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Case Report

Mycoplasma Pneumoniae Induced Rash and Mucositis (MIRM) in the Differential Diagnosis of Drug Allergy

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ABSTRACT

Mucocutaneous eruptions associated with *Mycoplasma pneumoniae* (MP) infection has been newly termed 'MP-induced rash and mucositis (MIRM)'. A 17-year-old male developed a rash, bilateral purulent conjunctivitis, and oral and genital ulcers after the first dose of amoxicillin-clavulanic acid, initially considered as a drug allergy. Following hospitalization under a preliminary diagnosis of Stevens-Johnson syndrome and initiation of systemic steroids, he developed pneumonia. Laboratory tests confirmed MP infection, leading to a refined diagnosis of MIRM. The patient fully recovered within two weeks following treatment with azithromycin and intravenous immunoglobulin. This case underscores the importance of considering MIRM in the differential diagnosis of drug allergies and aims to enhance awareness of this condition.

Key Words: Adolescent, Drug allergy, Mucositis, *Mycoplasma pneumoniae*, Rash

INTRODUCTION

Mycoplasma pneumoniae (MP) is a common respiratory pathogen that causes community-acquired pneumonia (CAP), occurring more frequently in children than in adults (1). Although most MP infections are typically mild, about 25% of patients may develop severe extrapulmonary complications, such as mucocutaneous blistering (2). Mucocutaneous eruptions associated with MP infection exhibit a wide range of morphological variations (3). Therefore, previously these eruptions have been categorized within the spectrum of erythema multiforme (EM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) due to their multifaceted nature (3). Canavan et al. (3) initially described a new term as MP induced rash and mucositis (MIRM) and proposed diagnostic criteria. In this report, we present a case of an adolescent initially suspected of having a drug allergy, who was ultimately diagnosed with severe MIRM.

CASE REPORTS

A previously healthy 17-year-old boy was prescribed oral amoxicillin-clavulanic acid one week ago for fever and cough. One hour after the first dose of the drug, he developed a rash over his entire body. On the second day, he experienced redness, burning sensation, light sensitivity in the eyes, and the formation of fluid-filled blisters in the mouth. On the fourth day of taking the drug, as his symptoms persisted, he presented to our clinic with a suspected amoxicillin-clavulanic acid allergy. He had widespread ulceration of the oral mucosa, swollen eyelids and bilateral purulent conjunctivitis (Figure 1A-1B). Target-like lesions that did not tend to coalesce were observed on the extremities, anterior surface of the trunk, and back (Figure 1C, 1D). Ulcerative lesions were present on the glans penis and suprapubic region. There were no fever, lymphadenopathy, or organomegaly. Complete blood count revealed a white blood cell count of 11.700/mm^3, hemoglobin concentration

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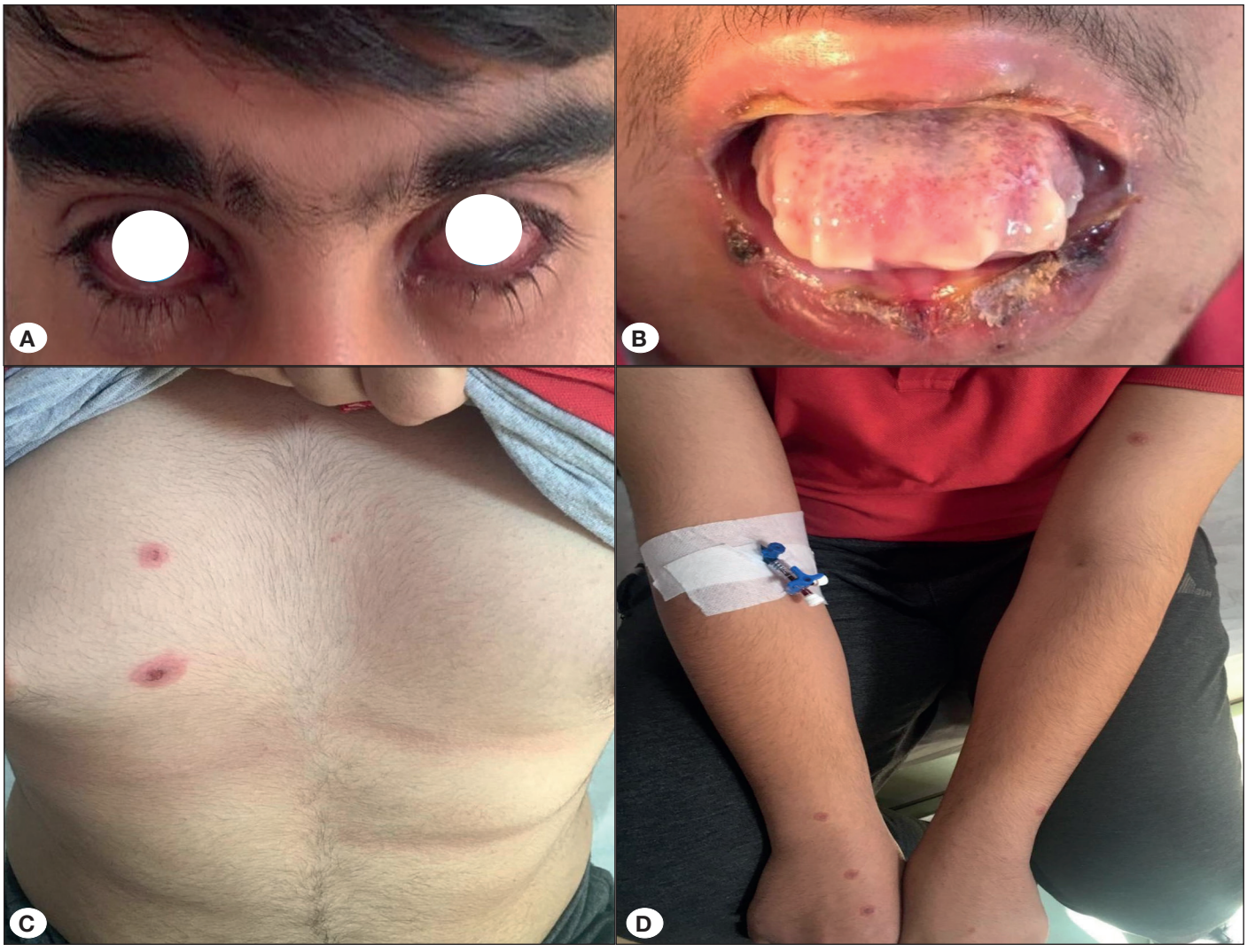

Figure 1: A) Due to MIRM bilateral purulent conjonctivitis, **B)** Due to MIRM ulceration of the oral mucosa, **C,D)** Due to MIRM targetoid lesions of the trunk and extremity

of 13 g/dL, platelet count of 405.000/mm^3, and CRP level of 172 mg/L (N: 0-5). Liver and kidney function tests were normal. The patient was admitted with a preliminary diagnosis of Stevens-Johnson syndrome. Treatment was initiated with intravenous methylprednisolone at a dose of 60 mg/day. Ophthalmology started treatment for ocular involvement including dexamethasone, bacitracin, moxifloxacin eye drops, and artificial tears. A symblepharon ring was placed. Urology inserted a urethral catheter due to genital involvement. Intravenous hydration and high-calorie formula were initiated for the patient with inadequate oral intake. On the 5th day of hospitalization, the patient required supplemental oxygen and bilateral crackles were heard at the lung bases. Serum *Mycoplasma pneumoniae* IgM were found to be positive. The PCR test performed on the nasopharyngeal specimen was positive for MP. Based on these findings, the patient was diagnosed with MIRM. The patient received a 5-day course of azithromycin treatment and a total of 400 mg/kg of intravenous immunoglobulin (IVIG) divided over 5 days. On the 2nd day of azithromycin therapy, the patient's oxygen requirement decreased. By the 14th day, regression of skin lesions was observed; methylprednisolone was gradually tapered off, and the patient was discharged. The patient has been consistently monitored without any complications for a period of three years. Written informed consent was obtained from the parents of the patient for publication.

DISCUSSION

Here, we report a case initially consulted for a suspected drug allergy and subsequently diagnosed with typical MIRM after clinical and laboratory evaluations. We want to bring attention to MIRM, a recently established term in the field of differential diagnosis for drug allergies.

Accurate drug allergy diagnosis is crucial to prevent severe or potentially life-threatening reactions and to avoid unnecessary drug restrictions that can impact patients' health and lead to

increased medical expenses (4). Skin rashes are commonly seen in children treated with beta-lactam antibiotics. Many children are mistakenly labeled as penicillin-allergic, yet less than 10% of these patients develop a rash during an oral provocation test. The rash is more likely to be related to the underlying infection rather than an allergic reaction to the antibiotic (5-7). We did not think of drug allergy in our patient without the need for provocation, only on the basis of history and the nature of the rash. In the presented case early type drug allergy was not suspected as the rash that appeared one hour after the initial dose amoxicillin-clavulanic acid did not exhibit urticarial characteristics. Additionally, the rapid onset of mucosal involvement and rash also ruled out the possibility of a delayed-type reaction linked to the drug. The duration of drug induced- SJS/TEN may vary depending on the specific drug but there is typically a latent period between administration of the drug and the onset of rash (8).

Initially, the patient was admitted with a diagnosis of SJS. Although the mucosal involvement suggested SJS, the limited cutaneous involvement and the subsequent development of clinically and laboratory-confirmed pneumonia led to the suspicion of MIRM. Our case meets all the diagnostic criteria of MIRM (Table I). Key feature that help to distinguish MIRM from SJS include predominance mucosal involvement and relatively sparse cutaneous involvement and excellent prognosis. The oral mucosa is primarily affected (94%) followed by the ocular (82%) and genital mucosa (63%) characterized by vesiculobullous lesions and ulcerations (3). The patient had involvement in all three mucosal areas.

We added IVIG to the treatment due to the development of pneumonia and the need for oxygen under the steroid treatment initiated during our patient's hospitalization. In a systematic review, Lofgren et al. (9) reported that 77% of patients diagnosed with MIRM were treated with antibiotics, 37% with corticosteroids, and 11% with IVIG. Considering the low IVIG requirement reported in the literature, we believe that we may have acted hasty in initiating IVIG. Corticosteroids also have been used in the treatment of SJS/TEN for many years, but their use remains controversial. Proponents argue that high-dose corticosteroids administered early can help reduce inflammation, while opponents suggest they may increase the risk of sepsis. The available studies on corticosteroid use in SJS/TEN are all case series, mostly retrospective, with no randomized controlled trials (10). The treatment decision should be made under the guidance of experts.

Table I: Proposed diagnostic criteria for classic cases of MIRM

Detachment	<10% BSA
No. of mucosal sites involved*	≥2
Few vesiculobullous lesions, or scattered atypical targets	Yes
Targetoid lesions	±
Evidence of atypical pneumonia	
Clinical	Fever, cough, positive auscultatory findings
Laboratory	Increase in MP IgM antibodies, MP in oropharyngeal or bullae cultures or PCR, and/or serial cold agglutinins

BSA: *Body surface area,* ***PCR:*** *Polymerase chain reaction,* ***MP:*** *Mycoplasma pneumonia, *Rare cases have \ two mucosal sites involved (3).*

Our patient was hospitalized for a duration that could be considered as relatively long. The prolongation of the patient's hospitalization was caused by delayed adequate oral intake due to mucositis and the onset of pneumonia symptoms on the fifth day of hospitalization. In support of this, significant prolongation of hospitalization was observed in patients with MIRM compared to those with non-mycoplasma EM, and an increase in oxygen requirements was noted in patients with MIRM compared to those with CAP alone (11).

In patients with MIRM, while 81% of them achieve complete recovery, some individuals may experience ocular complications such as conjunctival synechiae, corneal ulcerations and dry eyes as well as oral and genital synechiae, post-inflammatory pigmentary changes, and, more rarely, complications such as B-cell lymphopenia, restrictive lung disease, and bronchiolitis obliterans have been reported (3,12-15). During the long-term follow-up of our patient, none of these complications developed.

In conclusion, MIRM is characterized by widespread mucosal involvement, minimal skin involvement, and it predominantly affects young males. When diagnosed early and supported by appropriate care, including the use of preferred treatment options such as antibiotics and systemic steroids, MIRM exhibits a favorable long-term prognosis. During the differantial diagnosis of a drug allergy it is important to keep in mind. On the other hand, since SJS/TEN is a more mortal diseases; such patients should be consulted with pediatric allergists for a definitive differential diagnosis with drug allergy; to prevent underdiagnosis of drug induced SJS/TEN.

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