



# Recurrent palmo-plantar pustulosis at the site of insertion of therapeutic titanium

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**Recurrent palmoplantar pustulosis at the site of insertion of therapeutic titanium**

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24   The patients in this manuscript have given written informed consent.

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26   the manuscript. T.F. and A.Y. contributed to data collection and interpretation of the

27   results. All authors have read and approved the final manuscript.

28   **KEYWORDS:** metal allergy, titanium, palmoplantar pustulosis (PPP), dermcidin

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39 ***Dear Editor,***

40 Palmoplantar pustulosis (PPP) is a refractory inflammatory disease characterized  
41 by pustular eruptions on the palms and soles.<sup>1-3</sup> The etiology of PPP is unknown, but it  
42 may be caused by metal allergy, tonsilitis, and smoking.<sup>1-4</sup> The mechanism by which  
43 metal allergy causes PPP has not been elucidated yet. A systematic review of 519  
44 patients with PPP revealed that metal allergens triggered PPP.<sup>3</sup> Conversely, another  
45 retrospective analysis suggested that dental metal removal did not improve PPP  
46 symptoms.<sup>1</sup> Herein, we report a case with PPP presenting with recurrence of  
47 non-bacterial pustular eruptions only at the site of insertion of therapeutic titanium for  
48 bone fracture healing.

49 A 62-year-old man had PPP on the palms and soles for 15 years and had been  
50 in remission at the time of the present case report. The patient had a bone fracture in his  
51 left lower leg, which was treated with a therapeutic titanium implant. After 5 months, he  
52 presented with non-bacterial pustular eruptions with erythematous scaling only at the  
53 site of insertion of therapeutic titanium (Figure 1a–e). The skin biopsy from the pustule  
54 on the left lower leg showed PPP manifestations (Figure 1f). First, we hypothesized that  
55 the operation led to an eccrine sweat glands disorder resulting in sweat leakage in the  
56 dermis of the affected area. However, a thermoregulatory sweat test using the

starch-iodine method with sweating revealed neither hypohidrosis nor hyperhidrosis of the affected area (Figure 1g–h).<sup>5</sup> Moreover, immunohistochemical staining for dermcidin, the major sweat antimicrobial peptide, did not show sweat leakage (Figure 1i–j).<sup>5</sup> The patch test with metal allergens revealed the erythema result for titanium and iron, both of which are included in the insertion although the iron content is low (<1%) (Figure 1k). Patient's symptoms responded to the difluprednate ointment, but when the treatment was discontinued the symptoms recurred.

PPP may be caused by various factors.<sup>1,3,4</sup> In the present study, we showed that the potential contribution of metal allergy to the etiology of PPP is in line with the systematic review by Brunasso et al.<sup>3</sup> However, no similar cases have been reported and it is difficult to confirm whether a metal allergy is the main cause, because therapeutic titanium cannot be removed from the bone. Also, it is challenging to propose a mechanism explaining how it would lead to the symptoms of PPP. Although titanium allergy is rare, titanium used for orthopedic surgery for left distal radius fracture reportedly led to PPP.<sup>4</sup> Murakami et al. performed the immunohistochemical staining of dermcidin as a marker for sweat secretion and revealed the contribution of the abnormal eccrine sweating to PPP.<sup>2</sup> However, the sweat secretion, as well as sweat function, were normal in this case. Further studies are needed to elucidate the mechanism through

75 which metal allergies cause PPP, and whether the Koebner phenomenon by bone  
76 fracture and/or operation may induce a PPP lesion. Nevertheless, our results show the  
77 potential contribution of metal allergy to PPP etiology.

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## References:

1. Kouno M, Nishiyama A, Minabe M, et al. Retrospective analysis of the clinical response of palmoplantar pustulosis after dental infection control and dental metal removal. *J Dermatol.* Jun 2017;44(6):695-698. doi:10.1111/1346-8138.13751
2. Murakami M, Ohtake T, Horibe Y, et al. Acrosvringium is the main site of the vesicle/pustule formation in palmoplantar pustulosis. *J Invest Dermatol.* Aug 2010;130(8):2010-6. doi:10.1038/jid.2010.87
3. Brunasso Verneti AMG, Puntoni M, Massone C. Palmoplantar Pustulosis and Allergies: A Systematic Review. *Dermatol Pract Concept.* Apr 2019;9(2):105-110. doi:10.5826/dpc.0902a05
4. Kono T, Oda T, Akaiwa K, Nakamura K, Sasaoka K, Tanaka H. Remission of Palmoplantar Pustulosis after On-Pump Coronary Artery Bypass Grafting in a Patient with Titanium Allergy. *Ann Thorac Cardiovasc Surg.* Jun 20 2020;26(3):170-173. doi:10.5761/atcs.cr.18-00031
5. Fukumoto T, Tsuchiyama S, Fukunaga A, Nishigori C. Hypohidrosis and metal allergy: Trigger factors for unilateral lichen planus. *J Dermatol.* Aug 2017;44(8):963-966. doi:10.1111/1346-8138.13836

**Figure 1. Clinical and histopathological findings of the patient with palmoplantar pustulosis at the site of insertion of therapeutic titanium in the left lower leg**

(a–e) Clinical appearance of palmoplantar pustulosis at the site of insertion of therapeutic titanium in the left lower leg, showing pustular eruptions with erythematous scaling.

(f) Hematoxylin and eosin staining of the skin biopsy from the left lower leg, showing a micro abscess in the epidermis with inflammatory cell infiltration. [ $\times 20$ , scale bar = 500  $\mu\text{m}$ ]

(g, h) No significant difference was observed in the number of black dots as perspiration points between the soles of the feet.

(i, j) Immunohistochemical staining of dermcidin (mouse monoclonal antibody to dermcidin [G-81]; Santa Cruz Biotechnology, Dallas, TX) showing no significant sweat leakage in the affected area. [i:  $\times 40$ , scale bar = 500  $\mu\text{m}$ , j:  $\times 200$ , scale bar = 100  $\mu\text{m}$ ]

(k) The patch test reaction using titanium (10.0 % Titanium in petrolatum, Cat. T-042, CHEMOTECHNIQUE DIAGNOSIS, Sweden) showed the slightly edematous erythema.



