

Typical target lesion with a central blister in erythema multiforme major caused by drug allergy in a toddler

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Abstract

Erythema multiforme (EM) is an uncommon acute mucocutaneous illness with target lesions primarily on the face and limbs. Slow-onset hypersensitivity reactions to infections (including herpes simplex virus and mycoplasma pneumonia) and medicines (including antibiotics, anticonvulsants, and nonsteroidal anti-inflammatory drugs) cause EM. A 4-year-old male with EM after taking metamizole, ampicillin, cloxacillin, and an unknown puffer, the major developed lip sores and blisters on various places of his body. Dermatological examination revealed haemorrhagic crusts on the lips. On both hands and feet, typical target lesions with central blisters, purplish red in color, well-defined boundaries, round to oval in form, and variable size were seen. There were erythematous macules and genital oedema. A blood test revealed higher levels of leucocytes and CRP. Serological testing revealed no IgG, IgM, or anti-HSV1&2 antibodies. The X-ray of the chest was normal. Clinical improvement occurred after elimination of suspected drugs and intravenous dexamethasone, gentamicin, and paracetamol, oral cetirizine, fusidic acid 2% cream, 0.9% NaCl compress, and sterile gauze. The diagnosis of EM was established based on the presence of multiple typical target lesions with central blisters, symmetrical distribution on the extremities (dorsal surfaces of hands and feet), and involvement of lip and genital mucosal lesions after taking drugs. Negative IgG and IgM Anti HSV 1&2 test results lead to the diagnosis of drug allergy-related Erythema Multiforme Major.

Keywords: Erythema Multiforme; Erythema Multiforme Major; Drugs Allergy; Toddler

1. Introduction

Erythema Multiforme (EM) is a rare acute mucocutaneous illness characterized by targeted lesions, particularly on the face and limbs⁽¹⁾. The clinical course of this disease can range from moderate symptoms with no or little involvement of the mucous membranes, known as EM minor, to more severe clinical symptoms with the participation of two or more mucosae, known as EM Major^(1,2).

EM can occur at any age, but it is most common in adolescents and young adults, with males being more common than girls (males outnumber females by a factor of three). The number of cases discovered yearly ranges from 0.5 to 1 per 1,000,000 people. EM minor is more prevalent than EM Major^(1,9).

EM is thought to be caused by a delayed-type hypersensitivity reaction to infection (90% of the time) or particular medicines (10% of the time)^(2,3,5). Herpes simplex virus (VHS) and *Mycoplasma pneumoniae* are the most common infections that cause EM^(13,16). Antibiotics (particularly sulfa group, penicillin, erythromycin, nitrofurantoin, and

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tetracycline), anticonvulsants (phenytoin and carbamazepine) and nonsteroidal anti-inflammatory medicines are the most frequently related with EM episodes (7,12,14).

Except in EM Major (EMM), where there is fever ($t > 38.5\text{ }^{\circ}\text{C}$), prodromal signs are uncommon. Early EM lesions are often spherical, regular papules or plaques of varied sizes. EMM has a more severe, extensive, and progressive clinical course; clinical symptoms can be identified with a target acral lesion, occasionally with body involvement involving less than 10% of the body surface area, and two or more mucosal involvement (eyes, mouth, and/or genitals)^(1,2,12). Events 3 weeks before EM should be explored for precipitators, emphasizing signs and symptoms of HSV, respiratory tract infection, and drug use history. The primary goal of EM management is to identify and eliminate causal causes^(10,11). EM treatment is determined by the underlying cause and severity^(11,19).

In this study, a toddler was diagnosed with EM Major, which was thought to be caused by an allergy to metamizole, ampicillin, cloxacillin, and powder drugs whose ingredients were unknown. This case was recorded since it is unusual and can help with the diagnosis of EM Major, as well as the discovery of causes and management.

2. Case

A 4-year-old boy with complaints of red-brown sores on his lips and bigger blisters growing on both hands, feet, thighs, and genitals that were worsening after taking metamizole, ampicillin, and cloxacillin while in the hospital. Three days before hospitalisation, the patient complained of fever and cough, went to the health facility and was given a powder drug whose ingredients were unknown. Blisters formed on the lips after taking the powder drug, and the blisters extended to the back of the hands, instep, thighs, and genitals. There was no history of topical treatments, applying oil or ointment to wounds and blisters, and the lesions were not painful to touch.

Physical examination revealed moderate general condition and compost mentis awareness. Axillary temperature 37°C , respiration 18 times per minute, pulse 82 times per minute, SpO₂ 98%, body weight 11 kg, height 99 cm, malnourished status. Within typical bounds, generalist status.

On July 26, 2022, dermatological status revealed multiple hemorrhagic crusts, distinct boundaries, geographic shape, and size $0.8 \times 1.5\text{-}1 \times 2\text{ cm}$ in the labialis region. Multiple typical target lesions in the extremities region superior and inferior dextra and sinistra with dicentral blisters, purplish-red color, firm boundaries, round to oval shape, and varied sizes. Erythematous macules with irregular boundaries and irregular shape, $1.5 \times 2.5\text{ cm}$ in size, with vaginal edema (Figure 1).

On July 26, 2022, a complete blood examination revealed haemoglobin of 11.6 g/dl (10-12), leukocytes of $14.5 \times 10^3\text{ L}$ (6-17), erythrocytes of $4.61 \times 10^6\text{ L}$ (4.0-6.0), platelets of $540 \times 10^3\text{ L}$ (150-440), hematocrit of $37.6 \times 10^3\text{ L}$ (40-52), lymphocytes of 23.6% (25-50), monocytes of 12. On July 26, 2022, a serological investigation revealed a Quantitative CRP of 33.34 mg/L (3-10). On July 26, 2022, a chest photo examination revealed normal.



Figure 1 Erythema Multiforme Major with Multiple Hemorrhagic Crusts and Multiple Typical Target Lesions with Blisters in the Center on Day 1 of Treatment

The patient's working diagnosis was erythema multiforme major associated with allergies to metamizole, ampicillin, cloxacillin, and powdered drugs whose contents were unknown, with a differential diagnosis of *causa herpes simplex virus* based on anamnesis, physical examination, and supporting examinations.

Treatment: discontinue the suspected drug (ampicillin, metamizole, cloxacillin, and an unknown powder drug), administer D5 12 NS 1000cc infusion fluids within 24 hours, dexamethasone 1mg intravenous injection every 8 hours (first day), gentamicin 55 mg intravenous injection every 12 hours (if renal function is good), paracetamol 110 mg intravenous drip every 8 hours if fever (axillary temperature $>38^{\circ}\text{C}$), Skin complaints and lesions are evaluated, and the patient's family is educated.

3. Evaluation

On the sixth day of treatment, July 31, 2022, there was no itching or body heat, and hunger had begun to improve. Physical examination revealed that the patient's general health was good, that he was aware of *compost mentis*, that his axillary temperature was 36.4°C , that his respiration rate was 18 times per minute, and that his pulse rate was 78 times per minute.

Dermatological examination revealed very some blackish erosion and crusting in the labialis region. In the superior and inferior dextra and sinistra extremities, there are numerous well-defined hyperpigmented macules, blisters, and erosions. Minimal vaginal erosions and hyperpigmented macules.

On July 30, 2022, a serological examination revealed negative IgG - IgM Anti HSV1 and HSV2 (normal negative levels).



Figure 2 Treatment Evaluation Day 6. There are Multiple Hyperpigmented Macules with Crusts on them

4. Discussion

This is a rare example of erythema multiforme major caused by medication allergies in a toddler. On physical examination, a target lesion is round with clear boundaries and consists of 3 distinct zones, of which two concentric rings with discoloration surrounding the central circular zone, which tends to appear blackish, manifest as damage to the epidermis in the form of bullae or crusts, lesions are found primarily on the face and extremities^(1,15).

The presence of a target acral lesion, sometimes with the involvement of the body and blisters in the center of the target lesion involving less than 10% of the body surface area, and the presence of two or more mucosal involvements (eyes, mouth, and/or genitals) are used to determine EMM^(11,20,21). In EM, prodromal signs are uncommon; moderate symptoms such as cough, rhinitis, and low-grade fever are more common. In one-third of patients, EMM fever symptoms are greater than 38.5°C ⁽¹⁾. A toddler was reported to have a target lesion with blistering in the core of the lesion affecting the thorax and extremities, involving the oral and genital mucosa, and exhibited prodromal symptoms in our case report.

Erythema Multiforme is caused by a delayed-type hypersensitivity reaction mediated by T lymphocytes. The herpes simplex virus (VHS) and *Mycoplasma pneumoniae* are regarded to be the most common causes of Erythema Multiforme^(1,17,21). Drugs cause about 10% of EM^(5,18). According to the anamnesis, the patient's symptoms felt burdensome when given ampicillin, metamizole, cloxacillin, and an unknown substance.

The underlying etiology, the clinical picture of mucosal involvement, and the severity of the disease all influence EM therapy. The most crucial treatment is eliminating causal causes, including infectious diseases and medications. The initial step is to treat the suspected contagious condition or discontinue the causative medicine. Hospitalization is recommended for EM cases with severe mucosal involvement producing eating problems or EM Major with suspicion of SJS^(1,11). Intravenous fluid administration, electrolyte replacement and steroids may be considered for hospitalised cases^(11,15,17). Systemic corticosteroids have been extensively studied as adjuvant therapy for EM because they have a beneficial immunosuppressive effect on hypersensitivity reactions, but their use is still controversial due to the complications they can cause^(3,15). According to various studies, the recommended systemic corticosteroid regimen is prednisone 0.5-1 mg/kg/day or methylprednisolone 1 mg/kg/day for three days, then decreased in 7-10 days to 4 weeks^(3,4). Systemic corticosteroids, such as Prednisone 40-60 mg/day, are gradually tapered over 2-4 weeks⁽¹⁵⁾. In our situation, the treatment included discontinuing the suspected medicine, administering electrolyte fluids, administering systemic corticosteroids (dexamethasone 0.02-0.3 mg/kg/day), and providing other symptomatic relief.

After the sixth clinical day of treatment, the patient no longer complained of itching or body heat, and his appetite began to improve. Lip lesions have started to peel, bullae have begun to crust, and no new blisters have formed.

5. Conclusion

Erythema multiforme major caused by drug allergy is rare; if it occurs, it should be investigated alongside other differential diagnoses for urgent care and follow-up. The most crucial treatment is eliminating causal causes, including infectious diseases and medications. Some specialists propose that in EM cases with extensive mucosal involvement causing eating disorders, hospitalization is needed for intravenous fluids, electrolyte replenishment, and corticosteroid delivery. Although systemic corticosteroids are still contentious due to the difficulties they produce, some specialists have recognized that immunosuppressants can effectively manage lesions in EM, which is supported by the positive response in our patients. In this case, the prognosis is *dubia ad bonam*.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest regarding the publication of this document.

Statement of informed consent

Informed consent was obtained from all individual participants included in the case report.

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