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ADVERSE DRUG REACTIONS TO ANTIBIOTICS: A CASE REPORT

Pharmaceutical Science

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ABSTRACT

WHO has defined an adverse drug reaction(ADR's) as any response to a drug that is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy. ADR's due to antibiotics are often reported in clinical practice . ADR's are associated with increased morbidity and mortality, prolonged hospitalization, and increased medical expenses. We report here a case of 23 year old male patient with history of road traffic accident with lacerated wound and fracture on left lower limb who went on to develop repeated wound infection. Subsequent to 2 weeks of medical therapy as well as debridement, the patient was put on maintainance therapy of clindamycin and aztreonam. After 14th day of clindamycin,9th day of piperacillin tazobactum and 3rd day of aztreonam therapy patient developed maculopapular rash initially on chest and abdomen followed by face and pinna on the next day. The reaction subsided after clindamycin aztreonam, piperacillin tazobactum were withdrawn. Tablet pheniramine maleate 25 mg was started along with Clobetasone cream 0.05% and liquid paraffin for local application was started and continued for 5 days. Rash subsided after 2 days after which piperacillin tazobactum was restarted. Also linezolid started during the course of therapy resulted in hepatotoxicity on 5th day which subsided on its withdrawal . In review of literature there is no documented cases of cross reactivity between aztreonam and clindamycin ,however cross reactivity between aztreonam and penicillins is demonstrated in vivo. Also linezolid induced hepatotoxicity is commonly reported. The causality assessment was done as per WHO-UMC scale and it is probable in this case for clindamycin, aztreonam and linezolid. Although the incidence of clindamycin, aztreonam and linezolid induced adverse reaction is rare, clinicians should be aware of such reactions with these drugs.

KEYWORDS

Adverse drug reactions, clindamycin, aztreonam, linezolid, Piperacillin tazobactum

INTRODUCTION

WHO has defined an adverse drug reaction (ADR's) as any response to a drug that is noxious and unintended and that occurs at doses used in man for prophylaxis, diagnosis or therapy. Antibiotics are one of the most commonly used agents to treat various kinds of infections. ADRs caused by antibiotics accounts for 40.9% of all ADR's and are associated with several serious outcomes.[1] Among all ADRs 75-80% are classified into type-A(predictable) whereas 20-25% as type-B (unpredictable).Unpredictable ADRs may be of immediate (<1hr)or delayed(>1hr) type that occur in susceptible individuals. Immediate reactions are usually IgE-mediated whereas delayed reactions are usually non-IgE or T-cell mediated.[2,3] Clinically these ADRs could be cutaneous (e.g., maculopapular rashes, erythroderma, exfoliative dermatitis and fixed drug reactions), organ-specific (e.g., blood dyscracias, hepatitis, interstitial nephritis), systemic (e.g.,anaphylaxis, drug induced hypersensitivity syndrome) or various combinations of these. Severe cutaneous ADRs such as Stevens Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Acute Generalized Exanthematous Pustulosis (AGEP) could be life threatening.[2,4] Beta-lactam antibiotics were found to be the commonest cause of these ADRs.[1]ADR's are associated with increased morbidity and mortality, prolonged hospitalization and increased medical expenses.

Clindamycin use has increased significantly due to its excellent coverage for skin/soft tissues and bone infections, it is a good alternative for Methicillin-Resistant Staphylococcus Aureus (MRSA). Although allergic reactions caused by clindamycin are rare, immediate and delayed skin reactions have been previously reported.[3] Aztreonam, a monobactum antibiotic is also known to cause skin rash, but cross reactivity with clindamycin is not known. However, cross reactivity with penicillins is demonstrated in vivo[5].Linezolid is a oxazolidinone class antibiotic commonly used for resistant pseudomonas infections is also known to cause hepatotoxicity if used for longer duration.[6]

We report here a case of Cutaneous Drug reaction caused by Clindamycin and/or Aztreonam and organ specific reaction (hepatotoxicity) caused by linezolid.

Case Report

A 23 year old male patient was admitted following a road traffic accident with lacerated wound over left lower limb. On examination GCS was 15/15, pulse and blood pressure were within normal range. All other clinical findings were normal with exception of findings on local examination of left foot i.e. contused lacerated wound (15cm×8cm×3mm) on anterior aspect ,bone was exposed , swelling and tenderness was present, heel pad avulsion was present, Anterior Tibial Artery pulsations were absent and Posterior Tibial Artery pulsations were present which were later confirmed with the help of CT angiography. On X-ray compound fracture of lower end of left fibula and compound fracture of left calcaneum with ankle dislocation was seen. Other investigations like complete blood count,renal function tests and liver function tests were within normal limits during admission. Compond fracture of left fibula and left calcaneum was surgically treated with external fixator for tibia and tens nail for fibula. Pre and post surgical procedure patient was started on Injection Gentamicin 60 mg BD and Injection Cefoperazone sulbactum 1.5gm BD and Injection Metronidazole 400mg TDS. After 1 week patient was shifted to plastic surgery ward for Anterolateral thigh(ALT) free flap placement with secondary suturing and debridement after which patient was started on Injection Clindamycin 600mg IV BD for 7 days followed by Tablet Clindamycin, Injection Amikacin 500mg IV BD, Injection Piperacillin tazobactum 4.5g IV BD as post operative antibiotics.

Injection Amikacin 7 day course was completed and stopped. Patient was having continuous spikes during this period and no rash was seen and wound culture was showing growth of pseudomonas sensitive to aztreonam and so injection aztreonam 1g iv TDS was started ,but on 4th day patient developed maculopapular rash on chest and abdomen and on the next day rash worsened and extended till face and pinna.After development of rash aztreonam and Clindamycin and Piperacillin tazobactum were stopped and rash was treated with tablet pheniramine maleate 25 mg and Clobetasone cream 0.05% and Liquid paraffin for local application for 5 days. Rash subsided after 2 days after which Piperacillin tazobactum was restarted and patient was posted for ALT free flap advancement with secondary suturing and split thickness skin grafting with pre and post operative antibiotic therapy of injection Metronidazole 400 mg TDS continued for 3 days. On day 30, tablet linezolid was started for pseudomonas growth on wound culture, but on 5th day liver enzymes(SGOT and SGPT)were increased to 8 times, so linezolid was withdrawn as it is known to cause

hepatotoxicity. Liver enzymes showed gradual improvement over 15 days after discontinuation of linezolid. On urine culture growth of klebsiella and pseudomonas was seen and therefore injection tigecycline 50mg iv BD was started and continued for 14 days and later readded in next month as culture report showing growth of same organisms and was continued for 21 days. Also on wound culture pseudomonas growth was still present so ceftazidime was added 1g BD for 5 days and later patient was discharged on Amoxycllin clavulanic acid for 5 days.[Total admission was for 80 days and patient was given discharge on request as he wanted to go to his hometown]

DISCUSSION

Adverse drug reactions of clindamycin are infrequent and mostly limited to abdominal pain, diarrhea, metallic taste, transient abnormal hepatic function tests and agranulocytosis. Hypersensitivity reactions, including rash and urticaria, have been reported, as well as rare cases of anaphylaxis, Drug Rash with Eosinophilia and Systemic Symptoms (DRESS) syndrome and Stevens-Johnson Syndrome (SJS).[7-10] However, delayed cutaneous allergic reactions are relatively uncommon and reported exclusively in adults.[11]The most reported presentation was delayed maculopapular eruptions, usually develop 5 to 10 days after clindamycin initiation.[12] In our patient reaction was developed on 14th day of clindamycin,9th day of piperacillin tazobactum and 4th day of aztreonam so exact drug to which reaction occured could not be found out. As per previous case reports delayed hypersensitivity with clindamycin was more commonly seen and aztreonam shows cross reactivity with penicillins is known in vivo,[5]so the reaction can be due to clindamycin or azetreonam or due to cross reactivity between Piperacillin tazobactum and azetreonam.

Therapy with linezolid has been associated with mild and transient elevations in serum aminotransferase and alkaline phosphatase levels in 1% to 10% of patients, although similar rates of elevations occur in patients with infections treated with comparable agents, and enzyme elevations were not found in normal volunteers given linezolid for short periods. On the other hand, SGPT elevations during therapy have been higher with higher doses of linezolid, but in all instances the elevations occurred without symptoms and resolved with discontinuation of the drug[6]. In our case ALP levels were within normal range and SGOT and SGPT were elevated 8 times of normal value.

According to WHO-UMC scale and ADR was probable in this case for clindamycin, aztreonam and linezolid.

CONCLUSION

Adverse drug reactions due to antibiotics is one of the major concern. Although the incidence of clindamycin, azetreonam and linezolid induced drug reaction is rare, but it has the propensity to cause serious life threatening conditions and prolong hospital stay. Thus, the clinicians should be aware of such reactions before prescribing and during course of therapy.

This case was reported to ADR monitoring centre in Pharmacovigilance cell, Goa Medical College. Such ADR's reporting is a continuous process which aids clinician in having a sound and adequate knowledge while prescribing drugs belonging to different classes and categories to their patients.

ADR's monitoring should be encouraged and practiced right from the remote to the tertiary care centre for betterment of prescribing practices.

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