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Unusual Manifestation of Post-Infectious Erythema Multiforme

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Abstract **Case Report**

Erythema multiforme presents as an acute skin rash characterized by symmetrical, round-shaped erythematous papules. It is typically triggered by herpes infections, Mycoplasma pneumoniae, or certain medications. In this case report, we describe a 12-year-old boy with no significant medical history who was admitted with gingivostomatitis and a generalized rash persisting for 5 days, accompanied by an unnoticed fever and declining overall health. Upon examination, the patient exhibited a fever of 39.2°C, gingivostomatitis characterized by erythematous plaques covered with vesicles across the lips, oral thrush, a maculopapular skin rash resembling erythema multiforme in a cockade pattern, and crusty lesions on an erythematous background in the genital area (penis and glans). The diagnosis confirmed erythema multiforme and gingivostomatitis caused by Chlamydia pneumoniae through respiratory PCR test and serological testing, which revealed elevated levels of IgM antibodies. Treatment with Clarithromycin resulted in significant clinical improvement, with lesion regression and achievement of a fever-free state within 72 hours. This case highlights the potential for atypical manifestations of Chlamydia pneumoniae infection in children.

Keywords: Erythema multiforme, Chlamydia Pneumoniae, children, infection, pediatric.

INTRODUCTION

Erythema multiforme is an acute skin rash characterized by the emergence of symmetrical, round-shaped erythematous papules. It is commonly triggered by herpes infections, Mycoplasma pneumoniae, or certain medications. Here, we report a case of Chlamydia pneumoniae infection presenting as erythema multiforme after consent of its parents. Our objective is to investigate potential atypical manifestations of Chlamydia pneumoniae infection in children.

OBSERVATION

A 12-year-old boy, with no significant medical history, was admitted for gingivostomatitis and a generalized rash persisting for 5 days, accompanied by an unnoticed fever and a decline in overall health.

The admission examination revealed a febrile child with a temperature of 39.2°C, exhibiting gingivostomatitis characterized by an erythematous plaque covered with vesicles forming a bouquet across the lips, as well as oral thrush. Additionally, there was a maculopapular skin rash resembling erythema multiforme in a cockade pattern, and crusty lesions on an erythematous background in the genital area (penis and glans) (Figure 1). The initial blood tests showed lymphopenia at 910 cells/mm3 and a CRP level of 30.44 mg/l. Chest x-ray results were normal. A respiratory PCR test was performed, revealing Chlamydia pneumoniae. The diagnosis confirmed erythema multiforme and gingivostomatitis caused by Chlamydia pneumoniae through serological testing, which revealed elevated levels of IgM antibodies.

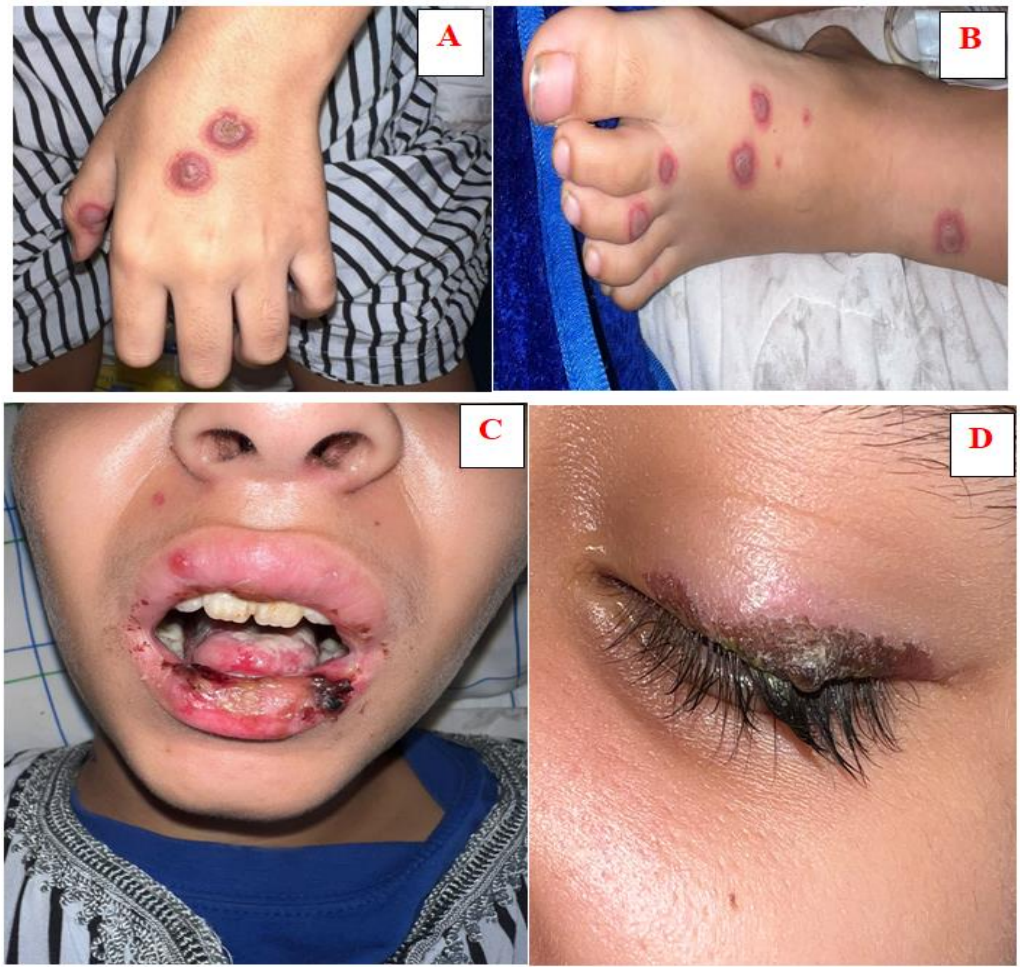

Figure 1: Various forms of geographically distributed non-exudative erythematous eruptions. (A), (B) (C)

The patient was prescribed Clarithromycin at a dosage of 50mg/kg/day in 2 divided doses, Paracetamol at 15mg/kg/6h for fever management, and local treatment of the lesions. There was significant clinical improvement noted by lesion regression and achieving a fever-free state within 72 hours (Figure 2).

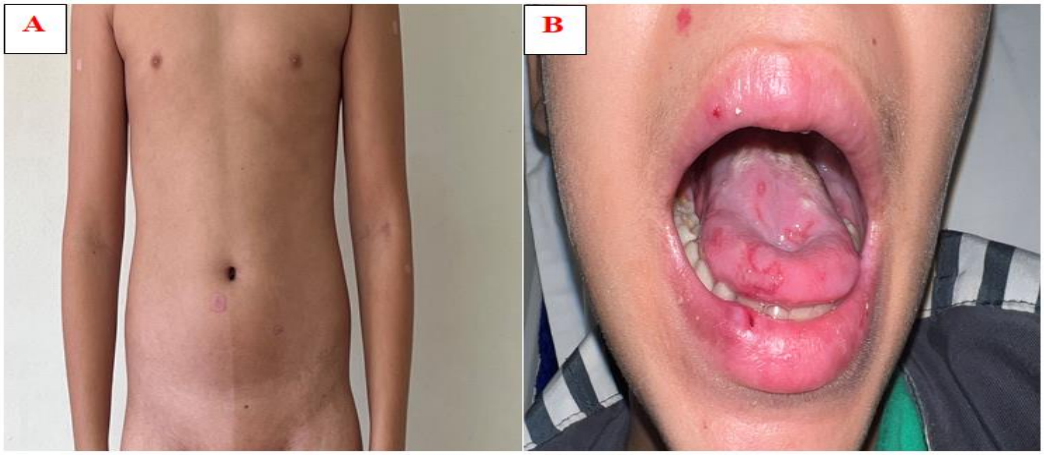

Figure 2: The evolution of our patient's condition after a few days of treatment initiation (A, B)

DISCUSSION

Erythema multiforme (EM) is an immune-mediated disorder affecting both the skin and mucous membranes, often presenting with characteristic "target" lesions. These lesions typically start as annular macules on the skin, which may progress to papules and sometimes merge into plaques. Initially, lesions are isolated, but they can coalesce over several days, making their "target" appearance less distinct [1]. In children, the lesions commonly appear on the extremities without

specific preference between the arms and legs. Unlike other childhood rashes, EM does not follow a predictable course, with new lesions appearing gradually or rapidly.

Histological studies indicate inflammatory changes around blood vessels, interface infiltration, hyperkeratosis, granulation tissue, mucinosis, and acanthosis. Viral infections, particularly herpes simplex virus type 1, account for the majority (80% to 90%) of EM cases, although other viruses such as herpes simplex virus type 2, cytomegalovirus, Epstein-Barr virus, influenza, Chlamydia pneumoniae, and COVID-19 have also been implicated. Additionally, vulvovaginal candidiasis and Mycoplasma pneumoniae infections are associated with EM [2].

Certain medications, including antibiotics, antiepileptic drugs, nonsteroidal anti-inflammatory drugs, and vaccines, can trigger EM. EM is also linked with various medical conditions including inflammatory bowel disease, hepatitis C, leukemia, lymphoma, and solid organ cancers [3].

There are two types of EM: EM minor, characterized by a mild, self-limited rash, and EM major, which presents as a severe, potentially life-threatening rash involving mucous membranes. While EM typically occurs in individuals aged between the second and third decades of life, it can also manifest in childhood.

Infection and exposure to drugs are suspected triggers for EM. Notably, herpes simplex virus (HSV), especially in recurrent cases of EM, is a well-documented association. Additionally, Mycoplasma pneumoniae (Mp) infection has been reported in some cases of EM. Recently, there has been emerging interest in the possible involvement of Chlamydia pneumoniae (Cp) infection in EM. In a 2013 study by Shinsaku *et al*., seven cases of EM minor were found to be associated with Cp infection. Diagnosis of Cp infection was made through HITAZYME-ELISA testing, revealing elevated IgM antibody titers against Cp. Among seven patients diagnosed with EM in our clinic over two years, one had systemic lupus erythematosus (SLE), while others had no significant underlying conditions [4]. Treatment varied, with some patients receiving intravenous drips and others specific medications, but most cases resolved within 5-7 days. Of particular interest was Case 1, who had recurrent EM episodes, with Cp infection identified during the fourth episode. Notably, anti-Cp IgM titers were elevated, while anti-HSV titers were negative. Case 2, diagnosed with SLE, showed slightly lower anti-Cp IgM titers, possibly due to immunosuppressive treatment. Cases 3-7 were the first occurrence of EM, with three showing positive anti-Mp antibody titers and other viral infections. Furthermore, there is a possibility of co-infection with Mp, which warrants consideration. While previous reports suggested that Mp-associated EM tends to be more severe, our case presented as the minor type.

The characteristic clinical features and mechanisms underlying Cp-related skin eruptions remain poorly understood, emphasizing the need for further research. Overall, routine testing for Cp infection in EM cases, alongside HSV and Mp, is recommended to better understand and manage this condition [4].

When assessing a child suspected of having EM, it's important to ask about recent infections or symptoms indicative of such infections, as well as any medications they may have been taking. In many cases, a diagnosis can be established based on the patient's history and physical examination alone, without the need for further testing. However, in instances of more severe presentations, particularly those involving mucous membranes or significant pain, initiating empiric therapy may be warranted. Skin biopsy is seldom necessary, but in rare or prolonged cases where diagnosis remains uncertain, consultation with a dermatologist can help determine whether biopsy is advisable [5].

There are several potential differential diagnoses for EM, including urticaria, which is commonly found in children. Distinguishing between EM and urticaria can be challenging, particularly in the early stages. EM typically presents with fixed lesions persisting for several days, whereas urticaria tends to manifest as transient, appearing and disappearing repeatedly, and often resolves within a few days. However, in some cases, the distinction between the two conditions is difficult, leading to the term "urticaria multiforme" [6].

The most critical differential diagnoses for EM involving mucous membranes are Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis. While all three conditions are immune-mediated epidermal disorders with varying clinical presentations, SJS and toxic epidermal necrolysis carry high mortality rates and lack effective treatments. Although previously considered part of a continuum, these conditions are now recognized as having distinct features and outcomes, necessitating different management approaches. Erythema multiforme typically presents with papular lesions and target-like appearances, while SJS often features widespread erythematous or purpuric macules with blisters [7, 8].

Treatment for children with EM is generally supportive, focusing on observation. Some may benefit from topical steroids or antihistamines. The use of systemic steroids in children remains controversial, with reserved use for severe cases to suppress cytokine and chemokine responses, T cell function, and reduce adhesion of inflammatory molecules to blood vessel endothelium. In cases where herpes infection is suspected, early antiviral treatment (e.g., acyclovir) may help reduce the severity and duration of EM eruptions, particularly if precipitated by sun exposure. Prophylactic acyclovir treatment may also be considered, although

evidence is limited. For cases involving oral mucous membranes or systemic symptoms, hospital admission for hydration and supportive care should be considered, especially if the child is in significant pain or discomfort [9, 10].

CONCLUSION

When encountering erythema multiforme associated with gingivostomatitis, it's important to consider a Chlamydia pneumoniae infection. Diagnosis should be supported by microbiological examinations and molecular biology. Early and appropriate treatment is essential to ensure prompt improvement of the lesions.

Competing interests: None declared

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