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Case Report

Maculopapular skin rash due to amoxicillin tri-hydrate hypersensitivity reaction: a case report

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ABSTRACT

Amoxicillin tri-hydrate (AMT) is a commonly used penicillin group of antibacterial agent to combat various bacterial infections. Penicillin group of drugs are known to cause cutaneous drug eruptions as a hypersensitivity reaction. Most of the time, these eruptions are mild in nature, however, sometimes they represent the early manifestation of rare and severe drug-induced cutaneous reactions, such as; Stevens–Johnson syndrome and toxic epidermal necrolysis. Here, we report a case of maculopapular skin rash developed due to AMT hypersensitivity reaction in a 48-year-old Indian male patient. Pheniramine maleate, hydrocortisone and skin protecting lotion were prescribed to manage the situation. This case is being reported to emphasize the need for reporting of drug induced complications and their management procedures.

Keywords: Amoxicillin tri-hydrate, Hypersensitivity reaction, Maculopapular skin rash, Pheniramine maleate, Hydrocortisone

INTRODUCTION

Amoxicillin (amoxycillin tri-hydrate [AMT]) is a beta-lactam antibiotic, introduced in clinical practice first time in UK in 1972.[1] AMT is a broad spectrum antibiotic, with promising antibacterial action against both Gram-positive and Gram-negative bacterium. Chemically, classified under semi synthetic penicillin due to structural similarity with native penicillin by the presence of β-lactam ring. Broad spectrum action of AMT is due to benzyl group present in the side chain, which increases its sensitivity to inhibit the bacterial cell wall synthesis.[2,3] AMT is indicated in a variety of infections in ear, nose and throat, infection of genito urinary tract, infection of the skin and skin structure, infection of lower respiratory tract, sexually transmitted disease, and in triple therapy of *Helicobacter pylori* infection.[4] Common adverse effects of AMT are pain at injection site, nausea and diarrhea on oral administration, thrombophlebitis etc. Hypersensitivity reactions include; maculopapular or morbilliform type of skin rash, itching, urticaria, vomiting, fever, wheezing, angioneurotic edema and serum sickness. Exfoliative dermatitis is less common, and anaphylaxis reactions are rare.[4,5] Lymphocytes from both drug-induced immediate and delayed cutaneous hypersensitivity reactions form the basis of diagnosis with such offending drugs.[6,7] Management of hypersensitivity skin reactions is mainly discontinuation of the offending drug along with administration of pheniramine maleate and corticosteroids.[8] Here, we discuss a case of AMT induced cutaneous hypersensitivity reaction, which appeared immediately after the administration of the first dose of AMT.

CASE REPORT

A 48-year-old Indian male patient visited out-patient department (OPD) of general surgery on October 15, 2014 at around 09:00 AM with a complaint of pain and swelling in penis and was diagnosed as "paraphimosis." He was prescribed with following medicines;

1. Capules AMT 500 mg b.i.d
2. Tablet Zix-S b.i.d (acelofenac 100 mg, paracetamol

500 mg and serratiopeptidase 15 mg)
3. Tablet pantoprazole (pantop) 40 mg OD
4. Tablet multivitamin OD.

After administration of first amoxycillin capsule; within few hours patient developed itching and redness of the skin, as cutaneous complications, which appeared initially over face and spread rapidly toward neck, chest and rest of the body. On the same day, he revisited the hospital at 07:00 PM due to cutaneous complications.

On examination (O/E) patient was

- Conscious and coherent
- Afebrile
- Bi-lateral air entry: positive
- Cardiovascular sound, respiratory sound and per-abdomen was found to be normal at diagnosis (NAD)
- Blood pressure (BP) was elevated to 150/100 mmHg
- Pulse rate was also found to be slightly higher as 105 beats/mins
- Itching and redness of the skin were present.

Provisionally he was diagnosed as "reaction to amoxicillin' and was prescribed with injection avil 45.5 mg intra muscular stat (pheniramine maleate).

Soon after administration of injection avil, he developed shivering and was referred to Department of General Medicine for admission and was admitted on the same day at 9.30 PM.

On admission; O/E patient was:
- Conscious and coherent
- Maculopapules and rashes all over the body were present.

His lab reports:
- Hemoglobin: 10.5 g% (13.0-17.0 g%)
- Total leukocyte count: 6500/cumm (4000-11000/cumm).

Differential count:
- Polymorphs: 65% (45-70%)
- Lymphocytes: 40% (20-40%)
- Reactive lymphocytes: 03%
- Eosinophils: 03% (1-4%)
- Monocytes: 02% (0-1%).

Blood smear: anisocytosis with microcytosis hypochromic anemia.

Platelets: reduced (1.5-4.5 lakhs/cumm).

Liver function test:
- Total serum bilirubin: 0.6 mg% (0.3-1.0 mg%)
- Serum glutamic pyruvic transaminase: 18 IU/L (0-45 IU/L).

Alakaline phosphatase: 43 IU/L (44-147 IU/L).

Random blood sugar: 90 mg/dl (80-160 mg/dl)

Blood urea: 25 mg/dl (10-45 mg/dl).

Serum creatinine: 1.3 mg/dl (0.5-1.5 mg/dl).

Serum electrolytes:
- Sodium: 140 mEq/L (135-150)
- Potassium: 4.6 mEq/L (3.5-5.5)
- Chloride: 130 mEq/L (95-105).

Based on medical history, clinical examination and laboratory findings; patient was diagnosed as a case of "drug reaction to amoxicillin" and was freshly prescribed with:
1. Intravenous (IV) fluid ringer lactate 1 unit and normal saline 2 units
2. Injection hydrocortisone 100 mg IV t.i.d
3. Injection avil 45.5 mg IV OD (pheniramine maleate)
4. Colosoft lotion for topical application (calamine I.P 8.0% W/W, *aloe vera* gel 10.0% W/W, light liquid paraffin I.P 10.0% W/W).
5. Tablet betnesol 0.5 mg b.i.d (betamethasone)
6. Tablet atarax 10 mg b.i.d (hydroxyzine hydrochloride)
7. Tablet PCM 500 mg t.i.d S.O.S (paracetamol).

On day 2 (October 16, 2014) patient was conscious and coherent, afebrile, pulse rate 80 beats/mins, BP 110/70 mmHg and rashes were decreased. He was prescribed with;
1. Injection hydrocortisone 100 mg IV t.i.d
2. Injection avil 45.5 mg IV b.i.d (pheniramine maleate)
3. Colosoft lotion for topical application (calamine I.P 8.0% W/W, *aloe-vera* gel 10.0% W/W, light liquid paraffin I.P 10.0% W/W)
4. Injection rantac 150 mg IV b.i.d (ranitidine).

On day 3 (October 17, 2014) patient complained of itching and the same medication was continued. On day 4 (October 18, 2014) itching was present, but other vitals were NAD and the same medication was continued with discontinuation of ranitidine and addition of pantop 40 mg OD. On day 5 (October 19, 2014) no fresh complaint was there, and itching was also decreased substantially; his vitals were NAD. Hence, same medication was continued for that day also. On day 6 (October 20, 2014) itching was completely resolved without any fresh complaints, and his vital was found to be NAD. Patient was fit to discharge from the hospital and was advised with following the prescription upon discharge:

Tablet allegra 120 mg b.i.d (fexofenadine) for 5 days.

He was directed to visit the OPD of general medicine after 1 week for further examination and informed that, paraphimosis treatment will be restarted if no fresh complaint arrived during this period (Figure 1).

DISCUSSION

Prescribed medicines frequently cause adverse drug reactions manifesting in diverse forms. Maculopapular skin rash is one such manifestation associated with AMT; developed due to an immune-mediated hypersensitivity reaction.[9,10] Maculopapular skin rashes consist of macules (distinct flat areas) and papules (raised lesions). They may or may not be associated with itching but are commonly erythematous in nature. Manifestation may be localized or may spread all over the body causing generalized eruptions. These reactions are frequent in pediatric population but occur in adults too.[8] Reported literature has revealed that, AMT induced hypersensitivity cutaneous reactions are immediate or rapid i.e. within minutes to an hour in most of the cases. Same was observed in this case, with a development of cutaneous reaction within 2 hrs of first dose of AMT administration. However some rare adverse effects may develop even after several days.[11] Evidence suggests that, longer the interval between drug intake and appearance of the reaction, less the probability of being immunoglobulin-E mediated.[12] Management of AMT induced cutaneous reactions includes; early identification and withdrawal of the offending drug,[13] rapid initiation of supportive care by fluid and electrolyte replacement,[14] symptomatic treatment with antihistaminic drugs like diphenhydramine and topical emollients like calamine and liquid paraffin,[15] helps relieve itching and skin rash. However, serious anaphylactic reactions require the urgent administration of adrenaline to counter the cardiac collapse as well as corticosteroids to counteract the effect of inflammatory mediators released from the mast cell.[11] Although clinical evidence for the use of systemic immunosuppressive therapy is lacking, but in common practice this is often prescribed.[13] In our case, AMT was withdrawn and corticosteroids (hydrocortisone), anti-histaminics (pheniramine maleate) were used along with intravenous fluid and topical skin protecting lotion (calamine, *aloe vera* and light liquid paraffin), which resulted in complete remission of rashes within 6 days.

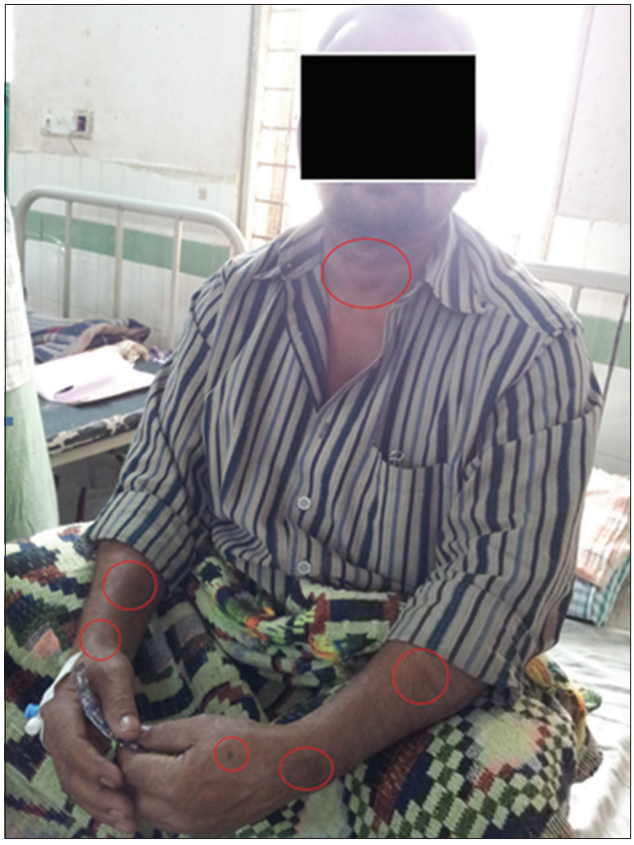

Figure 1: Maculopapular skin rashes on body on 3rd day of hospital stay.

CONCLUSION

We can conclude that, early detection and subsequent withdrawal of the offending drug is the very first step for the management of such incidences. Supportive care with continuous monitoring can be beneficial to overcome such cutaneous drug reactions and further therapeutic measures should be administered as required. Continuous Continuing Medical Education program in order to motivate drug induced hypersensitivity reporting will help clinician for proper identification and management of such incidences. Furthermore the patient should describe proper history of such drug allergy to the clinician to avoid such incidences in future.

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