Pediatric Pearls

Use of steroids for erythema multiforme in children

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ABSTRACT

QUESTION I recently diagnosed an erythema multiforme rash in several patients, two of whom had the major variant, Stevens-Johnson syndrome. Should these patients be managed with corticosteroids?

ANSWER In most cases, mild erythema multiforme is self-limited and resolves in 2 to 4 weeks. Stevens-Johnson syndrome is a serious disease that involves the mucous membranes and lasts up to 6 weeks. There is no indication for using steroids for the mild form. Use of steroids for erythema multiforme major is debatable because no randomized studies clearly indicate which children will benefit from this treatment.

RÉSUMÉ

QUESTION J'ai récemment diagnostiqué un érythème polymorphe chez quelques patients dont deux souffraient de la variante plus grave, soit le syndrome de Stevens-Johnson. Ces patients devraient-ils être traités avec des corticostéroïdes?

RÉPONSE Dans la plupart des cas, l'érythème polymorphe bénin se résorbe de lui-même et disparaît en deux à quatre semaines. Le syndrome de Stevens-Johnson est une maladie grave qui s'attaque aux membranes muqueuses et dure jusqu'à six semaines. Il n'est pas indiqué d'utiliser des corticostéroïdes pour la forme bénigne. L'utilisation des stéroïdes pour l'érythème polymorphe grave est discutable parce qu'aucune étude randomisée n'a clairement démontré quels enfants peuvent bénéficier d'un tel traitement.

Erythema multiforme (EM) is an acute, self-limited illness characterized by the presentation and distinctive distribution of fixed red papules.[1,2] Over time, these primary lesions typically grow larger and produce well demarcated plaques that undergo variable concentric changes; some have central blisters with a necrotic blister roof, while others have areas of central epidermal necrosis without circumscribed blister formation. Because of their annular appearance, complete with red border and a central white-gray area, these lesions are known as "iris" or "target" lesions.[3]

Although there has been some debate about the accuracy of the classification scheme,[2] EM is classically separated into two clinical forms.[4] Erythema multiforme minor is characterized by symmetric involvement of the extremities and predominantly affects the extensor surfaces, usually sparing the trunk and mucous membranes. The duration of EM minor from onset to healing ranges from 2 to 4 weeks.[3]

In contrast, the course of EM major is longer; healing occurs within 6 weeks in most cases.[3] Erythema multiforme major is also known as Stevens-Johnson syndrome (SJS); in SJS, the mucous membranes are heavily affected.[3-5] Generally, two or more mucosal surfaces are affected, including the ocular, nasal, buccal, and anogenital mucosae.[3,5] In extreme cases, complications can include visual impairment, systemic symptoms, and damage to the internal viscera.[3,4]

Causes

Both type III and type IV host-specific hypersensitivity reactions have been put forth as the possible

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pathogenesis of EM, based on the common histologic findings of T lymphocytes, basophils, a monocytic infiltrate, and no leukocytoclastic vasculitis.[4-6] The list of antigenic stimuli linked to the development of EM is considerable,[3] with the most well documented being herpes simplex virus (HSV) infections, *Mycoplasma pneumoniae* infections, and reactions to systemic drugs such as sulfonamides and penicillins.[2-7]

Management

When the precipitant can be identified, initial management of EM should involve correcting or treating the cause. A macrolide or tetracycline is usually given in *Mycoplasma*-induced illness to treat infection.[6] For HSV, oral acyclovir has been shown to be effective in preventing further episodes of HSV-associated EM.[8] If any drug is identified as the culpable agent, it should be discontinued immediately.

Since EM minor is a self-limited and relatively benign illness, treatment is predominantly to alleviate symptoms.[3,6,7] Management of EM major is far more complicated, as there is no generally accepted standard of treatment.[4]

In light of proposed pathogeneses, some have recommended using systemic corticosteroids for treating EM major. Renfro et al[6] suggested that the immunosuppressive and anti-inflammatory properties of corticosteroids could decrease the severity of the disease if they were administered early in the course of the illness, thereby shortening convalescence time and preventing development of serious complications.

Three reported cases demonstrate a dramatic improvement in patients after initiation of methylprednisolone therapy. In one study, body temperatures were brought under control, and vesicular eruptions halted and began to resolve within 2 to 3 weeks.[6] Martinez and Atherton reported two cases where administration of intravenous methylprednisolone arrested progression of acute attacks and recurrences of the disease. Patients recovered within 2 weeks and had no serious sequelae.[9]

Though corticosteroids' immunoregulatory and anti-inflammatory effects are not fully understood, some of the proposed mechanisms might explain why they are of benefit in treatment of EM. By maintaining vascular integrity, promoting synthesis of lipocortins, and decreasing the expression of leukocyte adhesion molecules, corticosteroids negatively affect the inflammatory response.[7,10] In terms of immune modulation, corticosteroids down-regulate cytokine gene expression, which is thought to result in inhibition of several immune functions.[10]

No concrete evidence in the literature, however, proves that corticosteroids are efficacious for EM major. A retrospective pediatric study by Rasmussen[11] linked corticosteroid therapy with delayed recovery time and serious complications. Thirty-two children with severe EM major were treated with large doses of systemic prednisone or supportive care only. While an antipyretic effect was seen, patients receiving corticosteroids had to stay longer in hospital than those in the supportive care group. Also, all patients with complications (including pneumonia and gastrointestinal bleeding) were in the steroid-treated cohort.[11]

Another retrospective review reached similar conclusions concerning steroid use for EM.[12] A case series illustrated successful management of patients without use of systemic steroids,[13] and a large case-control analysis implicated corticosteroids in development of EM major.[14]

Conclusion

Because of conflicting reports and the lack of controlled studies examining therapy, indications for corticosteroid use in children with EM are unclear.[15,16] The small sample sizes and anecdotal nature of the evidence presented by proponents of systemic steroid use could be considered flaws in their arguments.[7,9] In retrospective studies by Rasmussen[11] and Ginsburg,[12] the point of initiation of corticosteroid therapy in the course of the disease was not reported. If given later in the course of the illness, corticosteroids might not be found helpful and could contribute to an increased risk of infection, which could account for the complications

reported in the Rasmussen study.[11] Future studies also need to consider route of administration and dose of corticosteroids because they vary greatly among published studies, making comparison difficult.[7,9,11,12] Until the appearance of prospective, double-blind or randomized controlled trials that address these issues, whether to administer corticosteroids to children with EM major will remain controversial.

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