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Shiitake Dermatitis-like Eruption Due to Tegafur/Gimeracil/Oteracil Combination Usage

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ABSTRACT
S-1 is a combination drug of tegafur, gimeracil and oteracil potassium that is designed on the basis of 5-fluorouracil. We report here for the first time that S-1 is a causative agent of drug eruption mimicking shiitake dermatitis. A 58-year-old Japanese man presented with pruritic erythemas arranged in a linear fashion. He had been treated with S-1 for esophageal cancer. Although differential diagnosis included shiitake dermatitis and dermatomyositis, he had not eaten raw shiitake mushroom, and he did not have other cutaneous lesion such as Gottron's sign and abnormalities of peripheral blood examination including Jo-1 antibody and antinuclear antibody. Histopathological examination revealed necrotic keratinocytes in the Malpighian layer, vacuolar change in the basal layer, and lymphocytic and eosinophilic infiltration in the upper dermis. Based on clinical and histological findings, we made a diagnosis of drug eruption due to S-1.

Key words dermatomyositis; drug eruption; linear erythema; shiitake dermatitis; S-1

Tegafur/gimeracil/oteracil (S-1) is a combination drug that is designed on the basis of 5- fluorouracil (5-FU). It is used for treatment of patients with various cancers such as gastric, head and neck, lung and pancreatic cancers.[1–3] S-1 is used as a single agent or in combination with platinum-base anticancer drugs such as cisplatin. For FU agents, such as 5-FU, tegafur and tegafur/uracil (UFT), drug eruptions of discoid lupus erythema-like and photosensitive types are well known, but linear erythema or scratch dermatitis type is extremely rare.[4] Here we present a rare case of drug eruption due to S-1 showing a unique skin eruption of linear erythema and scratch marks that were almost identical to shiitake dermatitis.

PATIENT REPORT
A 58-year-old man presented with pruritic erythemas arranged in a linear fashion. He received with S-1 monotherapy for esophageal cancer. One month after administration of the drug, he developed rashes on his trunk and extremities. He was referred to us for evaluation. His medications included S-1 and loratadine. On physical examination, multiple, pruritic linear erythemas and papules were seen on his trunk and extremities (Fig. 1a). There was no Gottron's sign, heliotrope rush, elongation of the epionychium or muscle weakness. He had no previous history of intake of raw shiitake mushroom. Results of peripheral blood examinations including Jo-1 antibody and antinuclear antibody were all within normal ranges. We did not perform drug-induced lymphocyte stimulation test. A skin biopsy specimen taken from the upper back revealed necrotic keratinocytes in the Malpighian layer, vacuolar change in the basal layer, and infiltrate of lymphocytes in the upper dermis intermingled with eosinophils (Fig. 1b). Because of our tentative diagnosis of drug eruption, administration of S-1 was discontinued. He was treated with topical clobetasol ointment and olopatadine. The skin eruption gradually improved within 1 month and therapy was discontinued without any recurrence of the eruption. However, after restarting treatment with S-1, his eruption deteriorated, and it was thus concluded that S-1 was the causative agent in our patient.

DISCUSSION
Shiitake dermatitis is caused by the consumption of raw shiitake mushroom and it shows flagellate erythema.[5, 6] Histologically, however, our case exhibited necrotic keratinocytes in the epidermis and infiltration of lymphocytes and eosinophils in the dermis, suggesting a drug eruption rather than shiitake dermatitis, which is histologically characterized by a spongiotic epidermis, papillary dermal edema and lymphocytic infiltration.[6] Such a necrotic change of keratinocytes had been found in acute cutaneous reactions including drug eruptions. Bleomycin is a representative drug inducing flagellate erythema and the presence of necrotic keratinocytes in the epidermis as in our case.[7]

Dermatomyositis is also an important differential

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Abbreviations: 5-FU, 5-fluorouracil; S-1, Tegafur/gimeracil/oteracil; UFT, tegafur/uracil

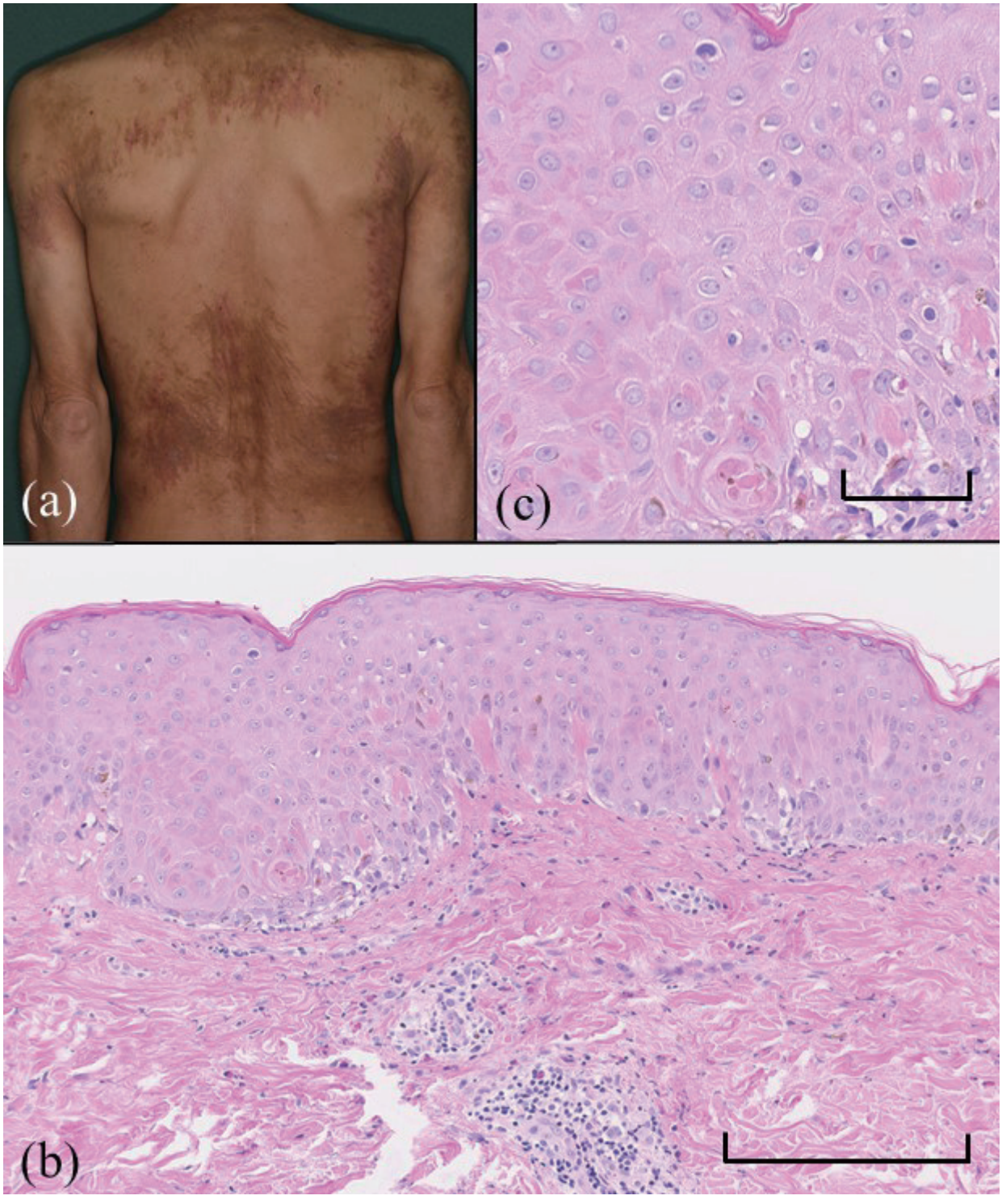

Fig. 1. a: Physical findings. Linear erythemas and scratch marks were seen on the patient's trunk.
b: Histopathological findings. Marked necrotic keratinocytes were seen in the Malpighian layer (H&E staining). Bar = 200 μm.
c: Marked necrotic keratinocytes were seen (H&E staining). Bar = 50 μm.
H&E, hematoxylin and eosin.

diagnosis of linear erythema of trunk. Furthermore, dermatomyositis is sometimes related with malignant tumor and this patient had esophageal cancer. Histopathologically, liquefaction in basal layer, dermal edema and mucin deposition in the dermis are characteristics of dermatomyositis. In addition, necrotic keratinocytes which were seen in our patient are occasionally found in patients with dermatomyositis.[8] Therefore, there is a possibility of dermatomyositis as a differential diagnosis in our patient. However, there was no other cutaneous lesion such as Gottron's sign, heliotrope rush or elongation of epionychium, and the result of blood examination did not support the diagnosis of dermatomyositis. Thus, we excluded the possibility of dermatomyositis.

Since S-1 is a combination anticancer agent consisting of drugs of tegafur, gimeracil and oteracil potassium, we could not specify the causative agent. However, our case provided an important implication that an anticancer drug, S-1, may show flagellate erythema mimicking shiitake dermatitis.

The authors declare no conflict of interest.

REFERENCES

1 Yamanaka T, Matsumoto S, Teramukai S, Ishiwata R, Nagai Y, Dukushima M. Safety evaluation of oral fluoropyrimidine S-1 for short- and long-term delivery in advanced gastric cancer: analysis of 3,758 patients. Cancer Chemother Pharmacol. 2008;61:335-43. PMID: 17922276.

2 Ueno H, Okusaka T, Furuse J, Yamao K, Funakoshi A, Boku N, et al. Multicenter phase II study of gemcitabine and S-1 combination therapy (GS Therapy) in patients with metastatic pancreatic cancer. Jpn J Clin Oncol. 2011;41:953-8. PMID: 21715364.

3 Kader A, Miyatani K, Takaya S, Matsunaga T, Fukumoto Y, Osaki T, et al. Changes in Standard Treatments and Postoperative Outcomes for Advanced Gastric Cancer at One Institute over an 11-Year Period. Yonago Acta Med. 2015;58:77-80. PMID: 26306057.

4 Adachi A, Nagai H, Horikawa T. Anti-SSA/Ro antibody as a risk factor for fluorouracil-induced drug eruptions showing acral erythema and discoid-lupus-erythematosus-like lesions. Dermatology. 2007;214:85-8. PMID: 17191054.

5 Chu EY, Anand D, Dawn A, Elenitsas R, Adler DJ. Shiitake dermatitis: a report of 3 cases and review of the literature. Cutis. 2013;91:287-90. PMID: 23837150.

6 Mendonca CN, Silva PM, Avelleira JC, Nishimori FS, Cassia Fde F. Shiitake dermatitis. An Bras Dermatol. 2015;90:276-8. PMID: 25831007.

7 Biswas A, Chaudhari PB, Sharma P, Singh L, Julka PK, Sethuraman G. Bleomycin induced flagellate erythema: Revisiting a unique complication. J Cancer Res Ther. 2013;9:500-3. PMID: 24125992.

8 Mendese G, Mahalingam M. Histopathology of Gottron's papules--utility in diagnosing dermatomyositis. J Cutan Pathol. 2007;10:793-6. PMID: 17880586.