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CASE REPORT

Toxic epidermal necrolysis secondary to *Mycoplasma pneumoniae* and herpes simplex virus infection

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Summary Toxic epidermal necrolysis (TEN) is a life-threatening skin reaction associated with a high mortality rate. Most TEN is induced by drugs, but some cases are caused by other insults. *Mycoplasma pneumoniae* and herpes simplex virus are the most common infectious pathogens associated with TEN. In identifying the etiology of TEN, it is crucial to include not only a detailed drug history but also potential infection sources. Any suspicious infections should be treated in a timely and efficient manner to improve survival rates. In this article, we report on five patients who developed TEN related to *M. pneumoniae* and herpes simplex virus infections. We also reviewed the relevant literature. We performed a retrospective medical chart review of five patients with TEN, which was considered secondary to *M. pneumoniae* and herpes simplex virus infections. We compared patients with infection-induced and drug-induced TEN. We found that patients with infection-induced TEN were younger in age and had lower SCORTEN scores, less renal dysfunction, shorter hospitalization periods, and higher survival rates compared with patients with drug-induced TEN. Identifying the etiology of TEN requires the inclusion of not only a detailed drug history but also infection sources, such as *M. pneumoniae* and herpes simplex virus. Our findings corroborate previously reported clinical

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and etiologic association with TEN. TEN induced by *M. pneumoniae* and herpes simplex virus manifested less severe clinical courses than its drug-induced counterpart.

1. Introduction

Toxic epidermal necrolysis (TEN) and Stevens—Johnson syndrome (SJS) are uncommon but life-threatening skin conditions. Skin detachment of $<$ 10% of total body surface area (TBSA) is classified as SJS, $>$ 30% detachment is classified as TEN, and between 10% and 30% detachment is classified as overlap SJS/TEN.[1,2] Most TEN has an acute onset and is a result of an adverse drug reaction. However, other conditions, such as infections, can also be a trigger. Of the 101 patients with TEN in our previous study, five patients had TEN caused by infection.[3] Of these five patients, three had TEN associated with *Mycoplasma pneumoniae* and two had TEN associated with herpes simplex virus infection.

M. pneumoniae is a well-known cause of SJS, which is an intracellular pathogen responsible for atypical respiratory infection. It has been reported as the most common infectious agent associated with SJS affecting children and young adults.[4] It is rarely the cause of TEN.[5–7] Herpes simplex virus is located in the basal keratinocyte and lower spinous cell layers. Expression of viral DNA fragments in the keratinocyte layer leads to activation of CD4 positive T-helper cells, which induce various reactions, including cytokine production and subsequent inflammatory response. CD4 positive T-helper cells are also the predominant cells in the blister fluid of patients with TEN,[8] and the cytokine they produce is responsible for the pathologic findings in skin lesions.[9] It is crucial that an etiology of TEN includes not only a detailed drug history but also infection sources. In this article, we report on five patients in whom TEN developed because of *M. pneumoniae* and herpes simplex virus infections, and we review the relevant literature. Additionally, we compare patients with TEN associated with viral infections and patients with drug-induced TEN.

2. Patients and methods

A retrospective medical chart review was performed for five patients admitted between January 1992 and December 2009 to a burn intensive care unit (BICU) with TEN, which was considered secondary to *M. pneumoniae* and herpes simplex virus infections.

The severity of TEN was measured using the patients' SCORTEN scores. The SCORTEN (Severity-of-Illness Score for Toxic Epidermal Necrolysis) score is an illness severity index used exclusively for TEN developed by Roujeau in 2000 and is defined by the EuroSCAR group.[11] The score is designed to predict the mortality rate through seven independent factors that are scored within 24 hours from patient admission (Table 1). Each factor contributes one point to the overall SCORTEN level, with a higher score correlating with a higher mortality rate. The treatment protocol that was applied for these patients with infection-induced TEN was the same as the protocol for patients with drug-induced TEN. Early diagnosis, prompt withdrawal of suspected drugs, and confirmation of possible infection sources were considered the most critical to manage this condition. Fluid resuscitation was begun after admission according to body surface defect percentage and adjusted according to urine output. Hydrotherapy was administered to all patients to remove the lytic skin carefully. Membrane dressings were used for wound care. Aquacel® Ag Hydrofiber® dressing (Convatec Inc. USA) or Acticoat® (Smith & Nephew, Inc.) USA was used routinely for both patients with drug- and infection-induced TEN. These were most effective for children because of their poor cooperation and compliance when changing dressing. Elastic cotton bandages were then wrapped around the dressing. The dressing is changed every 2—3 days. The wound was evaluated twice per week; all dressings were removed and hydrotherapy was performed. Efficacy was determined by measuring wound healing time to achieve 95% re-epithelialization of the involved area. The database from our previously published study[3] was used for comparisons between patients with infection- and drug-induced TEN, such as severity, length of hospitalization periods, and prognosis. All demographic data, including sex, age, TBSA, and SCORTEN score, and laboratory data and outcome were obtained. In this study, renal dysfunction was defined as serum creatinine 1.5 times that of known baseline or urine production of $<$ 0.5 mL/kg for 6 hours according to the International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group.[10]

2.1. Statistical analysis

Values were expressed as mean $\pm$ standard deviation. Categorical and continuous variables were compared with means and normal distributions using the Chi-square and Mann—Whitney *U* tests. Any p value $<$ 0.05 were considered statistically significant.

3. Results

Three cases were diagnosed as TEN associated with *M. pneumoniae* and two were diagnosed as TEN associated with herpes simplex virus infection (Table 2). The presence of these viruses was confirmed by positive serologic findings. The patients consisted of three boys and two girls, with an average age of 8.6 years (range 6—12 years). All cases were referred to the BICU at the acute stage with an average duration from disease onset of 4.2 $\pm$ 3.1 days. The average rate of TBSA epidermal detachment among our