Erythema Multiforme

Erythema multiforme (EM) is an acute, immune-mediated, and sometimes recurring skin condition that is considered to be a type IV hypersensitivity reaction. It is associated with some infections such as HSV or Mycoplasma pneumoniae, or less frequently medications. The presence of EM is characterized by the appearance of distinctive target-like lesions on the skin in a symmetrical distribution. Mild symptoms is classified as EM minor while mucosal involvement is classified as EM major. The disease is self-limiting but topical ointments may provide symptomatic relief.



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Pathogenesis

Type IV Hypersensitivity Reaction

Hiker-sensitive Guy with Type 4 Fork

The pathophysiology of EM is not clearly understood. The current understanding of its pathogenesis is primarily derived from studies investigating EM secondary to HSV infection, which is thought to involve a Type IV hypersensitivity reaction to viral antigens deposited in lesional skin. This kind of hypersensitivity reaction is delayed and cell-mediated and is the only type of hypersensitivity reaction that involves sensitized T lymphocytes instead of antibodies. It appears that this immune-mediated response can be triggered by a variety of stimuli including viral, bacterial, and chemical products.

HSV

Herpes-harp Virus

Infections account for approximately 90% of EM cases, and herpes simplex virus (HSV) is the most commonly identified trigger overall. EM does not occur in the majority of people infected with HSV, and it doesn't appear with every recurrence of HSV infection in individuals who have a history of HSV-related EM. The reason for this has not been identified.

Mycoplasma Pneumoniae

Mic-plasma Nude-Mona

In children particularly, Mycoplasma pneumoniae infection is an important trigger for EM.

Drugs

"Drugs" Pill Bottle

Studies estimate that approximately 10% of EM cases are drug-induced. Higher rates of drug-induced EM have been reported for children, particularly associated with penicillin. In the general population, a wide variety of medications have been seen to cause EM eruptions, but NSAIDs, sulfa drugs, antiepileptics (phenytoin), and antibiotics (?-lactams) have been more commonly identified as triggers.

Characteristics

Targetoid Lesions

Target Leeches

Targetoid lesions are the hallmark of EM. At initial onset, multiple types of erythematous lesions (macules, papules, vesicles) may develop, which are typically not itchy. These lesions then evolve into the classic target lesions: three distinct color zones with a central dusky (dark) center showing epithelial disruption/erosion. The three zones include the central erosion/blister, a darker red inflammatory zone surrounded by a pale ring of edema, and a red halo surrounding the periphery of the lesion. Targetoid lesions in EM are typically less than 3 cm in diameter.
Atypical target lesions may also appear as raised, palpable lesions with only two zones of color change and a poorly defined border.

Symmetrical Distribution

Symmetrical Prickly Cactus

EM lesions most commonly appear in a symmetrical distribution and favor extensor surfaces and acrofacial sites (face, hands, and feet). Lesions then spread centrally and may also involve flexural surfaces of extremities and/or the trunk.

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EM Minor: Mild Symptoms

Mild Miner

EM minor refers to EM with minimal or no mucosal involvement and without associated systemic symptoms.

EM Major: Mucosal Involvement

Major Mucus

EM major is used to describe EM with severe mucosal involvement and possibly associated systemic symptoms such as fever, generalized discomfort, or muscle aches. Mucosal lesions can involve the oral, ocular, and/or genital mucosa and commonly appear as diffuse areas of mucosal redness, painful erosions, and/or blisters.Oral involvement occurs most commonly. Lesions tend to affect the vermilion border of the lip and mucosal surfaces, including the buccal mucosa (inner cheek), labial mucosa (inner lip), unattached or marginal gingiva surrounding teeth, and the tongue. Rarely, involvement can extend to the pharynx and upper respiratory tract.

Self-Limiting

Self-limited Selfie Kid

In most patients, EM spontaneously resolves within a few weeks without long-term consequences. EM lesions typically don’t scar, but postinflammatory hyperpigmentation may remain for months after resolution. The primary treatment is usually symptomatic, including oral antihistamines, analgesics, local skincare, and soothing mouthwashes for mucosal involvement. Suspected infections should be treated appropriately after cultures and/or serologic tests. Prophylaxis with oral acyclovir may be helpful in reducing the recurrence of HSV-associated EM and should be considered in patients with greater than 5 attacks per year. For frequent recurrences and persistent cases unresponsive to routine treatment, continuous therapy with valacyclovir has been reported to be effective.

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