Systemic Nickel Allergy Presenting as Papuloerythroderma-like Eruptions

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Accepted May 25, 2010.

Papuloerythroderma is characterized by erythroderma with widespread coalescent solid or lichenoid papules, and eruptions often spare skin folds. Below is reported an old women experiencing pruntic pupules for a long period.

CASE REPORT

An 82-year-old woman had had pruritic papules on her entire body for 4 years. Her medical history included hypertension controlled with cilnidipine. On examination, there were numerous red-brown lichenoid papules on her trunk and extremities. The papules tended to aggregate or coalesce to form diffuse erythematous plaques with sparing flexors, mimicking papuloerythroderma (Fig. 1). Laboratory data revealed elevated levels of blood eosinophils (1204/μl) and lactate dehydrogenase (354 U/l), but no other abnormal findings. Histologically, lichenoid papules showed irregular acanthosis with hyperkeratosis. There was a cellular infiltrate comprising lymphocytes and eosinophils in the upper dermis (Fig. 2). Extensive examinations, including serum tumour markers, computed tomography and fiberscope examination of the gastrointestinal tract, did not reveal any evidence of internal malignancy. The condition had been resistant to topical corticosteroids prior to admission, but the skin lesions improved after external application of petrolatum and without cessation of cilnidipine. Lymphocyte stimulation test and patch-testing for cilnidipine (10% and 20% in petrolatum) were negative. She did not have a history of allergic reactions to metals. However, patch-testing for metals revealed positive reactions for $NiSO_4$ (5% aq) and $K_2Cr_2O_7$ (0.5% aq) at 48 h, 72 h and 7 days. Oral challenge test with 12 mg $NiSO_4 \cdot 6H_2O$ (2 mg Ni) (1, 2) induced diffuse erythema with pruritus on her trunk and extremities, but similar effects were not seen with 7.5 mg K_2CrO_4 (2.5 mg Cr) or placebo control (NaCl 10 mg) (Fig. 3); the reaction peaked at 2 days after challenge. Examination revealed that her dental materials contained nickel, as determined by X-ray fluorescence spectroscope. In addition, the patient had been consuming boiled Japanese barnyard millet as part of her diet. She was advised to avoid this food and to commence a low-nickel diet (3) together with sodium chromoglycate.

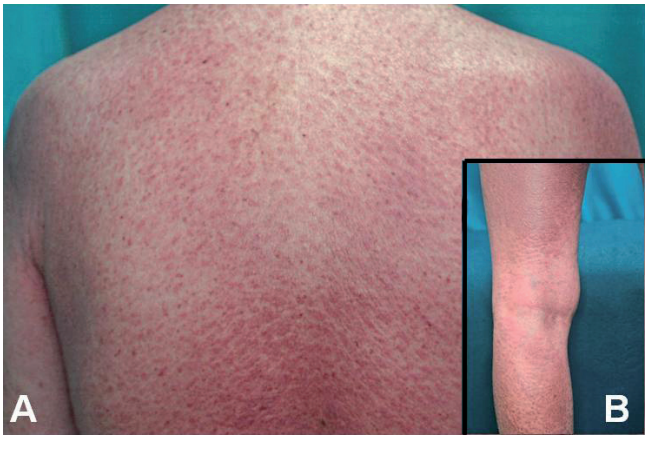

Fig. 1. Clinical features of skin lesions. (A) Numerous lichenoid papules were distributed on the trunk. (B) Eruptions spared popliteal fossa.

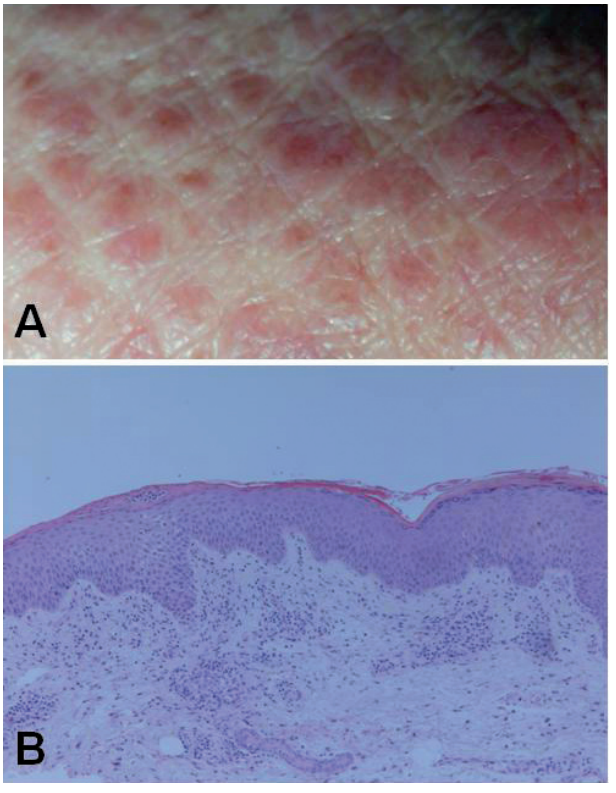

Fig. 2. Clinical and histological manifestations of lichenoid papules. (A) Polygonal, red, solid papules on the arms. (B) Papules showed parakeratotic hyperkeratosis and acanthosis with dermal cellular infiltrates. (Haematoxylin and eosin staining, original magnification ×100).

DISCUSSION

Papuloerythroderma was first described by Ofuji et al. (4). Papuloerythroderma has been reported to be associated with internal malignancy (5, 6), and recent reports have shown that it may occur due to ingestion of aspirin or furosemide (7, 8). The present case exhibited papuloerythroderma-like eruptions characterized by aggregated lichenoid papules on the entire body, but it was intriguing that the present patient had a nickel allergy, as demonstrated by the positive skin patch-test and oral challenge test with $NiSO_4$. Nickel is known to be a common cause of contact allergies, and it is present in various metal compounds, such as coins, ornaments, utensils and dental braces. Systemic intake of nickel can induce pompholyx and/or systemic contact dermatitis (9, 10). However, we are not aware of any

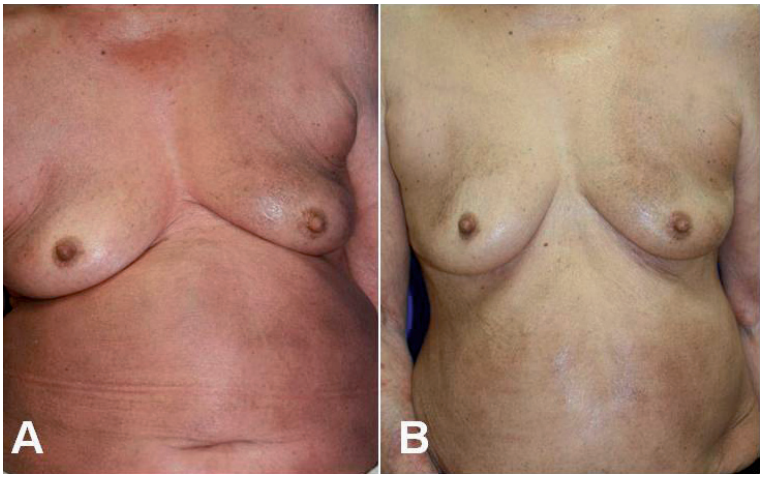

Fig. 3. Oral challenge test. (A) Twenty-four hours after challenge with $NiSO_4$. Diffuse erythema on the trunk. (B) Challenge with placebo control (NaCl). No erythema.

prior reports of papuloerythroderma-like eruption as a systemic symptom.

Notably, the patient had been consuming boiled Japanese barnyard millet as a health supplement, which contains large amounts of nickel (535 μg/100 g) (3). It was estimated that her nickel intake was 160 μg/day. Thus, in our patient, this health supplement could have been a major source of nickel that may have caused skin symptoms, although nickel derived from dental braces might also have contributed to some extent. This notion was supported by the finding that skin symptoms improved after hospitalization with the cessation of Japanese barnyard millet, and the removal of dental braces was not necessary.

Oral challenge with $NiSO_4 \cdot 6H_2O$ induced acute diffuse erythema, but not lichenoid papules. Continuous administration of nickel may be required for the gradual development of papular lesions characteristic of papuloerythroderma.

The present case suggests that eruptions presenting as papuloerythroderma may be a manifestation of a systemic allergy to metals, in addition to indicating an underlying malignancy, or a reaction to drugs.

The authors declare no conflict of interest.

REFERENCES

1. Veien NK, Hattel T, Justesen O, Norholm A. Oral challenge with metal salts. (I). Vesicular patch-test-negative hand eczema. Contact Dermatitis 1983; 9: 402–406.
2. Veien NK, Hattel T, Justesen O, Norholm A. Oral challenge with metal salts (II). Various types of eczema. Contact Dermatitis 1983; 9: 407–410.
3. Takamatsu N, Arita T, Muramatsu T. Dietary management of systemic metal allergy: metal content of nickel, chromium, cobalt, and zinc in substitute foods for food allergy and health-promoting foods. J Environ Dermatol Cutan Allergol 2008; 2: 167–172.
4. Ofuji S, Furukawa F, Miyachi Y, Ohno S. Papuloerythroderma. Dermatologica 1984; 169: 125–130.
5. Nazzari G, Sabattini C. Ofuji's papuloerythroderma. An association with early gastric cancer. Eur J Dermatol 1999; 9: 317–318.
6. Schepers C, Malvehy J, Azon-Masoliver A, Navarra E, Ferrando J, Mascaro JM. Papuloerythroderma of Ofuji: a report of 2 cases including the first European case associated with visceral carcinoma. Dermatology 1996; 193: 131–135.
7. Sugita K, Kabashima K, Nakashima D, Tokura Y. Papuloerythroderma of Ofuji induced by furosemide. J Am Acad Dermatol 2008; 58 Suppl 2: S54–55.
8. Sugita K, Koga C, Yoshiki R, Izu K, Tokura Y. Papuloerythroderma caused by aspirin. Arch Dermatol 2006; 142: 792–793.
9. Dou X, Liu LL, Zhu XJ. Nickel-elicited systemic contact dermatitis. Contact Dermatitis 2003; 48: 126–129.
10. Guillet MH, Wierzbicka E, Guillet S, Dagregorio G, Guillet G. A 3-year causative study of pompholyx in 120 patients. Arch Dermatol 2007; 143: 1504–1508.