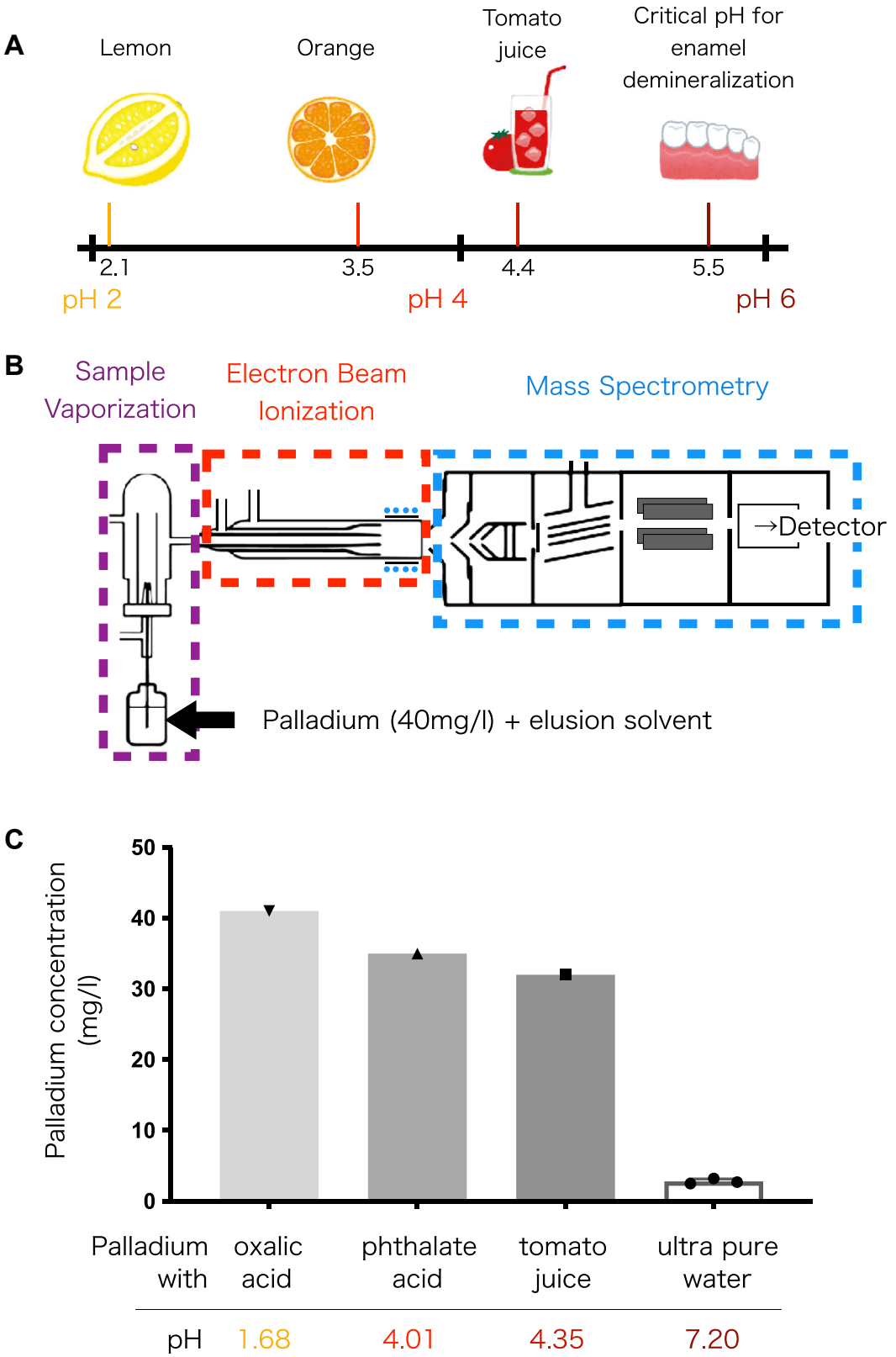


FIG 2. Analysis of palladium ionization under various pH conditions via inductively coupled plasma mass spectrometry. **A,** Graphic schema illustrating the pH levels of various acidic substances and highlighting the acidic nature of common foods. **B,** Schematic representation of the inductively coupled plasma mass spectrometry analytic method used to assess palladium ionization. **C,** Results depicting palladium concentration in the leachate obtained by using different acidic solvents, demonstrating the ionization behavior of palladium under varied pH conditions.

delayed-type hypersensitivity, identified primarily through patch testing. Although patch tests are a fundamental diagnostic tool for allergic contact dermatitis, their results may vary, potentially resulting in underestimation of the prevalence of palladium sensitivity.[4] Notably, in our case, the patient did not exhibit a reaction within the standard 1-week period but did demonstrate a positive response 2 to 3 weeks after application. Although its mechanism remains unknown, this late delayed reaction is reminiscent of findings similar to those reported for gold, suggesting the need to adjust the timing of interpreting patch test results based on the specific metal and other relevant factors.[5] Such considerations are crucial for the accurate diagnosis of metal-induced allergic reactions and underscore the need for a nuanced understanding of the temporal dynamics of hypersensitivity responses.

Our study also investigated the correlation between the consumption of "sour foods" and the occurrence of palladium-induced SCD. In a cohort of 925 individuals suspected of having dental metal allergies, 14.8% exhibited positive results of patch tests to palladium.[6]

Palladium chloride can form palladium chloride ions under acidic conditions such as exposure to lactic acid at pH 4, which have been implicated in allergic sensitization and reactions.[7,8] We compiled the pH levels of various foods into a graphic representation, as shown in Fig 2, *A*, illustrating that the pH values for lemon, orange, and tomato juice are approximately 4 or less. This suggests that the ingestion of these acidic foods may lower the pH of the oral cavity, potentially facilitating the onset of allergic symptoms.

To test this hypothesis, we conducted an *in vitro* analysis to examine the ionization of palladium under acidic conditions. Palladium chloride, the same compound found in the patch testing reagents, was selected as the test sample (Torii Pharmaceutical Co, Tokyo, Japan). The elution solvents used were an oxalic acid standard solution at pH 1.68 (Nacalai Tesque, Inc, Kyoto, Japan), a phthalate buffer at pH 4.01 (Wako Co, Ltd, Tokyo, Japan), 100% tomato juice at pH 4.35 (Kagome Co, Ltd, Aichi, Japan), and ultrapure water at pH 7.20. Inductively coupled plasma mass spectrometry (Agilent Technology, Santa Clara, Calif) was utilized to analyze the anatomic process.[9] After 24 hours of exposure of palladium to each solvent, the leached sample solution was vaporized and the electron beam–ionized elements were detected and quantified by mass spectrometry, as depicted in Fig 2, *B*. Although the complete dissolution of palladium would result in a concentration of approximately 40 mg/L, the rate of detection in water at pH 7.20 was less than 10%. Our findings demonstrated that nearly all palladium was ionized in the oxalic acid solution at pH 1.68 and approximately 90% was ionized in the phthalate buffer at pH 4.01 (Fig 2, *C*). Despite the exposure duration exceeding that typical *in vivo* conditions, approximately 80% of the palladium was ionized after exposure to tomato juice, underscoring the significant ionization potential of palladium in acidic environments similar to those found in dietary substances.

Collectively, although the initial investigations focused on food allergies as a potential cause of the patient's symptoms, the late delayed positive patch test result for palladium redirected our focus toward SCD due to palladium. Our findings highlight the need to adjust the timing of interpreting patch test results based on the specific metal in question and to explain the potential risks of SCD before dental metal treatment. Furthermore, this case underscores the importance of considering not only food allergies but also the potential for SCD induced by dental metal ionization in acidic oral environments. This comprehensive diagnostic approach (see Fig E1 in this article's Online Repository at www.jaci-global.org) is crucial for the accurate diagnosis and effective treatment of affected individuals.

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