Case Report

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Mucocutaneous Manifestations of *Mycoplasma pneumoniae* Infection: Case Reports of SJS, MIRM, and Fuchs Syndrome

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Objective: After lifting COVID-19 restrictions, increased spread of *Mycoplasma pneumoniae* has been observed in both adults and children, with a growing number of cases showing extrapulmonary involvement. We present reports of three cases: pneumonia with infection-related Stevens–Johnson syndrome affecting 7-8% of body surface area and leading to pulmonary obstruction in a child; pneumonia with rash and severe mucositis in an adolescent; and Fuchs syndrome in an adult. We further discuss the pathogenesis of extrapulmonary manifestations, focusing on the role of the CARDS exotoxin and host immune responses.

Keywords: *Mycoplasma pneumoniae*, Extrapulmonary, Mucositis, Stevens–Johnson syndrome, Mycoplasma-induced rash with mucositis

Introduction

During the COVID-19 pandemic, non-pharmacological interventions (NPIs) temporarily reduced circulation of respiratory pathogens. After relaxation of NPIs, rhinovirus resurged from 2020 onward,[1-3] followed by RSV in spring summer 2021,[4] and invasive pneumococcal disease in children during 2021–2022.[5,6]

In contrast, the incidence of *Mycoplasma pneumoniae* remained at "quarantine-level" values,[7,8] raising concerns for a delayed but amplified epidemic. Owing to "immunity debt" the growing pool of individuals lacking immunity[7-9] a sharp rise in cases among adults and children has been documented since 2023–2024.[10,11]

Extrapulmonary manifestations accompany *M. pneumoniae* pneumonia in up to 25%

of adults and 10% of children,[12,13] with frequency increasing during epidemics. The most commonly affected systems are cardiovascular, nervous, gastrointestinal, cutaneous, renal, musculoskeletal, and sensory organs.[13] We report three cases of *Mycoplasma pneumoniae* with mucocutaneous involvement, all admitted to the Republican Clinical Infectious Diseases Hospital, Ulan-Ude, in autumn 2024.

Case Reports

CaseA (SJS)

A 6-year-old boy was admitted on day 5 of illness with a history ofnon-productive cough, fever up to 39.9 °C. As reported by the accompanying relative, a maculopapular rash had appeared earlier the same day.

Prior to hospitalization he had received only symptomatic care without antibacterial treatment. On admission, vesicular stomatitis, keratoconjunctivitis OU, and oxygen saturation of 89% were noted. Oxygen therapy was initiated with a target saturation of 98%. Empirical amoxicillin–clavulanate and acyclovir (pending laboratory results for HSV-1/2 and VZV) were started. Because of persistent respiratory distress (respiratory rate 40/min, audible wheezing), ipratropium bromide and budesonide were added, reducing respiratory rate to 26/min.

Within 24 hours the rash progressed from maculopapular to vesicular. On hospital day 2, following a positive PCR result for *Mycoplasma pneumoniae* and the onset of urethritis and balanitis, clarithromycin and ceftriaxone were initiated. By day 5, bullous eruptionsup to 3 cm had appeared (Figure 1)

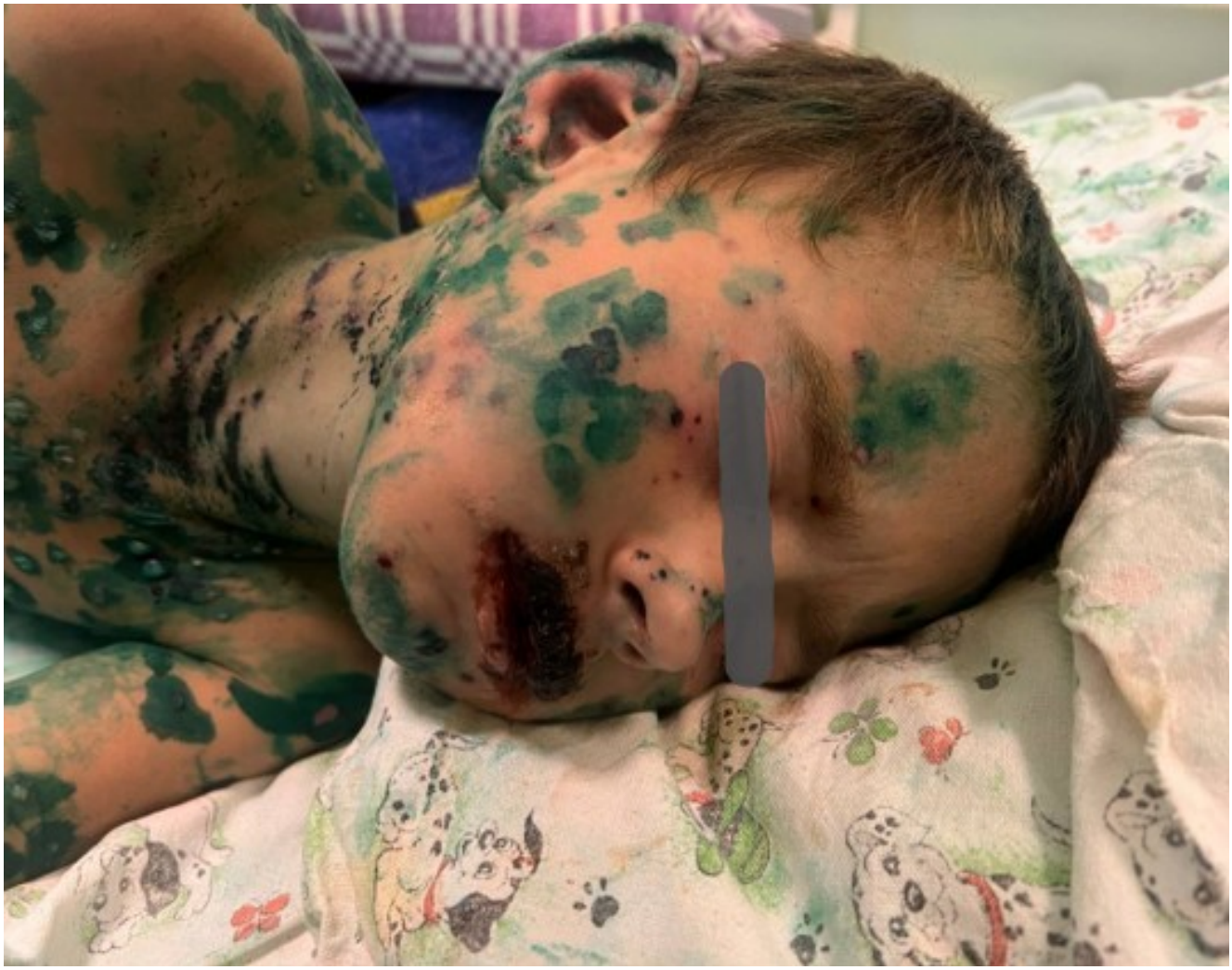

Figure 1. Oral mucositis and cutaneous lesions, including bullae and scabs, on the face, neck, and upper torso.

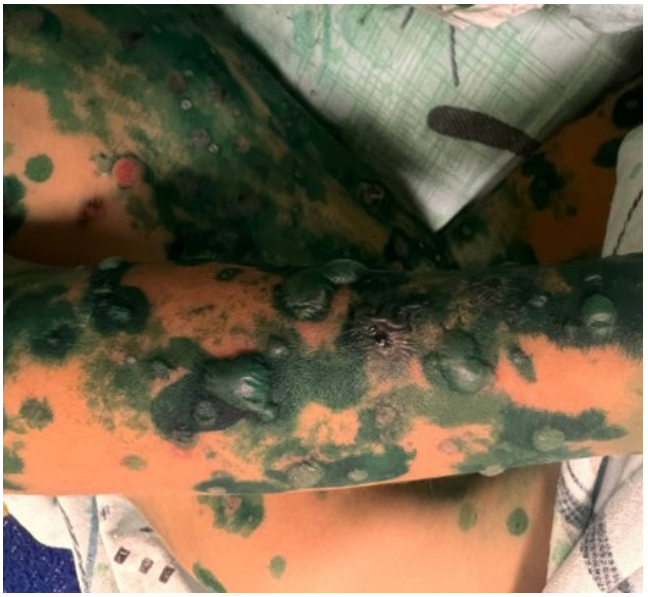

Figure 2. Merging bullae on torso and arms.

Despite the further increase in number and size of lesions (leading to detachment of 7-8% of body surface area, predominantly affecting face, neck and upper torso), they were attributed to the infection rather than a drug reaction, given absence of temporal relation to drug dosing and the mucosal involvement consistent with infection-related Stevens–Johnson syndrome.

Because of persistent respiratory distress and progressive skin involvement, systemic glucocorticoids were introduced, leading to gradual improvement with resolution of systemic symptoms, respiratory distress, and pruritus. The patient was transferred from the ICU to the ward on day 8 of hospitalization.

However, by day 17, exercise intolerance and wheezing recurred. Despite ongoing therapy, no improvement was achieved, and MSCT was ordered. On day 22, he was readmitted to ICU with respiratory failure; MSCT revealed bronchiectasis, and he was transferred to the pulmonology department for further care.

Case B (MIRM)

A 17-year-old male developed fever and dry cough on the fourth postoperative day after laparoscopic varicocelectomy. Despite outpatient treatment, symptoms progressed, though CXR at re-evaluation was normal. On the sixth day of illness, he developed conjunctival injection (Figure 3), productive cough,dysuria, and was admitted.

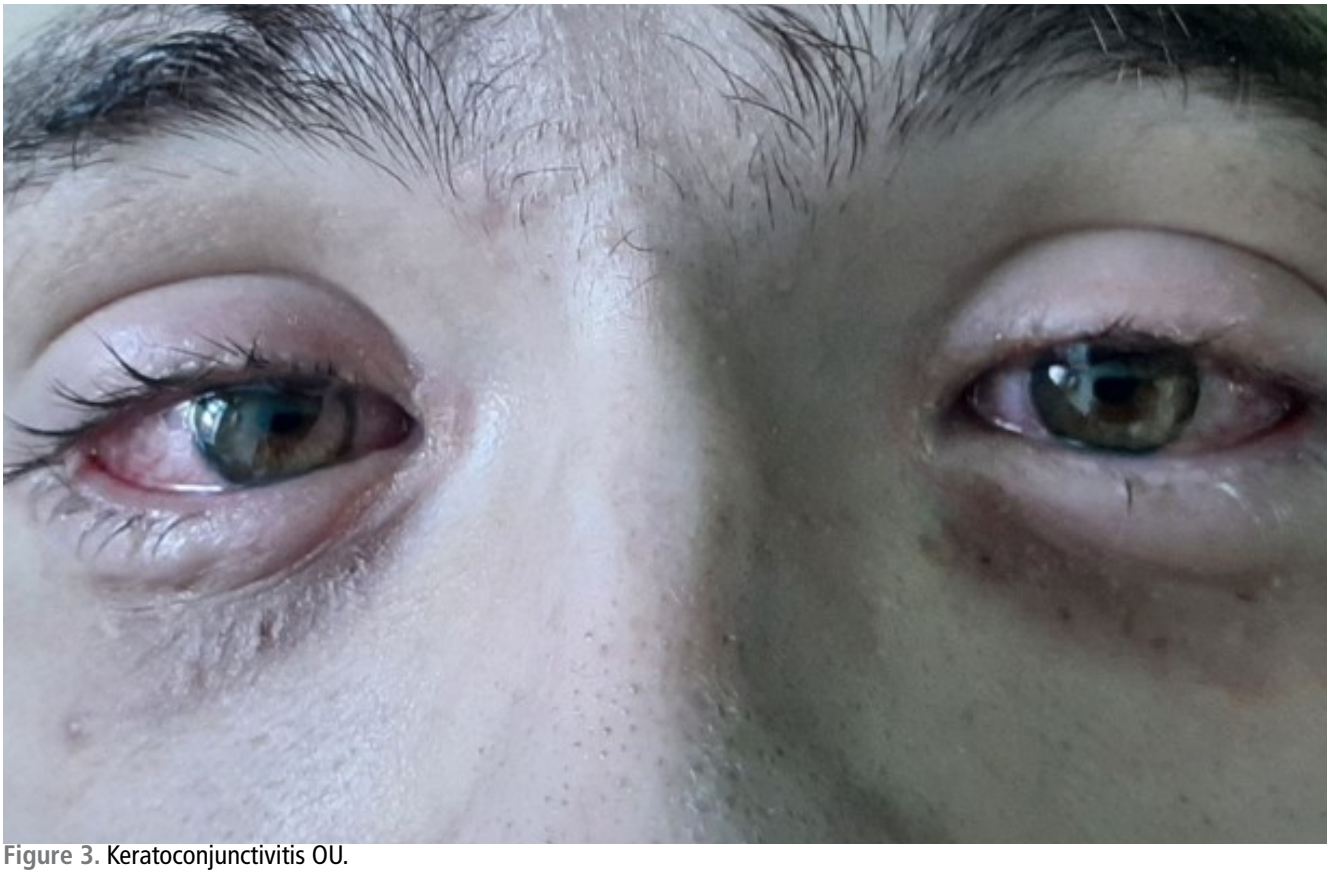

Figure 3. Keratoconjunctivitis OU.

Later that day, sparse vesicular eruptions and oral aphthae and balanitis appeared, progressing the next morning to bullae and targetoid bullae up to 6 mm (Figure 4, 5) and increasing oral lesions (Figure 6).

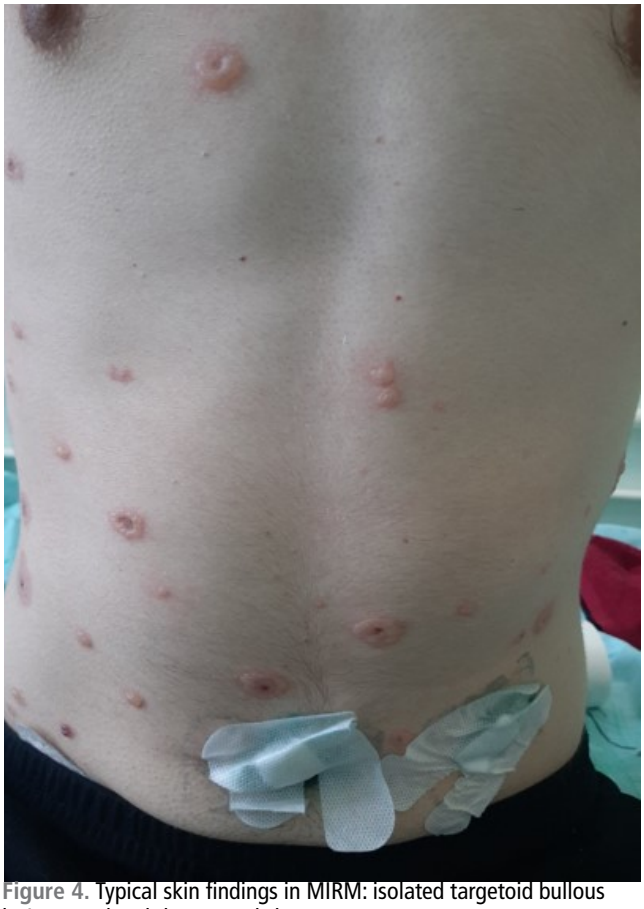

Figure 4. Typical skin findings in MIRM: isolated targetoid bullous lesions on the abdomen and chest.

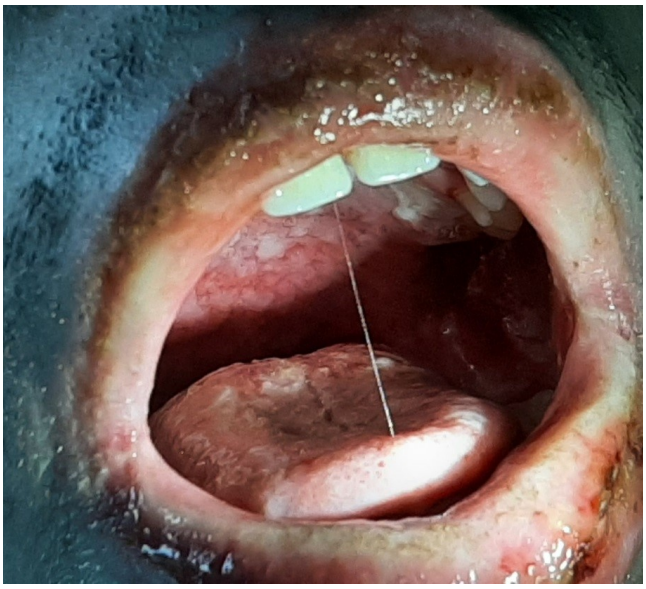

Figure 6. Oral mucositis: swelling of the tongue and palatal mucosa accompanied by blistering of the lips.

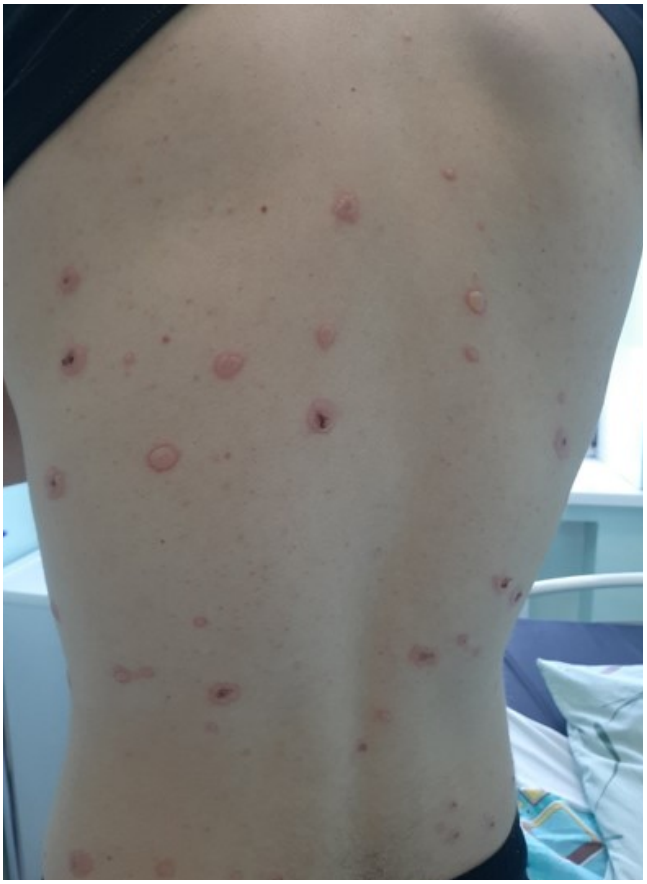

Figure 5. Several isolated bullous lesions on the back.

On hospital day 2, CXR showed polysegmental pneumonia of the left lung, and PCR for *M. pneumoniae* was positive; clarithromycin and ceftriaxone were started, later supported by positive IgM serology. The most extensive mucocutaneous involvement was documented on hospital days 6–7 with some bullae enlarging up to 2 cm and oral blistering, followed by gradual clinical recovery.

Case C (Fuchs syndrome)

A 26-year-old male presented with dry cough and fever up to 39 °C, initially treated as outpatient without improvement. CXR showed bronchitis, and clarithromycin led to partial relief. On day 9 of illness, painful oral aphthae appeared, followed by fever and urethritis; patient was admitted and doxycycline was added. PCR for Mycoplasma pneumoniae was negative, but IgM serology later returned positive. During hospitalization, the patient developed

bilateral conjunctivitis, scleritis, and retinal angiopathy. Despite widespread mucositis (stomatitis, urethritis, conjunctivitis), no skin rash was observed; a presentation consistent with Fuchs syndrome, characterized by widespread mucositis in the absence of skin rash. Continuation of antimicrobial therapy resulted in gradual recovery.

Discussion

Pathogenesis of Extrapulmonary Involvement

The key virulence factor of *M. pneumoniae* is the CARDS exotoxin (Community-Acquired Respiratory Distress Syndrome), described by Kannan T.R. and colleagues.[14,15] This toxin promotes vacuole formation with proteolytic enzymes, disrupts mucociliary clearance and leads to respiratory epithelial cell death. In addition to pneumonia *M. pneumoniae* is also linked with asthma, [16-19] and recent evidence suggests associations to COPD and bronchiectasis.[20,21]

The CARDS toxin further activates NLRP3 inflammasomes, promoting procaspase-1-mediated maturation of pro-IL-1β.[22] Elevated interleukin-1 levels drive both local and systemic inflammation, while excessive production predisposes to extrapulmonary complications and diverse inflammatory diseases.[23-26]

Persistence within host cells and antigenic variation allow *M. pneumoniae* to evade immune recognition and induce autoimmunity.[23] Cytokine cascades, recruitment of neutrophils, eosinophils and monocytes, and macrophage activation promote Th1/Th17 responses, resulting in delayed-type hypersensitivity.[27] Formation of immune complexes causes vasoconstriction and thrombotic injury, while perivascular edema can progress to vasculitis.[13] Together, direct cytotoxicity and immune-mediated mechanisms account for organ damage in tissues rich in macrophages, granulocytes, and Th1/Th17 cells—most notably, the skin.

Pathogenesis of Cutaneous Manifestations

The most frequent cutaneous manifestations of *M. pneumoniae* infection includeerythema multiforme (EM), Stevens–Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), and Mycoplasma-induced rash with mucositis (MIRM). Less common are mucositis without rash (Fuchs syndrome), erythema nodosum, nonspecific erythema, urticaria, petechiae, Raynaud's phenomenon, vasculitis, Sneddon–Wilkinson disease, thrombotic thrombocytopenic purpura, and Sweet's syndrome.[28-34]

Erythema multiforme is an immune-mediated polymorphic dermatosis usually triggered by viruses (e.g., *HSV*), *M. pneumoniae*, or medications. It arises through helper and cytotoxic T-cell responses to keratinocyte antigens cross-reactive with *M. pneumoniae* adhesins, leading to keratinocyte apoptosis. Based on extent of papular eruptions and mucosal involvement, EM is categorized as minor or major.[35]

M. pneumoniae is the leading infectious trigger of SJS/TEN, responsible for up to 50% of infectious cases. Early recognition of this association allows for appropriate analgesia (avoiding agents harmful in allergic SJS/TEN), prevents unnecessary allergological investigations, and ensures timely etiological antibacterial therapy.

The clinicalentity of MIRM has gained recognition in recent years. The prevailing model proposes that *M. pneumoniae* drives B-cell expansion, producing large numbers of uniform antibodies that form immune complexes, deposit in tissues, and activate complement.[36,37] Molecular mimicry between *M. pneumoniae* adhesins and keratinocyte antigens may also contribute. [38]

The pathogenesis of extrapulmonary involvement in *M. pneumoniae* reflects a combination of direct cytotoxic effects, immune evasion, molecular mimicry, and immune complex–mediated injury. It explains the broad clinical spectrum ranging from erythema multiforme to SJS/TEN and MIRM, as well rarer syndromes. Early recognition of *M. pneumoniae* as an underlying cause of severe mucocutaneous disease is critical, as it directs timely etiological therapy, prevents unnecessary investigations and improves patient outcomes.

List of Abbreviations

Non-pharmacological interventions NPIs
Respiratory syncytial virus RSV
Oculus uterque (both sides involved -latin) OU
Herpes simplex virus HSV
Varicella zoster virus VZV
Polymerase chain reaction PCR
Multislice spiral computed tomography MSCT
Chest radiograph CXR
Community-Acquired Respiratory Distress Syndrome exotoxin CARDS exotoxin
Chronic obstructive pulmonary disease COPD

Erythema multiforme EM
Stevens–Johnson syndrome SJS
Toxic epidermal necrolysis TEN
Mycoplasma-induced rash with mucositis MIRM

Conflict of Interest

The authors declare no conflict of interest.

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