Mycoplasma pneumoniae (Mp) is one of the most common causes of community-acquired pneumonia. It can induce a cellular immune response, leading to respiratory inflammation and injury. Mp infection is frequently accompanied by a variety of extrapulmonary manifestations, including arthritis, hepatitis, myositis, neurological involvement and cutaneous diseases. Cutaneous diseases, such as erythema nodosum, erythema multiforme, urticaria, vasculitis and Stevens-Johnson syndrome (SJS), develop in up to 25–33% of all Mp infections (1, 2). SJS associated with Mp infection is commonly observed in children, while adult SJS is caused mainly by drugs (3). Adult SJS associated with Mp infection has seldom been reported (4, 5). Here, we report 2 adult SJS patients with Mp infection and drug reaction, with possible synergistic effects on the development of SJS.

CASE REPORTS

Patient 1. A 33-year-old man visited our hospital with ocular and oral lesions. He had a high-grade fever, general fatigue and nasal discharge, for which he had been prescribed diclofenac and L-carbocisteine by his doctor one day after the appearance of symptoms. On the following day, he had a painful throat and eyes, and was admitted to our hospital. Physical examination revealed hyperaemic conjunctivae, corneal erosions and pseudomembranous formation. Erosions on the buccal mucosa and ulcers on the lips were also observed. No cutaneous lesions were seen. Laboratory tests revealed leukocytes 13.3×10⁹/l and C-reactive protein (CRP) 7.1 mg/dl (normal < 0.3). Liver function tests were within normal limits. Human immunodeficiency virus (HIV) infection was negative and no adenovirus antigen was detected in the conjunctivae. Herpes simplex virus (HSV) antigen on the lip was negative. On admission, a titre of particle agglutination (PA) test for Mp was 1:320 (normal < 40). No abnormal findings were seen on chest X-ray. A skin specimen could not be obtained because the patient declined biopsy of the labial lesions. Atypical SJS without appearance of skin lesions was suspected. Lymphocyte transformation test (LTT) was performed to identify culprit drugs on admission (6, 7). The LTT for diclofenac was positive (stimulation index level 2.56 (positive >1.80)). The patient was treated with oral prednisolone, 40 mg daily, and a glucocorticoid eye drop. The prednisolone was tapered gradually. A 4-fold reduction in PA titre was found 4 weeks after onset.

Patient 2. A 59-year-old man was referred to our hospital because of a high-grade fever and mucosal lesions. He had been treated with loxoprofen and clarithromycin for fever and sore throat for 4 days before presentation. The symptoms persisted and he noticed labial and oral lesions. Atypical SJS without appearance of skin lesions was suspected. Lymphocyte transformation test (LTT) was performed to identify culprit drugs on admission (6, 7). The LTT for diclofenac was positive (stimulation index level 2.56 (positive >1.80)). The patient was treated with oral prednisolone, 40 mg daily, and a glucocorticoid eye drop. The prednisolone was tapered gradually. A 4-fold reduction in PA titre was found 4 weeks after onset.
X-ray disappeared. The LTT for loxoprofen became negative 6 months after disease onset (Table SI). This case has been described in part elsewhere (8).

At the 1-year and 2-year follow-up of patients 1 and 2, respectively, no sequelae were detected.

DISCUSSION

In adult SJS, drug reactions, rather than infections, have been emphasized as the main causative agent; therefore, intensive investigation for the culprit drug is carried out (9). The co-involvement of infectious agents might be overlooked in the clinical setting in adult patients with SJS. In children, Mp infection has been postulated as the most common implicated factor for the development of SJS (10). The characteristics of paediatric SJS associated with Mp infection are severe mucocutaneous involvements, such as oral ulcers, and keratoconjunctivitis, in the absence of skin lesions. In this regard, atypical SJS cases have been reported as Fuchs syndrome (4, 11), Mp-associated mucositis (12, 13), and incomplete SJS (14).

The clinical characteristics of our 2 patients were similar to those observed in paediatric SJS associated with Mp infection. The results of our serological examination showed significant alterations in Mp antibody titres in the 2 cases, with infiltrative shadowing on the X-ray in 1 case. Thus, it is clear that the preceding Mp infection contributed to the development of SJS in these 2 cases. In addition, drugs were given before the appearance of mucosal lesions in these 2 cases. LTT was performed to determine the causative drug and the results were positive in both cases. Therefore, the involvement of drug reactions was suspected in our atypical SJS adult patients. Although challenge tests could not be performed because the Committee of Severe Cutaneous Adverse Drug Reactions advises against the use of these tests, no positive LTT levels for diclofenac or loxoprofen in healthy individuals were observed with our method, which supports the involvement of a drug reaction in the present cases. Although LTT levels cannot predict whether sensitization leads to clinical symptoms, it has been shown that strong immune reactivity is frequently associated with clinical symptoms (6), and LTT needs to be carried out at the acute stage of SJS to avoid false-negative results (7).

In the present cases, LTTs were performed at the acute stage of SJS to avoid false-negative results (7). At the 1-year and 2-year follow-up of patients 1 and 2, respectively, no sequelae were detected.

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