



**A CASE OF PIPERACILLIN-TAZOBACTAM INDUCED ACUTE
GENERALISED EXANTHEMATOUS PUSTULOSIS**

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ABSTRACT

Acute generalised exanthematous pustulosis (AGEP) is a rare cutaneous adverse drug reaction with an incidence of 1-5 patients per million per year. 80% of the cases have been attributed to antibiotics. A 50 year old diabetic male, presented with complaints of right lower limb pain and wound on the right heel and inter digital web space infection of the right foot since 15 days. On the basis of Ankle Brachial

Index & Angiogram, a diagnosis of Ilio-femoral-popliteal disease was ascertained and thus revascularisation was done. Postoperatively, he was started on Inj Piperacillin-Tazobactam 4.5 gm bd. Following the second dose of Inj. Piperacillin-Tazobactam he developed painful exanthematous scaling rashes with pustules on the trunk and upper limbs but no involvement of the lower limbs. Except for a rise in temperature [101 F], rest of the vitals were stable and the blood reports showed neutrophilia (N-83%). The causality assessment of this reaction as per the Naranjo's Scale was found to be 7 (Probable). Although rare, the clinicians should be aware of such an entity as knowledge of the clinical features and course of this reaction can prevent unnecessary therapeutic measures.

KEYWORDS: AGEP, cutaneous, Adverse drug reaction, antibiotics.

INTRODUCTION

Acute Generalised Exanthematous Pustulosis (AGEP) is a severe cutaneous reaction caused by drugs in over 90% of cases. It is a rare entity with an incidence of 1-5 patients per million per year. It has been reported maximally following administration of beta lactam antibiotics. However, this is only the third case of AGEP due to Piperacillin-tazobactam reported in literature till date. Thus, we report this adverse drug reaction in view of expanding medical knowledge, promoting drug safety and rational prescribing.

CASE HISTORY

A 50 year old diabetic male, presented with complaints of right lower limb pain and wound on the right heel and inter digital web space infection of the right foot since 15 days. On the basis of Ankle Brachial Index & Angiogram, a diagnosis of Ilio-femoral-popliteal disease was ascertained and thus revascularisation was done. Postoperatively, he was started on Inj cefuroxime 1.5 gm BD for 5 day . The patient was concurrently on Tablet (Tab) aspirin 150mg, Tab Cilostazol 100 mg , Tab Rosuvastatin 20mg, Tab Rabeprazole 40mg. As the patient was not responding to the given antibiotic, the pus was sent for culture and sensitivity and the patient was empirically started on Tab Fluconazole 150mg on 11/02/2014 followed by a fixed dose combination of Inj Piperacillin-tazobactam 4.5gm on 12/02/2014 at 6 pm.

After receiving the second dose of Injection (Inj) Piperacillin-tazobactam which was administered at 6 am, the patient developed painful exanthematous scaling rashes along with pustules first noticed on the trunk followed by the nape of neck, back, face, arms, forearms and hands including the palms bilaterally at 9am. There was no involvement of the lower limbs. The vitals were stable and the systemic examination didn't reveal any abnormality. The treating physician advised the administration of Inj. Paracetamol along with Inj.Pheniramine 1 ampoule which was heeded to. The subsequent doses of fluconazole and Piperacillin-tazobactam were withheld and a dermatology opinion was sought for.

On clinical examination, the presence of erythematous scaling macules with pustules led to the provisional diagnosis of acute generalised exanthematous pustulosis and due to its relationship with the time of drug administration the reaction was attributed to be due to the Piperacillin-tazobactam. Investigations were sent for and the blood reports on 15/02/2014 showed neutrophilia (N-83%,L-10%,M-02%,E-05%,B-0%) The pus culture obtained from the pustules was sterile. An interesting feature was that the patient had 4 spikes in temperature which went up to 101 degrees Fahrenheit in the subsequent 3 days of occurrence

of the reaction. All the above findings go hand in hand with the final diagnosis of drug induced AGEP.



Figure I. Exanthematous rashes on Day 3 Figure II. Rashes visible on the back on Day 3



Figure III. Healing lesions on Day 6



Figure IV. Complete resolution Day 9

CAUSALITY ASSESSMENT

The Causality assessment of the above reaction was found to be 7 (Probable) according to the Noranjo scale which was similar to the assessment by the WHO Probability scale. It was assessed as a moderate (level 4) reaction according to the Hartwigs scale for determining Severity of an adverse drug reaction. According to the Modified Shumock Thornton scale, it was a definitely preventable reaction. Therefore it becomes all the more important to report such incidences in order to increase awareness among the treating physicians.

REVIEW OF LITERATURE

Acute generalised exanthematous pustulosis (AGEP) is a rare but severe adverse drug reaction with an incidence of 1-5 patients per million per year.^[1] It is one of the severe

cutaneous adverse reactions that comes under the Severe Cutaneous Adverse Reactions (SCAR) study in Europe. It has been attributed to the beta lactam group of drugs most of the time.

The reaction is characterized by sudden occurrence of a generalized exanthema which develops within 1-2 days of the drug exposure. These symptoms are accompanied by fever and neutrophilia. The pustules resolve within 4-10 days once the causative drug has been withdrawn.^[2] Unlike other drug reactions AGEP has a short time to onset and spontaneous resolution of symptoms within a few days. Antibiotics (80%) are the predominant causative agents for the reaction.^[3] In this particular case the, patient had numerous non follicular sterile pustules occurring on a diffuse erythematous base on the face, trunk, back and arms. This is in accordance with the clinical presentation of the disease as reported previously.^[4] Since it occurred around 3 hours following the administration of the second dose of Piperacillin-tazobactam, a temporal relationship can be established. Also, the other medications were continued in the patient without any reaction being observed. There have been only two previous case reports regarding a similar reaction with the same drug combination.^[5] This is thus definitely a rare adverse drug reaction to a commonly used antibiotic Piperacillin-tazobactam and thus calls for care and judicious use of this drug in our routine medical practise.

The incidence of such a reaction still remains unknown in our country, therefore like the European nations, an increasing awareness of this condition can further enhance the reporting by the physicians.

CONCLUSION

Pharmacovigilance is defined as “the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problem”.^[6] Cutaneous adverse reactions are by far the most common adverse reactions observed in daily practices. However due to various reasons such as lack of knowledge, these reactions go unreported.^[7] AGEP is a rare entity that the physicians need to be aware of in order to avoid any unnecessary interventions to treat such a reaction and also to report it to the respective Pharmacovigilance centre.

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