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## Case Report

# Amoxicillin induced erythematous maculopapular rashes: a case report

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### ABSTRACT

Cutaneous adverse reactions (CAR) can occur with any class of drugs, however more widely caused by various antibiotics. Amoxicillin is a broad-spectrum, bactericidal, beta-lactam antibiotic, widely used for combating various infections. Cutaneous drug eruptions are known to be reported common while using penicillin class of drugs, specifically among children. These immune-mediated bizarre drug eruptions were range from mild to severe drug-induced cutaneous reactions, such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). The present case reported with maculopapular, erythematous rashes induced by amoxicillin in a nine-year-old male patient. Amoxicillin was prescribed for his hyperactive respiratory disease and subsequently after three days developed generalized maculopapular erythematous rashes as a result of an antibiotic-induced skin rash. The present case is being reported to add more data, also to emphasize and gather the information for evidence-based practice and to promote efficient pharmacovigilance adverse drug reaction reporting.

**Keywords:** Amoxicillin, Adverse drug reaction, Maculopapular erythematous rashes, Pharmacovigilance

### INTRODUCTION

Amoxicillin, a semi-synthetic, acid-stable drug belongs to penicillin ( $\beta$ -lactam) class of antibiotics. It is effective against various infections caused by a wide range of gram-positive and gram-negative bacteria.<sup>1</sup> Amoxicillin is used as an effective and safe therapy for sinusitis, otitis media, acute exacerbations of chronic bronchitis, epiglottitis, urinary tract infections, meningitis, and salmonella infections.<sup>2-4</sup> In India, a previous study reported that 1.78% of adverse reactions reported due to amoxicillin + clavulanate of 4.99% of total ADRs among pediatric patients, the ADRs include hypersensitivity reactions: angioedema, anaphylaxis, mild fever, rash, purpura, lymphadenopathy, generalized oedema, albuminuria, and hematuria.<sup>5</sup> Cutaneous adverse reactions like skin rashes, urticaria, itching, fixed drug eruption, angioedema are the common among the various adverse

drug reactions (ADR).<sup>6,7</sup> Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are a rare but serious form of ADRs affecting patient's life they are a wide spectrum of cutaneous reactions.<sup>6</sup> Herein, we present a case of maculopapular, erythematous rash induced by amoxicillin.

### CASE REPORT

A nine years old male patient presented with a history of hyperactive airway disease and admitted in a tertiary care hospital for which he was prescribed syrup amoxicillin and potassium clavulanate 457 mg twice daily (bid) and other concomitant drugs prescribed were tablet levocetirizine 2.5 mg and montelukast 4 mg once at night, syrup levosalbutamol/levalbuterol (1 mg/5 ml) twice daily, syrup chlorpheniramine maleate (4 mg/5 ml) and codeine (10 mg/5 ml)) twice daily and nebulizer

budesonide (200 mcg) and formoterol (6 mcg) once a day for 3 days. After consumption of the medications, the patient developed rashes all over the body with itching and fever, on the 4<sup>th</sup> day of treatment. Immediately, he consulted a dermatologist in a local clinic. All the medications were stopped immediately after the consultation. The maculopapular rashes lesions first appeared on the chest and then spread over to limbs and face. The rashes were gradually appeared all over the body (Figures 1-3).

### **General examination and investigation**

All the vital signs of the patient were normal, the patient was conscious, oriented. All the routine investigations were performed (laboratory haematological, renal and liver function test) and all parameters were within the normal range. However, the immunoglobulin levels and inflammatory markers were not measured.

On examination, the maculopapular erythematous rashes were irregular in shape and various size which was present over the chest, neck and face, also appeared on back, on arms, abdomen, palm, and foot. Later the affected area was found to become reddish pink but not bullae type. There was no “Nikolsky’s sign”. Multiple papule vesicles present over bilateral chest, neck, forearms, hands and backside. But there are no erosions and haemorrhagic crusting observed. However patient complaint with itching and pruritis.

### **Management**

Syrup Moxikind CV forte has been immediately stopped and the patient was observed for the progress of appearance of erythematous rashes. The patient was treated with intra muscular injections of corticosteroid and pheniramine maleate immediately on presentation to the clinic. The patient was then prescribed with prednisolone, levocetirizine and steroid ointment (fluticasone propionate) was applied to the affected area. Skin erosions were treated with moisturizers symptomatically.

### **Causality assessment of ADR**

Causality relationship of the maculopapular erythematous rashes with the drug was assessed using WHO causality assessment scale and Naranjo algorithm.<sup>8,9</sup> Both the scales revealed that the causality association of adverse drug reaction was probable/likely or probable with amoxicillin and potassium clavulanate. The assessment was confirmed by WHO causality of the drug to reaction (CIOMS V) method and confirmed probable reaction.

### **Reporting to the ADR monitoring centre**

This case was maculopapular erythematous rashes induced by amoxicillin was reported to regional pharmacovigilance centre, Government Kilpauk Medical

College Hospital, Chennai (report number: IN-IPC-2019-43982) under pharmacovigilance programme of India (PvPI), Indian Pharmacopoeia Commission.



**Figure 1: Onset of maculopapular rashes on the chest area.**



**Figure 2: Progression of maculopapular erythematous rash on the chest area.**



**Figure 3: Progression of maculopapular erythematous rash on the back.**

## DISCUSSION

Maculopapular skin eruptions are the most common of all cutaneous drug reactions to antibiotics. Cutaneous drug reactions present specific morphological patterns vary from mild skin irritation to toxic epidermal necrolysis.<sup>7,10</sup> Many skin diseases occur with cutaneous clinical signs. However, many skin diseases, it is essential to consider drugs as a possible cause of any eruption, because drug eruptions can take the form of any skin lesion.<sup>11,12</sup> Other than skin diseases and adverse drug reactions some systemic infections can cause skin rashes.<sup>13</sup> The pathophysiology of drug-induced adverse skin eruptions is not exactly known, however, immune-mediated reactions occur as a result of bizarre effects.<sup>14</sup> Mostly the symptoms vary from fatigue, fever, lymph node enlargement, dysfunction of the internal organs such as liver, kidneys or bone marrow.

In a previous retrospective analysis, it was found that other than antibiotics (31%) various other agents cause severe skin rashes the most common drugs implicated were antiepileptics (50%). Of the antiepileptics, carbamazepine was the most often implicated drug (27%) followed by phenytoin (13.6%).<sup>15</sup> In another study conducted in India reported that the drugs most often cause for the various cutaneous ADR were antimicrobials, anticonvulsants and NSAIDs. Among the ADRs, anticonvulsants were concerned in 41.6% of maculopapular rashes. Sulfonamides accounted for 43.3% and NSAIDs for 30.7% of fixed drug eruptions. Urticaria was associated with mainly by NSAIDs (24.3%) and penicillin class of drugs (20%).<sup>6,16</sup> However, specific drug-related ADR reports are more precise. Other than cutaneous type of reaction, amoxicillin causes various other ADRs such as acute generalized pustulosis, agranulocytosis, pancreatitis and Kuoni's syndrome.<sup>17-20</sup> The practice of reporting ADRs to WHO Uppsala Monitoring centre helps make more decision on framing usage guidelines for drugs. In India the pharmacovigilance program of India (PvPI) receiving the ADR reports from various regional PvPI centers and reporting to WHO centre. There were 64,441 individual case safety report (ICSR) received and updated.<sup>21</sup> The present probable case of amoxicillin Induced Erythematous Maculopapular Rashes was also reported to the PvPI. Fostering the practice of reporting any ADR can help to prevent and improve the drug therapy.

## CONCLUSION

Cutaneous skin rashes by amoxicillin/clavulanic acid are most likely responsible for the severe skin eruptions in the present case. This case report adds a drop of support to the active pharmacovigilance monitoring. Thus, effective ADR monitoring plays a vital role in the safety of the medicine. Hence, spontaneous reporting of such an event is necessary, pharmacovigilance holds the key in this regard.

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