SHORT COMMUNICATION

Mucosal Fixed Drug Eruption with Oral, Conjunctival, Nasal, and Anal Lesions: A Case Report

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Fixed drug eruption (FDE) is a localized variant of drug eruption that recurs at the same sites each time the causative drug is administered (1, 2). Cases of mucosal FDE (excluding the lips) without any skin involvement are extremely rare (1, 3). A previous study reported oral mucosal involvement in 17 of 450 cases of FDE (3.77%) (4). The palate and tongue are the most commonly affected sites in such cases (1, 5).

We report here an extremely rare case of mucosal FDE caused by ofloxacin, which presented with multiple oral lesions, including on the lips, buccal and gingival mucosae, tongue, and palate, accompanied by conjunctival, nasal and perianal lesions. No cases of mucosal FDE in which both the oral mucosa and other mucosae were affected have been reported previously.

CASE REPORT

A 62-year-old Japanese man in general good health had developed painful erosions in his oral cavity, nose, and perianal area, together with bilateral conjunctival hyperaemia 3 weeks prior to presentation. He had no known allergies and no history of smoking. Physical examination revealed erosions and ulcers on the lips; buccal, gingival, and glossal mucosae; and palate (**Fig. 1**a), as well as on the nasal and perianal mucosae (Fig. 1b). There were no cutaneous lesions.

As the patient denied taking any medication, mucous membrane pemphigoid (MMP) or paraneoplastic pemphigus (PNP) were considered. Laboratory tests, including complete blood count, liver and renal function, did not produce any significant findings. Enzyme-linked immunosorbent assays for antibodies to desmoglein (Dsg) 1, Dsg 3, BP180, BP230, and collagen VII were negative. Histopathological examinations of the tongue lesion revealed an ulcer and dense subepithelial infiltrates of inflammatory cells, including lymphocytes and neutrophils (Fig. 1c). Direct immunofluorescence (DIF) was negative. Indirect immunofluorescence (IIF) of normal human skin and 1M NaCl-split-skin was also negative. In immunoblot analyses using normal human epidermal extracts, immunoglobulin A (IgA) antibodies in the patient's serum reacted markedly with 210-kDa envoplakin and weakly with 190-kDa periplakin (Fig. 1d). Immunoblotting using normal human dermal extracts showed weak IgA reactivity with 200-kDa p200/laminin γ1 (Fig. 1e). No malignancy was suspected on whole-body computed

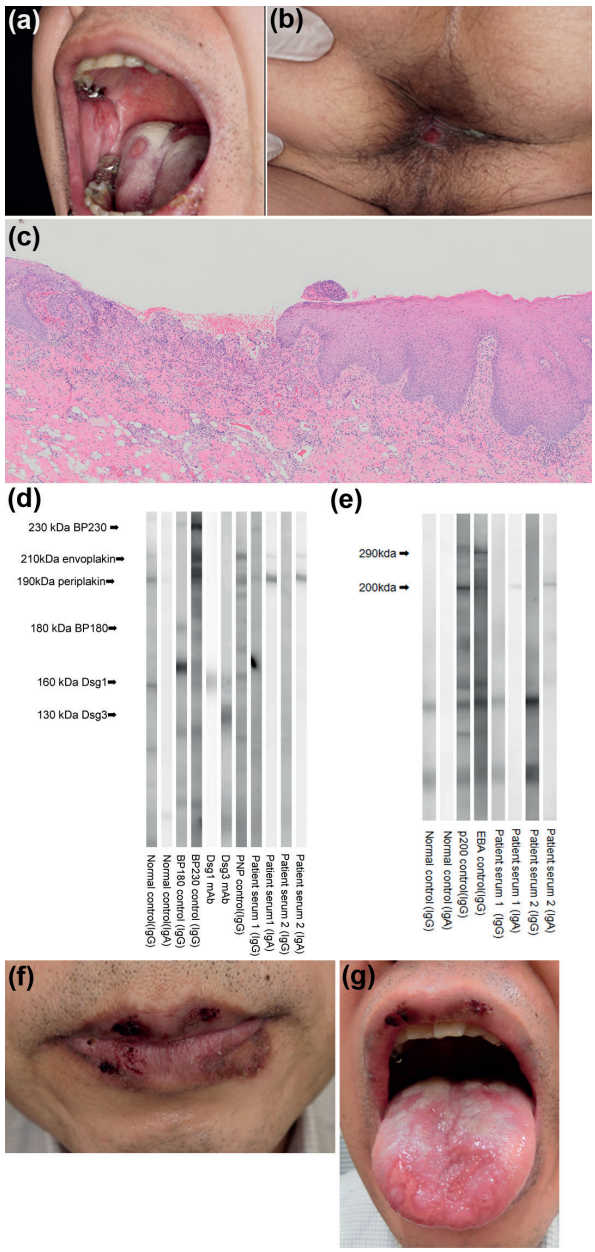

Fig. 1. Clinical and histopathological findings and the results of immunoblot analyses. (a, b) Clinical features at the first examination. Multiple oral mucosal lesions (a) and ulcerated perianal lesions (b) were seen. (c) Histopathological findings of a biopsy of the tongue lesion (haematoxylin & eosin, ×40). (d, e) Immunoblot analysis. (d) Normal human epidermal extract demonstrated marked IgA reactivity with 210-kDa envoplakin and weak IgA reactivity with 190-kDa periplakin. (e) Normal human dermal extracts showed weak IgA reactivity with 200-kDa p200/laminin γ1. (f, g) Clinical findings at the last episode. Haemorrhagic erosions coated by crusts were seen on the lip (f), and extensive erosions and ulcers were noted on the tongue (g).

tomography. These results were not indicative of MMP or PNP. Because the patient had difficulty in eating due to the oral erosions, oral prednisolone was considered. The initiation of treatment with 20 mg/day prednisolone resolved the mucosal lesions, and hence, the prednisolone was tapered and stopped within 2 weeks.

However, the patient experienced 3 more episodes of similar lesions at 3, 8 and 10 months after the first episode. Each time, the symptoms had persisted for 5–12 days before presentation. During the last episode, when he experienced a fever of 37.9°C, the patient developed painful haemorrhagic erosions and ulcers on his lip and in the oral cavity, which resembled lesions found in PNP or Stevens-Johnson syndrome (Figs. 1f and g). The patient repeatedly denied taking any medication. Treatment with 15 mg/day prednisolone was started but the oral lesions spread. The dose of prednisolone was increased to 30 mg/day 3 days later. The lesions were resolved in approximately 1 week. Prednisolone was gradually decreased and stopped within 2 weeks. IIF and immunoblot analyses of serum obtained during the second episode showed similar results to IIF and immunoblot analyses of the serum obtained during the first episode (Figs. 1d and e). DIF was also negative.

A detailed interview of the association between daily events and the development of the mucosal lesions revealed that the mucosal lesions developed after the patient underwent dental treatment. We consulted the patient's dentist regarding his medication history and found that he was prescribed ofloxacin for 3 days after each visit. In a provocation test, 1 dose of ofloxacin produced an itchy sensation on the oral, conjunctival, and perianal areas within 1 h, and erosions subsequently developed at the same sites, confirming the diagnosis of FDE. Ofloxacin was stopped, and no relapse has occurred since.

DISCUSSION

This is one of the first reported severe cases of multiple FDE to exclusively affect the mucosae. The patient was difficult to diagnose because multiple erosive mucosal lesions were found without typical cutaneous FDE lesions, the patient denied taking any medication, and the lesions continued to deteriorate even 3 days after the ingestion of ofloxacin. FDE lesions typically appear at the same sites within 0.5–8 h after drug intake and resolve within several days after drug withdrawal, although they may persist and increase in size and number several days after the discontinuation of the causative drug in some cases (2).

In the current case, MMP, PNP, and Stevens-Johnson syndrome were clinically suspected. The negative results obtained by DIF and various seroimmunological tests for IgG antibodies and the absence of underlying malignancies did not suggest either MMP or PNP. Stevens-Johnson syndrome could also be excluded because the patient did not develop any skin lesions, and the lesions at mucosal sites recurred very rapidly (within 1 h) after drug intake in a provocation test.

It is notable that IgA antibodies against envoplakin, periplakin, and laminin γ1 were repeatedly detected in the current case, although both DIF and IIF were negative. The patient's disease course suggested that these IgA antibodies were non-pathogenic. In addition, previous studies reported that antibodies against members of the plakin family were detected in toxic epidermal necrolysis (6), erythema multiforme major, and Stevens-Johnson syndrome (7). Therefore, the antibodies found in the current case and in the previous cases may occur as a secondary phenomenon due to the exposure of skin antigens as a result of epidermal damage (6, 7).

The current patient presented with an extremely rare clinical manifestations of FDE. Therefore, it was not possible to identify the relationship with the causative drug until the fourth episode, even though detailed medical and drug histories were taken. To solve this problem, a drug information-sharing system that includes all medical staff, including private practitioners, is needed.

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The authors have no conflicts of interest to declare.

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