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Title: Unusual post-patch testing erythema: a late, granulomatous, non-eczematous reaction to gold sodium thiosulfate

Running head: Late, granulomatous reaction to GSTS

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In patch testing, delayed reactions at day 7 or later are regarded as “late reactions”.¹ Neomycin, corticosteroids, paraphenylenediamine and gold are well-known allergens of late reactions.^{1,2} Of these, reactions to gold sodium thiosulfate (GSTS) can be significantly delayed, and some cases have been reported to be accompanied with granulomatous changes.^{3,4} Clinical reports of this reaction to GSTS are very limited. Here, we report a case of granulomatous reaction to GSTS, and we review the literature to reveal the features of this phenomenon.

A 54-year-old man presented to our department with a 7-day history of a strange eruption on the upper back (Fig. 1a). He had no remarkable medical history except for contact dermatitis on the scalp due to shampoo. The dermatitis was improved by topical steroid administration and shampoo cessation.⁵ As part of the diagnosis and medical tests for contact dermatitis due to the shampoo, we performed the standard patch test series (Sato Pharmaceutical Co., Ltd., Tokyo, Japan). At 2, 3, and 7 days, the test was negative for all ingredients. He noticed the eruption on the back 28 days after attaching patch-test chemicals. Examination revealed square, palpable erythema on the upper back (Fig. 1a). The lesion arose at the site of GSTS from the patch test. There were no other obvious eruptions. The skin biopsy specimen from the square erythema showed subepidermal and deep perivascular lymphocytic and histiocytic infiltration (Fig. 1b, 1c). Lymphocytes showed

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epidermotropism with vacuolar alterations; however, there were no signs of dermatitis, including

spongiosis (Fig. 1c). Multinucleated giant cells were also seen (Fig. 1d). The infiltrates contained

CD3⁺ T-cells (Fig. 1e) and CD68⁺ histiocytes (Fig. 1f). Based on these findings, the skin lesion was

diagnosed as a late reaction to GSTS. The eruption was totally excised.

There have been only 3 other cases of granulomatous reactions to GSTS.^{3,4} We reviewed all cases

including the present case, revealing that they have the following unique characteristics: (1) The

lesion appeared at 12 to 33 days after patch testing, (2) the lesion was limited to the site of the GSTS

patch test, (3) there were no histological findings of dermatitis, and (4) there was perivascular

lymphocytic infiltration in the dermis with granuloma formation.^{3,4}

The etiology and epidemiology of this phenomenon remain unknown. Of note, significantly delayed

reactions to GSTS are known to occur in people without apparent contact allergy to golds.⁴ In the

present case, the patient had no history of metal allergy. We did not try gold challenge test such as

wearing a golden ring, because he already had dental filling consist of gold. His dental metal filled 15

years earlier than his visit, and no mucosal or skin symptoms suggestive of metal allergy were noted.

We suspect that the late and granulomatous reaction to the gold sodium thiosulfate does not suggest

gold allergy. Thus, further investigations are needed to clarify the relationship between this delayed

positive reaction and true gold allergy.

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In summary, our case report and review suggests that patch-testing with GSTS can induce significantly delayed reactions with granulomatous formation. We dermatologists should pay attention to the testing region for an additional period to detect this phenomenon.

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Figure Legends

Fig.1. Late, granulomatous and non-eczematous reaction to patched gold sodium thiosulfate (GSTS).

(a) Palpable erythema on the site of patch-tested GSTS at day 35. The patient noticed this erythema at day 28.

The square erythema is flat and pale at day 2 (ICDRG: +?) and day 3 (+?), but is not apparent at day 7 (-).

(b) The histopathology of the square erythema on the back. The specimen shows subepidermal and deep perivascular lymphocytic infiltration with a focal aggregation of histiocytes. (c) The epidermis shows infiltration of lymphocytes, without spongiosis. (d) A multinucleated giant cell is also seen. (e, f) The infiltrates contain CD3⁺ T-cells and CD68⁺ histiocytes.

