Case Report

Co-infection of Mycoplasma pneumonia and Herpes Simplex Virus (HSV): A Case Report of a Boy with Erythema Multiforme

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Background: Erythema multiforme (EM) is an immune-mediated self-limited reaction that has mucocutaneous eruption manifestation.

Aim: The aim of this case report is to acknowledging the possibility of coinfection in EM to give the proper treatment.

Case Description: We report a unique case of Mycoplasma pneumonia and Herpes Simplex Virus-2 positive in immunocompetent patient with erythema multiforme. Coinfection of Mycoplasma pneumonia and Herpes Simplex Virus (HSV) infection is rarely presenting in an immunocompetent patient. The patient was admitted with a worsening blister and erosion on oral and genital mucosa, along with rashes on the extremities and trunk. The patient also had a fluctuating fever and productive cough. The skin examination showed multiple erythematous papules and plaques with dusky area and blister in some central plaques that resembled target lesion. The patient tested positive for Mycoplasma pneumonia and Herpes Simplex Virus (HSV) IgM and IgG serology. The patient received supportive therapy, levofloxacin, acyclovir, methylprednisolone, and therapy for ocular, oral, and skin lesions. Systemic symptoms and cutaneous lesion improved after hospitalization without sequelae.

Conclusion: Although it is rare, coinfection must be taken into consideration for the cause of EM.

Keywords: Erythema multiforme, Mycoplasma pneumonia, herpes simplex virus, mucocutanous eruption, Case-report

INTRODUCTION

Erythema multiforme (EM) is an immune-mediated self-limited reaction that has mucocutaneous eruption manifestation.[1] EM has several etiologies; one infection is caused explicitly by Herpes Simplex Virus-1 (HSV-1). Other infectious on agents often causing EM are hepatitis B and C, Mycoplasma pneumonia, and parvovirus B19.[2] Cutaneous lesion characteristics of EM are target lesions with the diameter <3 cm, circular-shape, well-defined border, and consisting of 3 different zones; 2 concentric rings with different colours around the circular zone usually with dusky appearance, indicating epidermal damage forming bullae or crust. The presence of EM manifestation does not increase patient mortality rate, although increasing patient's morbidity. Erythema multiforme generally occurs in young adults; nevertheless, it can occur in children. [1,3] Finding the exact etiology of EM in a patient can secure early prompt treatment and would make a better prognosis for the patient and less hospitalization duration with more cost-effective treatment. There is still a small number of publications reporting double infection of Mycoplasma pneumonia and HSV infection. In fact, this case report is the first in Asia.

METHODOLOGY

This is a case report and the authors certify that they have obtained all appropriate patient consent forms. The patient's parents have given their consent for clinical information to be reported in this study in the form. The patients' parents understand that name and initials will not be published. This case report already approved by the hospital ethical policy.

CASE REPORT

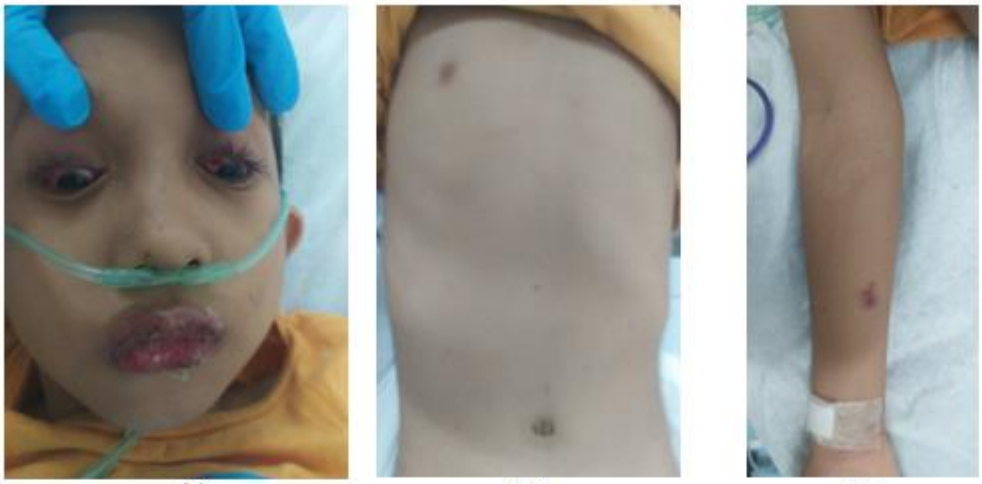
A 7-year-old boy presented with a worsening blister and erosion on oral and genital mucosa, along with rashes on the extremities and trunk 1 week before admission. He also had a fluctuating fever and productive cough two weeks before admission. He was treated with amoxicillin on 3rd day of the symptom, and the fever diminished. However, a week before admission, the fever and the productive cough recurred. Subsequently, he had blisters and erosion on the lips, genital and perianal area. Redness appeared on both eyes with productive mucous discharge and palpebral crust. The rash initially appeared as erythematous papule and then developed into plaque with a dusky area and blister in the centre of the plaque. The patient came to another clinic and was given azithromycin, acetaminophen, and oral topical steroid and referred to our hospital.

Physical examination revealed stomatitis with lip edema, erosion, brownish crust and pus. There was conjunctivitis on both eyes with purulent discharge and later pseudo-membrane on the conjunctiva tarsal. There were multiple papules and plaques with dusky area and blister in the center of some plaque that resemble target lesion on the lower and upper extremities, trunk, glans penis, and perianal, *Nikolsky* sign was negative. The patient was diagnosed with erythema multiforme major.

Initial laboratory results showed leukocytosis (12.950/μL) and increased erythrocyte sedimentation rate (20 mm/hour), C-reactive protein (43.4 mg/L) and positive for Mycoplasma pneumonia IgM and IgG with ELISA method. We did not find any immunocompromised evidence in the patient.

The patient received supportive therapy along with topical treatment for the ocular, oral, and skin lesions. The patient received gentamycin sulfate 0.3% antibiotic eye-ointment for ocular lesion, as well as Prednisolone acetate eye drop with routine pseudo-membrane removal by conjunctiva scrapping. We treated him with empirical Levofloxacin and methylprednisolone.

Infection marker was improved after antibiotic administration, but patient had persistent fever (but lower temperature than previous measurement) with progressing lesion. Mucosa and skin lesions continued to extend with atypical target lesions accompanied by blistering. Leukocyte and CRP were improving even though he still had a persistent fever and progressing lesion. We further performed other workups for EM, such as HSV serology evaluation and started empirical intravenous Acyclovir. We tapered off the methylprednisolone dose within a week. In the following days, the result of the IgM HSV-2 antibody was positive. After acyclovir administration, the skin lesion and the fever were improved. PCR test for SARS-CoV2 was performed in sequential manner and showed negative result.



(a) (b) (c)

Figure 1. (a), (b), and (c) show the mucosa and skin lesions when admitted to the hospital

(a) (b)

Figure 2. (a) and (b) the mucosa and skin lesions began to extend on the 3rd day of hospital admission

(a) (b) (c) (d)

Figure 3. (a), (b), (c), and (d) the mucosa and skin lesions began to extend on the 7th day of hospital admission

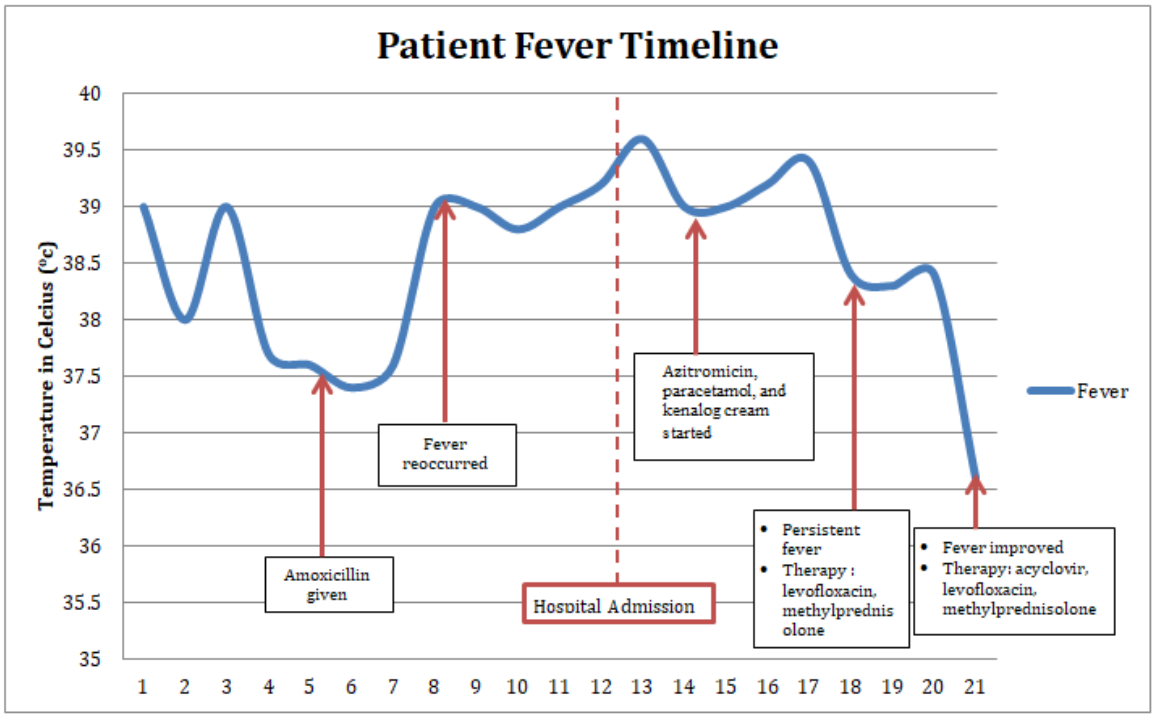


Figure 4. Patient Fever Timeline

DISCUSSION

Erythema multiforme generally occurs in young adults and initiates with prodromal symptoms followed by mucocutaneous symptoms.[1] The most common cause of EM is HSV infection. HSV infection causes EM in approximately 70% of patients.[4] Other common microbial agent causing EM is Mycoplasma pneumonia.[1] In this setting, Mycoplasma pneumonia and HSV1 are the cause of EM. There is still no literature explaining HSV and MP coinfection causing EM. One case report describes one EM patient caused by HSV and MP.[5]

Mycoplasma pneumonia serology test was evaluated because it is the leading cause of the erythema multiforme lesion in children with upper respiratory symptoms. We also did Tzank-test and HSV serology tests to evaluate whether HSV is the cause of EM as the partial response was found for methylprednisolon therapy. The differential diagnosis of this patient is SJS. Stevens-Johnson Syndrome and EM have similar mucosal manifestations with different dermatological manifestations. The most apparent difference between SJS and EM is the form of the lesion. The SJS lesion appeared as an erythematous or macula purpura or target lesion where EM is generally macular, not papular. Steven Johnson Syndrome's manifestation usually occurs in trunks and spreads distally, whereas EM dominantly has acral distribution. In our case, the patient was given steroids and antibiotics in the early phase. The patient had been given amoxicillin for five days. Then symptoms re-occurred within several days, so the antibiotic switched to azithromycin. Patient was diagnosed as SJS at the first time admitted to our hospital, therefore the suspected medication causing SJS (amoxicillin and azithromycin) were stopped. Subsequent evaluation did not find *Nikolsky* sign, therefore SJS diagnosis was excluded.[1,6]

In order to remain cautious of the SJS probability, the antibiotic treatment option for this patient is levofloxacin. Levofloxacin, a fluoroquinolone type antibiotic, serves as the second line antibiotic for MP patients who cannot receive macrolide type antibiotics. Based on one systematic review, there is no conclusive result

comparing the use of MP antibiotic spectrum (macrolide) and non-spectrum antibiotic on the activity against MP in pediatric patients. Despite of these considerations, macrolide is still the most common antibiotic used for MP patients. [7]

In the early phase, this patient was diagnosed with ocular Steven-Johnson Syndrome (SJS). The ocular manifestations of this patient are similar to ocular SJS clinical manifestation. Ocular manifestations in EM patients can present on up to 17%. Pseudomembrane and viral keratoconjunctival manifestations were found on the patient. Our patient was treated by routine conjunctival membrane scraping therapy and steroid administration, as well as an antibiotic eye ointment to protect the cornea from further infection or damage. Pseudomembrane can present by sedimentation of the virus on corneal mucosa, leading to corneal erosion. This patient did not have any major visual loss or persistent condition, but if not treated early, the side effects of visual loss and the development of symblepharon can be expected. Steroid administration is an important treatment following the formation of pseudomembrane and for the visual prognosis. Steroid eye-drop options for patients with such presentation are 0.12% prednisolone acetate, 0.1% fluorometholone, 1% Rimexolone, dexamethasone, and 0.001% loteprednol etabonate. It is also important to evaluate daily for any side effects of complications of topical steroid usage.[8, 9,10]

In this patient, the lesion on the genital area took a longer time to heal as the genital area is often in contact with urine, causing more humid conditions. The lesion improved after the patient was given systemic antibiotic, topical mupirocin ointment following the application of wet to dry gauze dressing with normal saline solution

The patient received methylprednisolone as a systemic steroid with a dose of 1 mg/kg/day for the anti-inflammatory in EM. In the following evaluation, the antibiotic and steroid administration only cause partial recovery with persistent fever and progressing lesion, although the frequency and the fever temperature reduced (below 38.5°c). On the follow-up the infection marker decreased but still above the normal range. Therefore, we thought of another coinfection and HSV test was examined with reactive IgM HSV-1. Acyclovir as the choice of therapy was given. Then we tapered off the steroid and stopped the antibiotic. Soon after acyclovir was given, the fever and the lesion were improved.

The advantage of this case is that it discusses rare cases of EM caused by MP+HSV in immunocompetent patients. Our case also discusses the manifestations found in the patient (mucocutaneous, ocular), hence inter-specialist collaboration is necessary in dealing with similar cases. The limitation of this case report is the lack of co-infection literature on EM.

CONCLUSION

Even if the patient is immunocompetent, it is still possible for co-infection of HSV and MP to occur. Identification of the lesion is important; therefore, it is necessary to carry out a supporting examination that is thought from the description of the lesion and treats according to the etiology. If there are no adequate facilities, the typical appearance of the lesion makes it possible to treat it first and observe the therapeutic response.

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None.

CONFLICTS OF INTEREST

There is no conflict of interest.

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