

Erythema multiforme in children

The steroid debate

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Abstract

Question In my office I occasionally see children who have rashes with “target lesions” and who are diagnosed with erythema multiforme (EM). When should these children receive steroids, and when should the illness be allowed to follow its natural course without steroid treatment?

Answer Erythema multiforme is relatively common in children. Current recommendations suggest not to treat EM minor with systemic steroids and that topical steroids might be of benefit. The use of systemic steroids for EM major remains controversial, as there is evidence both for and against treatment, and no randomized controlled trials have been done. Further studies need to address the benefit of steroids, and in the interim, physicians should decide on a treatment based on the severity of EM and in consultation with a dermatologist, if available.

Érythème polymorphe chez l'enfant

Le débat entourant les stéroïdes

Résumé

Question Je vois occasionnellement à mon cabinet des enfants qui ont des éruptions cutanées avec «lésions ciblées» chez qui on a diagnostiqué un érythème polymorphe (EP). Quand ces enfants devraient-ils recevoir des stéroïdes et quand devrait-on laisser le problème suivre son cours naturel sans traitement aux stéroïdes?

Réponse L'érythème polymorphe est relativement courant chez les enfants. Les recommandations actuelles sont de ne pas traiter l'EP mineur avec des stéroïdes systémiques, tout en indiquant que les stéroïdes topiques pourraient apporter des bienfaits. L'utilisation des stéroïdes systémiques demeure controversée, car il y a des données probantes en faveur et contre ce traitement, et aucune étude contrôlée randomisée n'a été effectuée. Il faudrait que d'autres études se penchent sur les bienfaits des stéroïdes; entre-temps, les médecins devraient décider du traitement en fonction de la gravité de l'EP et en consultation avec un dermatologue, si possible.

Erythema multiforme (EM) is an immune-mediated, mucocutaneous condition characterized by “target” lesions.¹ Classically, EM has been separated into 2 subgroups: EM without mucous membrane involvement (EM minor) and EM with mucous membrane involvement (EM major). In EM minor, lesions often present as papules, which might enlarge and eventually form the typical target lesion with erythema surrounding an area of central clearing. They might then evolve further, resulting in more confluent patches or annular lesions.¹ The rash in EM minor preferentially affects the limbs, specifically the extensor surfaces; however, it can also be seen throughout the body, excluding mucous membranes. While usually a self-limited condition, lasting less than 4 weeks, some patients might experience persistent or recurrent lesions.

Between 20% and 60% of patients with EM (pediatric and adult) present with EM major, which has mucous membrane involvement.¹⁻⁴ The oral mucosa is most commonly affected, initially with edema that progresses to superficial erosions.^{1,5} Other surfaces that might be involved include the anogenital, ocular, and nasal mucosa.

It is currently believed that EM is a result of an immune reaction to an inciting infectious or pharmacologic antigen. Although the full mechanism is not understood, it is in part due to a type IV hypersensitivity immune response, mediated by T lymphocytes.^{2,3} The most common infectious organisms in EM are herpes simplex virus types 1 and 2, as well as *Mycoplasma pneumoniae*.^{1,6} Nonsteroidal anti-inflammatory drugs, antiepileptics, and antibiotics (particularly penicillins and sulfonamides) are among the most common offending medications.^{1,5} Genetic predisposition to developing EM has also been suggested.¹ The diagnosis is typically made clinically, as there are no diagnostic laboratory tests for this process.^{1,3} For confirmation, a biopsy is needed.

Differentiating EM and Stevens–Johnson syndrome

Although previously thought to be on a similar continuum of EM, and histologically appearing the same,¹ Stevens–Johnson syndrome (SJS) is increasingly being considered a separate disease process.^{1,6,7} The rash in SJS has the same mucocutaneous lesions as in EM, but it is more widespread in distribution; lesions are more common on the trunk, the

limbs are less affected, and multiple mucous membranes are involved. The rash is also more macular than in EM.^{1,2} For children with suspected SJS, expert opinion should be sought, as complications might be life threatening. Other differentials that must be considered when diagnosing EM include fixed drug reactions, small-vessel vasculitis (eg, Henoch-Schönlein purpura), and urticaria.

Why consider steroids?

The first line of treatment for EM is removal of the inciting factor when possible.⁸ When herpes simplex virus infection is thought to be the cause, oral acyclovir is recommended to treat the child. For cases in which *Mycoplasma* infection is suspected to be the cause, treatment recommendations include a macrolide or tetracycline.³ For patients with EM minor, topical steroids might also provide some benefit and can be tried.^{1,5,9}

Systemic steroids have been suggested as adjuvant therapy based on their immunosuppressant effects.⁶ They suppress cytokine and chemokine response, as well as T cell function, and decrease adhesion of inflammatory molecules to blood vessel endothelium.^{6,10} To date, their use has been limited to EM major, as EM minor is self-limited.⁹

Currently there are no published randomized controlled trials looking at oral steroids in EM. It has been suggested that steroids used to treat EM major decrease the duration and severity of symptoms.¹¹ In a retrospective review of 22 adult patients with either EM major or EM minor, 13 were treated with oral steroids (60 mg of fluocinolone or prednisone for 5 to 7 days) and reported shortened duration of symptoms (15.7 days, compared with the reported typical course of 1 month) and no complications.² In another study of 11 patients aged 9 to 38 years with recurrent oral EM, the authors suggested that steroids facilitated faster treatment; however, data to support this were not presented.¹² In both of those studies,^{2,12} however, recurrence of disease was not different with steroid therapy. Kakourou et al reported that systemic steroids decreased the mean (SD) duration of eruptions (7.0 [3.3] days vs 9.8 [3.0] days; $P=.08$), as well as the severity of the rash in children with EM major, in a small prospective trial of steroids versus supportive treatment alone.¹³ Those who support use of steroids suggest that early treatment is important and might prevent complications of steroid use.^{6,13,14}

Other clinicians and researchers argue against use of systemic steroids, suggesting that steroid treatment might increase recovery time, as well as increase the risk of infections and other complications.^{6,15} In a retrospective review of EM major and SJS in pediatric patients,¹⁵ Rasmussen examined 32 children (aged 8 months to 14 years), 17 of whom received steroids, and reported that there were increased complications in the steroid group, and thus a longer hospital stay (21 days in the steroid group vs 13 days in the supportive group; $P<.01$).¹⁵ The most common complication was infection ($n=9$), followed

by upper gastrointestinal bleed ($n=3$).¹⁵ Two subsequent studies found similar results, with no evidence of faster resolution of symptoms of EM in those patients who received steroids versus those who did not.^{11,16}

Recommendations

Currently, systemic steroids are not recommended for EM minor; however, topical steroids might be of benefit.^{1,5,9} For patients with EM major, there is evidence both for and against treatment with steroids, with no clear guidelines.⁶ If steroids are used, treatment should occur early in the course of illness. Dosages should not exceed 40 to 60 mg/d, and tapering is needed when steroids are discontinued. Between 0.5 and 1.0 mg/kg of prednisolone daily tapered over 7 to 10 days is an alternative.³

Competing interests

None declared

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