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Erythema Multiforme

Erythema multiforme (EM) is an acute, self-limiting inflammatory skin disorder characterized by a diverse rash and mucocutaneous involvement, typically affecting the skin, mucous membranes, and, in severe cases, internal organs. The term "erythema multiforme" (meaning "multiple forms of redness") refers to the varied clinical manifestations of the condition. EM is often divided into two primary forms: EM minor and Stevens-Johnson Syndrome (SJS), which represent different severities of the same underlying disease process. While most cases are mild and self-limiting, SJS is a much more severe form, requiring urgent medical intervention.

Epidemiology and Demographics

EM is relatively common in dermatologic practice, particularly in young individuals, with approximately 50% of cases occurring in patients under the age of 20. The disease is rare in children younger than 3 years and adults older than 50 years. There is a slight male predilection, though the disease affects both genders equally. Recurrence is observed in about one-third of cases, and seasonal outbreaks have been documented, suggesting an environmental or infectious trigger.

Etiology and Pathogenesis

The pathogenesis of erythema multiforme remains incompletely understood, but it is believed to involve immune-mediated mechanisms, particularly hypersensitivity reactions that result in the apoptosis of keratinocytes. The disease is often triggered by viral infections, with herpes simplex virus (HSV) being the most common cause of EM minor, especially HSV-1 (cold sores) and HSV-2 (genital herpes). Other infectious triggers include Mycoplasma pneumoniae, bacterial infections, and rarely, fungal infections. In addition, medications, such as antibiotics (e.g., sulfonamides, penicillins), NSAIDs, and anti-seizure medications (e.g., phenytoin, phenobarbital) are frequently implicated in the development of both EM minor and SJS.

The immune system plays a central role in the development of erythema multiforme. It is theorized that the disease arises from an altered immune response, where cytotoxic T lymphocytes target epithelial cells, leading to keratinocyte death and skin ulceration. In more severe cases, such as SJS, this immune response extends to mucous membranes and internal organs, making it potentially fatal.

Clinical Presentation

EM manifests in different forms, ranging from mild skin involvement to life-threatening mucosal ulceration. The disease is typically divided into two major types: EM minor and SJS.

- ***Erythema Multiforme Minor:***

- *Preceding symptoms*: In most cases, there is minimal prodrome. When present, it consists of mild fever, malaise, or itching.
- *Skin lesions*: The rash begins as red, raised spots that evolve into targetoid lesions, with a characteristic bull's-eye appearance. These lesions are often concentrated on the palms, soles, and extremities, particularly over the dorsum of the hands and feet. In some cases, blistering may occur, especially around the lips and oral mucosa. The lesions typically resolve within 1 to 2 weeks, leaving behind residual hyperpigmentation.
- *Etiology*: The most common cause of EM minor is HSV reactivation. Other bacterial or viral infections can also trigger the condition. Recurrent episodes often follow the reactivation of an underlying infection or exposure to the same medication.

➢ ***Stevens-Johnson Syndrome (SJS):***

- *Severe manifestations*: SJS is the more severe form of erythema multiforme, with extensive mucosal involvement (including the oral cavity, eyes, and genital tract), and, in some cases, internal organ involvement. Blood blisters, erosions, and painful ulcers may appear, causing significant discomfort and difficulty in eating and swallowing.
- *Prodrome*: SJS often begins with flu-like symptoms such as fever, cough, malaise, and sore throat. These symptoms are often misdiagnosed as a viral infection, delaying appropriate treatment. The rash rapidly progresses over 1 to 14 days and may lead to widespread sloughing of the skin.
- *Complications*: Severe cases may result in sepsis, fluid loss, and respiratory failure. Mortality rates for SJS are estimated to be 5–15%, though improvements in early intervention have reduced this rate.

Diagnosis

The diagnosis of erythema multiforme is primarily clinical, based on the characteristic appearance of the rash and mucosal involvement. A thorough medical history and medication review are essential to identify potential triggers. In cases of suspected SJS, a skin biopsy may be performed to confirm the diagnosis by revealing epidermal necrosis and interface dermatitis.

Management and Treatment

➢ **Erythema Multiforme Minor:**

- *Self-limiting course*: In most cases, EM minor is self-limiting, with the rash resolving within 2 to 4 weeks without the need for specific treatment. Symptomatic management includes topical corticosteroids or antihistamines to alleviate itching.
- *Herpes simplex-induced EM*: For HSV-induced EM minor, oral antiviral medications (e.g., acyclovir [Zovirax], valacyclovir [Valtrex]) can be effective if started within the first few days of lesion appearance. In patients with recurrent episodes, prophylactic antiviral therapy may be considered.

➢ ***Stevens-Johnson Syndrome (SJS):***

- *Supportive care*: For SJS, hospitalization is often required, and management in a burn unit may be necessary to support skin and mucosal healing, fluid replacement, and infection prevention.
- *Immunosuppressive therapy*: Early intervention with intravenous immunoglobulin (IVIG), cyclosporine, or cyclophosphamide may significantly improve outcomes, especially if administered within the first 72 hours of symptom onset. Systemic corticosteroids may still be used in some cases, but they are generally avoided in patients with extensive mucosal involvement due to the risk of exacerbating infections.
- *Prevention of recurrence*: For patients with a known drug trigger, complete discontinuation of the offending medication is critical to prevent recurrence. If the same medication is used again, the eruption may occur within hours rather than days, increasing the risk of severe complications.

Conclusion

Erythema multiforme is a rare but significant dermatologic condition, ranging from the mild EM minor to the life-threatening SJS. Understanding the underlying immune mechanisms and identifying the causative triggers are crucial in managing this disorder. While EM minor typically resolves on its own, SJS requires urgent and aggressive intervention. The use of immunosuppressive therapies, early diagnosis, and supportive care has significantly improved outcomes for patients with SJS. As advancements in immunotherapy continue, early intervention remains key to preventing the potentially fatal consequences of severe forms of this disease.

References

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