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Case report

Mycoplasma pneumoniae-induced Stevens-Johnson syndrome without skin manifestations

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= Abstract =

Stevens-Johnson syndrome (SJS) presents with widespread blisters, erythematous or purpuric macules, and one or more mucous membrane erosions. Various etiologic factors, including infection, vaccination, drug administration, systemic diseases, physical agents, and food have been implicated as causes of SJS. *Mycoplasma pneumoniae* is the most common infectious agent to cause SJS in children. In recent literature, *M. pneumoniae*-induced SJS with mucositis that lacks the typical target lesions has been described. We report a case of a 6-year-old boy with swelling, peeling of the lips, and red eyes with photosensitivity. On physical examination, he showed severe oral mucositis and conjunctivitis with no evidence of skin lesions. Mycoplasma antibody, which was positive with titers of more than 1:2,560. For patients presenting with fever and mucositis of unknown origin, *M. pneumoniae* should be considered. **(Korean J Pediatr 2009;52:247-250)**

Key Words : *Mycoplasma pneumoniae*, Stevens-Johnson syndrome

Introduction

Stevens-Johnson syndrome (SJS) presents with widespread blisters, erythematous or purpuric macules and two or more mucous membrane erosions[1, 2]. *Mycoplasma pneumoniae* (*M. pneumoniae*) is a common cause of acute respiratory tract infections in children. *M. pneumoniae* infections can often be complicated by extra-pulmonary diseases affecting the skin, blood and central nervous system[3, 4]. *M. pneumoniae* is the most common cause of SJS in children[5]. In recent literature, *M. pneumoniae*-induced SJS with mucositis but lacking the typical target lesions has been described[6-10]. Here, we discuss a 6 year-old boy who developed severe mucositis associated with *M. pneumoniae*.

Case report

A 6 year old boy was referred to our hospital and presented with fever, swollen lips, sore throat and conjunctivitis. He was healthy until 3 days prior to admission when he developed fever, cough and sore throat. He had a conjunctival injection 2 days prior to admission. He was evaluated by a primary otolaryngologist. Upon admission, he was noted to have multiple ulcerations of his oral mucosa and photosensitivity and admitted with a presumptive diagnosis of aphthous stomatitis in the department of otolaryngology.

Upon physical examination, his body temperature was 39.5℃, heart rate was 90 beats/minute, blood pressure was 110/70 mmHg, and respiratory rate was 22 breaths/minute. His medication usage over the past 3 days consisted of amoxicillin, clenbuterol, and anti-tussive. There was no specific medical history. He had a small macular rash on his trunk, which disappeared after one day. He had multiple vesicles and ulcerations in his mouth and pharynx, swollen lips, and a bloody nose. Ocular involvement consisted of purulent conjunctivitis with photophobia and pain. Lung ascultation revealed coarse breathing sound. He received intravenous dexamethasone, analgesics, flomoxef and isepamicin for 7 days. The ophthalmologist removed the pseudomembrane on the conjunctivae and recommended ofloxacin eye drops with a pressure patch. After 2 days, his fever disappeared and his respiratory symptoms improved, however other symptoms worsened. Despite these therapies, his lips were fissured with serum and bloody encrestration and he was unable to eat, drink or speak due to the severe ulcera-

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tion in his oropharynx. His eyes deteriorated to resulting in pseudomembrane-induced traumatic corneal erosion (Fig. 1). On day 7 of admission, he was transferred to the department of pediatrics for further management and evaluation. After then, dexamethasone was stopped and the antibiotic regimen was changed to amoxicillin-clavulanate and clarithromycin. He was started on the treatment with wet-dressing and parenteral nutrition. The laboratory findings upon admission day were white blood cell count of 9,400/μL, C-reactive protein level of 15.49 mg/mL and ESR 45 mm/hr. The chest radiograph showed no specific findings. On day 7 of admission when he was referred to our department, further laboratory investigation was performed. Serologic tests failed to show herpes simplex virus (HSV), Epstein-Barr virus (EBV), Cytomegalovirus (CMV), or Chlamydiae pneumoniae except Mycoplasma antibody with titers of more than 2,560 (>1:2,560). Blood, throat, urine and stool cultures were negative (Table 1). He was discharged on day 14 with significant improvement of oral mucositis and conjunctivitis (Fig. 2). Seven days later after being discharged, the patient showed marked improvement.

Discussion

SJS is characterized by typical skin lesions, mucosal lesions on two or more sites such as oral, ocular, or genitourinary and constitutional symptoms. Typical cutaneous lesions in SJS generally consist of erythematous macules, the so-called target-shaped rash, that variably develop central necrosis to form vesicles, bullae, and an area of denudation on the face, trunk, and extremities, followed by bullous lesion and skin detachment[1, 2]. In SJS, oral lesions are present in all

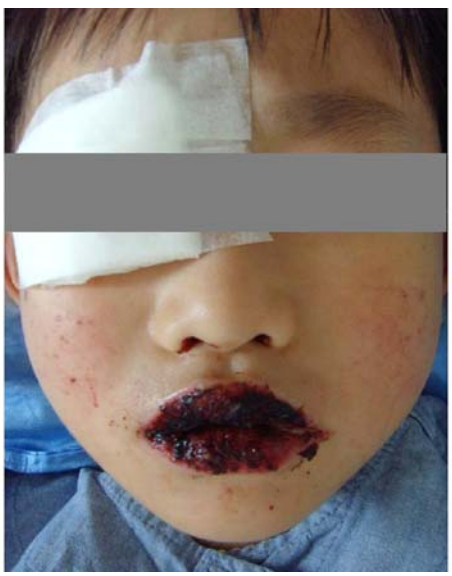

Fig. 1. Seven days after admission, the mucosa of the lips had fissures and bloody, melena-like crust. The patient could not open his eyes due to conjunctivitis and pain.

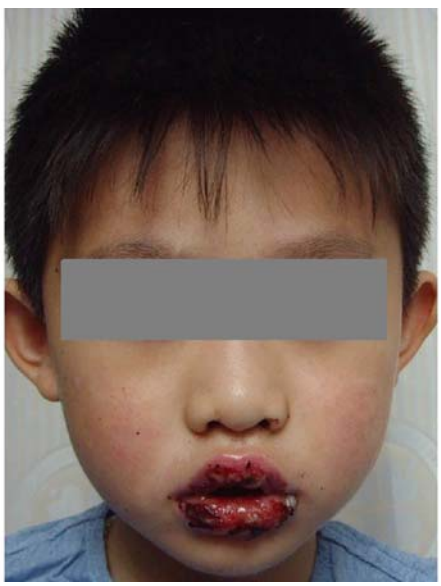

Fig. 2. Thirteen days after admission, the patient's oral mucosa lesions and conjunctivitis were improved.

Table 1. Laboratory Findings

Complete blood cell count	WBC count 9400/μL (neutrophil segment 78.5%, lymphocyte 9.5%, monocyte 11.9%), Hemoglobin 12.6 g/dL, ESR 45 mm/hr
Chemistry	CRP 15.49 mg/dL, IgE 695.2 IU/mL
Microbial serology	Mycoplasma Ab >1:2560, Cold agglutinin (-), Chlamydia pneumoniae IgM (-), ASO titer 346 IU/mL anti-HBs antibody (+), anti-HCV (-), CMV IgM (-), HSV IgM (-), HSV IgG (+), EBV viral capsid IgM (-), EA-DR IgM (-), EBNA (+),
Microbial culture	Blood culture (-), Throat culture (-), Urine culture (-)
Urine analysis	Protein (±), WBC 2-4, RBC 2-4

Abbreviations : ASO, antistreptolysin O, anti-HBs, anti-Hepatitis B virus surface antigen, anti-HCV, anti-Hepatitis C virus, CMV, cytomegalovirus, HSV, herpes simplex virus, WBC white blood cell, RBC, red blood cell

patients and ranged from isolated erosions and ulcers to involvement of the entire buccal mucosa, tongue, and pharynx with areas of denudation and pseudomembrane formation. Lip lesions have vesicle, ulceration, swelling, bleeding with or without crusting and peeling. The common ocular lesion is bilateral conjunctivitis that is often purulent and photophobia. Other known features are subconjunctival hemorrhage, conjunctival ulceration and corneal ulceration[1-4].

Various etiologic factors have been implicated as the cause of SJS. These include infection, vaccination, drugs, systemic diseases, physical agents, and food[1, 2]. In contrast to those of adults, infection is the most commonly identified cause of SJS in children[5]. Associated infection include HSV, *Mycobacterium tuberculosis*, group A streptococcus, Hepatitis B virus, EBV and *M. pneumoniae*. Among these, *M. pneumoniae* is the most common cause[5]. Many different eruptions have been described with *M. pneumoniae* infection. These include erythematous macular or maculopapular, vesicular, bullous, petechial and urticarial eruption[3, 4].

There are a few reports of *M pneumoniae*-induced severe mucositis and stomatitis in the absence of skin affections. Nomenclature of this manifestation is inconsistent in that it was referred to as 'SJS without skin lesion' or '*M pneumoniae*-associated mucositis'[6-10]. In our case, the lips were fissured with serum, blood, and crust, and the oral mucosa had multiple aphthous-like lesions. Our patient had purulent conjunctivitis with pseudomembrane formation. The skin and genital area were not affected except for a fleet rash on the chest. Here, other etiologies of mucosal lesions should be considered. The differential diagnosis includes herpetic gingivostomatitis and herpangina, in view of the extensive oral ulceration and inflammation, Kawasaki disease and Behcet disease in light of eye and oral mucosal lesions. Severe conjunctivitis is not an usual finding in herpetic gingivostomatitis and herpangina, but also serologic findings could exclude the herpetic gingivostomatitis. Kawasaki disease was excluded because the oral lesion associated with Kawasaki disease is a fissured dry lip with a strawberry tongue and there was no cervical lymphadenopathy. Behcet disease is very rare in children and is characterized by recurrent oral and genital ulcers and ocular inflammation with other systemic symptoms. Streptococcal infection was considered but was easily excluded, as it does not have ocular lesions, without the presence of a high ASO titer and pharyngeal culture. The clinical symptoms in our case correspond to the presentation of SJS without the presence of skin affection. The authors concurred that the most likely diagnosis was *M. pneumoniae* induced SJS with minimal or no skin manifestation.

The standard laboratory test to confirm Mycoplasma infection is to document a 4-fold or greater rise in the titer of *M. pneumoniae* antibodies between acute and convalescent sera[11, 12]. We used a particle agglutination assay Serodia-MycoII kit (Fujirebio, Tokyo, Japan) as a diagnostic method of Mycoplasma infection. Our patient showed Mycoplasma antibody titer with >1:2,560 on day 7 of admission, even though dexamethasone was used during the initial phase of admission. Steroids are known to suppress humoral immunity in patients on systemic dexamethasone[13, 14]. There may be an argument about *M. pneumoniae* as a pathogen in this case since we performed the test only one time during admission. Recently Kim et al. suggested that a single antibody titer of ≥1:640 as determined by the microparticle agglutination test could be used as a practical diagnostic criterion of acute *M. pneumoniae* pneumonia in children during the epidemic period and was comparable to PCR[12].

Medications including antibiotics, nonsteroidal anti-inflammatory drugs, pychoepileptics and antigout drug are the predominant inciting agent of SJS. Therefore, a thorough drug history must be obtained. The incubation time for drugs varies from a few days to 2-3 weeks, but may be up to 1 month[15]. Since our patient had only taken a few medications 3 days before his admission, we excluded medication as a cause of mucosal erosion.

There is no universally accepted specific treatment for acute SJS other than supportive and symptomatic care. Meticulous skin, mucous care and daily ophthalmologic examination are required. Steroid use for treating SJS remains controversial and debated topic. In this case, dexamethasone seemed to have no effect on natural course.

Our patient had high IgE titer. He and his family have had no allergy histories. Previous studies have demonstrated that *M. pneumoniae* infection is associated with a significant total IgE response and production of IgE specific to *M. pneumoniae*[16]. Further, a marked chronicity of increased serum total IgE was also revealed[16, 17]. Immune mechanisms play a major part in the pathogenesis of SJS and the precise mechanism of *M. pneumoniae*-related skin diseases is not known. Immune complex-medicated vascular injury, cell-mediated immune response/cytotoxic injury to epithelial cell, and autoimmune mechanism have all been proposed as a mechanism[11].

Here, we describe a patient with mycoplasma-induced SJS with minimal skin lesion. Mucositis with or without skin lesions is a extrapulmonary manifestation of *M. pneumoniae* infection. Therefore, a case for severe mucositis with the context of respiratory illness should be considered as a possible *M. pneumoonae* infection as a potential causative agent.

한 글 요 약

마이코플라즈마 감염에 의한 피부 병변을 동반하지 않은 Stevens-Johnson 증후군 1예

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Stevens-Johnson 증후군은 피부에 특징적 발진과 수포를 동반하고 두 개 이상의 점막 조직에 병변을 보이는 것을 특징으로 하는 질환으로 감염, 예방 접종, 약물, 전신 질환 및 물리적 자극 등이 원인이 될 수 있다. 이 가운데 *Mycoplasma pneumoniae*는 소아기의 Stevens-Johnson 증후군의 가장 흔한 원인이다. 최근 *Mycoplasma pneumoniae*에 의한 피부 병변 없이 심한 점막의 병변만을 보이는 경우가 보고되었다. 이러한 경우를 피부 병변이 없는 Stevens-Johnson 증후군이거나 혹은 다른 개별적 질환으로 보아야 할지에 대해서는 아직 논란이 되고 있다. 병력에서 특이 사항이 없는 발열과 심한 경구 및 입술의 병변과 결막염으로 입원한 6세 남아가 임상 검사에서 Mycoplasma 항체 증가 이외에는 특이 소견을 보이지 않아 저자들은 Mycoplasma에 의한 피부병변 없는 Stevens-Johnson증후군으로 진단하였고 이를 문헌 고찰과 함께 보고하는 바이다.

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