

## Case Report

# Morbiliform rashes due to erythromycin in a patient with herpes zoster infection

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**Abstract** Erythromycin is a macrolide antibiotic active against many gram-positive infections and few gram-negative bacteria, as well as mycoplasmas, spirochetes, chlamydiae and rickettsiae. Dermatological reactions appear to be rare with erythromycin and mainly include maculopapular rashes, pruritus, urticaria, and angioedema. Reports of morbiliform rashes due to erythromycin are rare. We report a case of morbiliform reaction due to erythromycin in a patient suffering from herpes zoster with established causality, severity and preventability assessments. Upon development of the adverse drug reaction, we stopped the drug and managed the patient with systemic corticosteroids.

### **Key words**

Erythromycin, morbilliform rashes, causality, severity, preventability.

## **Introduction**

Erythromycin is a macrolide antibiotic with an essentially bacteriostatic action against many gram-positive and to a lesser extent against gram-negative bacteria as well as mycoplasmas, spirochaetes, chlamydiae and rickettsiae.<sup>1</sup> Gastrointestinal disturbances such as abdominal discomfort, cramp, nausea, vomiting, and diarrhea are fairly common after both oral and parenteral administration. Other side effects include cholestatic jaundice, reversible hearing loss with large doses etc. Hypersensitivity

reactions appear to be uncommon and mainly include maculopapular rashes, pruritus, urticaria, and angioedema; anaphylaxis and acute respiratory distress have also been reported in literature. In addition, fixed drug eruption, urticaria, Stevens-Johnson syndrome (SJS),<sup>2</sup> toxic epidermal necrolysis (TEN)<sup>3</sup> have also been reported. Reports of morbilliform rashes due to erythromycin are not reported in the literature. We hereby report a case of morbiliform reaction due to erythromycin in a patient suffering from herpes zoster. We also carried out the causality, severity and the preventability assessments of the adverse drug reaction (ADR) by using the Naranjo algorithm,<sup>4</sup> Hartwig scale<sup>5</sup> and the modified Schumock and Thornton scales,<sup>6</sup> respectively.

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### Case report

A 23-year-old male presented to the dermatology out-patient department (OPD) of Manipal Teaching Hospital (MTH), Pokhara, Nepal on 6<sup>th</sup> July 2006 with complaints of itching and red rashes all over the body for the past 2 days. There was history of odynophagia but no burning micturation. On further enquiry, the patient gave history of small grouped blisters over the right side of chest and back, associated with pricking and shooting pains eight days earlier, for which he had applied silver sulphadiazine and acyclovir creams, along with oral ibuprofen and paracetamol. As the vesicles increased in size to form bullae, he was given tab erythromycin 500mg PO four times daily; within 24 hours of which he developed itchy rashes all over the body.

General and systemic examinations were within normal limits except for posterior pharyngeal wall congestion. Vital parameters were stable. Cutaneous examination revealed morbilliform rash all over the body (**Figures 1 and 2**) and tender erythematous plaque with irregular margin over the right mammary and scapular area, not crossing the midline. Investigations including HIV ELISA were negative. A probable diagnosis of drug reaction with healing herpes zoster of right T4, T5 dermatomal distribution was made.

The patient was admitted and started on intravenous steroids, namely dexamethasone 8mg twice daily, ranitidine 50mg IV bid, and calamine lotion for application over the morbilliform rashes. Oral erythromycin was stopped.



**Figure 1** Generalized morbilliform rash. Subsiding lesions of herpes zoster are also visible on right side of chest.



**Figure 1** Posterior view of patient.



**Figure 3** Disappearance of the rash after stopping the treatment .

The patient's condition improved within a matter of hours, and no new lesions were seen. The patient was discharged on the third day of admission with tapering dose of oral steroids. The patient followed up on 10 days from the day of discharge during which there was no new lesions except for healed hyperemic lesions of herpes zoster (**Figure 3**) and was advised not to take oral erythromycin thereafter.

Upon reporting the ADR to the Pharmacovigilance cell of the hospital through the ongoing spontaneous ADR reporting program, the pharmacists carried out the causality, severity and preventability assessments for the ADR. The causality assessment as per Naranjo algorithm was found to be 'probable' (Naranjo score 6), the severity assessment as per modified Hartwig and Siegel scale categorized the ADR to be 'moderate' (level 4a) and the preventability was identified as per the modified Schumock and Thornton scale was found to be 'not preventable'.

## **Discussion**

Morbilloform or maculopapular eruptions are the most common drug-induced reactions, which often start on trunk or areas of pressure or trauma, and consist of erythematous macules and papules that are frequently symmetric and may become confluent. Involvement of mucous membranes, palms, and soles is variable; the eruption may be associated with moderate to severe pruritus and fever. Morbilloform reactions usually develop within 1 week of initiation of therapy and last upto 1 to 2 weeks; however, reactions to some drugs, especially penicillin and drugs with long

half lives, may begin more than 2 weeks after therapy has begun and can last as long as 2 weeks after therapy has ceased.<sup>7</sup>

The pathogenesis of morbilliform rashes is unclear. A hypersensitivity mechanism has been suggested, although these reactions do not always recur following drug rechallenge. Diagnosis is rarely assisted by laboratory or patch testing; differentiation from viral exanthema is the principal consideration. Occasionally these eruptions may decrease or fade with continued use of the responsible drug.<sup>7</sup>

A distinct reddish-coloured morbilliform rash may be caused by ampicillin, its derivative amoxicillin and its esters bacampicillin, pivampicillin and talampicillin. The reaction will occur in almost all patients with infective mononucleosis (glandular fever) and is not always an indicator of true penicillin allergy although patients often self report penicillin sensitivity as a result of this reaction. A high incidence of this reaction also occurs in patients with cytomegalovirus infection. These are often transplant patients taking immunosuppressive drugs or patients with leukemia.<sup>8</sup>

Dermatological reactions due to erythromycin are rare. A report of contact sensitization and rare reports of skin irritation (e.g. erythema and peeling) have been reported with topical erythromycin ointment. The actual incidence of these ADRs is unknown.<sup>9</sup> One case of repeat drug eruption after administration of erythromycin has been described. The authors report it to be the first case of erythromycin as proven agent of such an

allergic reaction.<sup>10</sup> A 31-year-old woman developed SJS secondary to oral erythromycin. The patient had been prescribed a regimen of erythromycin therapy (333 mg every 8 hours) for otitis media. After the second dose, the patient developed oral ulcerations, tongue swelling, and a generalized erythematous rash. The symptoms quickly progressed to lesions (coalescing or bullae) that covered greater than 80% of her body. Although the patient developed numerous complications, she was discharged 32 days after admission. A temporal relationship of the SJS to the ingestion of erythromycin was suggested by the authors.<sup>11</sup> During the literature review, we could not locate any case of morbilliform rashes caused by erythromycin.

Establishing the causal relationship between the drug and the ADR is an important aspect in pharmacovigilance. Naranjo algorithm is a commonly used algorithm to carry out the causality assessment, which categorizes adverse drug reactions as possibly, probably or definitely due to a certain drug. In this patient, the ADR was found to be 'probably' related to erythromycin. Establishing the severity of an ADR is essential in categorizing the ADR reports. In general the severe ADRs require special care and may need hospitalization. Hartwig scale is used to categorize the reported ADRs into different levels as mild, moderate or severe based on the treatment and whether or not hospitalization is required for the management of the ADRs. In this case, the ADR was found to be moderate (level 4[a]) indicating that the ADR increased length of stay by at least one day.

Morbilliform eruptions are usually treated by discontinuing the suspected medications. Oral antihistamines, emollients, and soothing baths are useful. Short courses of potent topical corticosteroids can reduce inflammation and symptoms and are probably helpful. The role of systemic corticosteroids is not clear.<sup>7</sup> This patient was managed by IV dexamethasone and topical calamine lotion. The patient responded well to the treatment.

Preventability assessment helps in assessing the preventability status of an ADR. Modified Shumock and Thornton scale is a scale used to assess the preventability of an ADR. In this patient, the ADR was found to be not preventable. Broadly ADRs can be classified as type A and B. Type A ADRs are usually dose-dependent and are often preventable.<sup>12</sup> However, in this patient, the ADR could not be prevented.

## **Conclusion**

Erythromycin is used in several infective conditions. Dermatological reactions like morbilliform rashes can pose a significant morbidity to the patients. It may also lead to non-compliance and thus leading to treatment failure. Although this type of ADR is not reported with erythromycin, care should be taken for the prevention and early detection of this type of ADRs.

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