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DRUG INDUCED HYPERSENSITIVITY SYNDROME WITH PANCYTOPENIA AND SEPSIS DUE TO PIPERACILLIN- TOZABACTUM AND MEROPENEM: A RARE CASE

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ABSTRACT

Dress response with systemic symptoms and eosinophilia (DRESS) is a rare adverse drug reaction that can be lethal. Visceral damage, dermatitis, and haematological abnormalities are possible outcomes of this sickness, which has a long latency period. Clinical signs and symptoms of DRESS might vary. We describe a 34-year-old female who presented with lethargy, giddiness, and severe monthly bleeding. The laboratory examination indicated pancytopenia with leukocytosis, a peripheral blood smear suggestive of blasts, and clinical symptoms consistent with acute Leukemia. The antibiotics used here are meropenem and piperacillin/tazobactam (Pip/Taz). As a result, both systemic and eosinophilic symptoms appeared. These symptoms were all connected to DRESS. After Ceftriaxone was administered and the sensitising drug was stopped, the symptoms gradually subsided. Physicians should be alert for indications of abnormal behaviour.

Keywords: Pancytopenia, DRESS, Sepsis, Piperacillin tazobactam, Meropenem.

1. INTRODUCTION

A broad-spectrum antibiotic, meropenem eradicates both gram-positive and gram-negative bacteria. Used to treat a variety of illnesses, including meningitis and pneumonia.[1,2] This beta-lactam antibiotic belongs to the carbapenem subgroup, along with imipenem and ertapenem. It obtained FDA approval in July 1996.[2] Pip/Taz is an injectable antibiotic that combines a β-lactamase inhibitor (Taz) with a penicillin antibiotic (Pip) in a 1:8 ratio[3]. Skin rashes are uncommon, but in human abuse potential studies, they elicited aberrant responses. Adverse medication reactions occur in 0.1% to 1% of patients, and drug-induced skin problems are classed as acute or chronic[1]. The most prevalent adverse effects were diarrhoea (4-5%), nausea and vomiting (1-4%), and it seldom causes sepsis, septic shock, or pancytopenia.[2]

Drug response with eosinophilia and systemic symptoms, or drug-induced hypersensitivity syndrome (DIHS), is an uncommon and possibly lethal adverse drug reaction that has a high fatality rate. Its symptoms often resemble those of sepsis, potentially leading to a misdiagnosis.[4] Adverse reactions to 'A' or 'Augmented' pharmaceuticals are rapid and low-fatality, but other penicillin class treatments have a high mortality rate (Type 'B' or 'Bizarre')[5]. The proliferation of immature myeloid precursors is a hallmark of acute myeloid leukaemia (AML), a clonal haematopoietic stem cell disease. Nonspecific symptoms like fatigue, bleeding, or infections could be the first signs.

Table 1: RegiSCAR Diagnostic Criteria for DRESS

Criteria	Findings in this Case
Hospitalization	Yes
Drug-related reaction	Yes
Acute rash	Not specified
Fever > 100.4°F	Yes
Lymphadenopathy in ≥2 locations	Yes
Involvement of ≥1 internal organ	Yes (hematologic, liver suspected)
Abnormal CBC (eosinophils, lymphocytes, platelets)	Yes

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2. CASE PRESENTATION

A 34-year-old woman was brought to the hospital after complaining of giddiness and easy fatigability for the previous 15 days. These symptoms were both subtle at first and developed gradually. Additionally, she reported heavy menstrual bleeding for 11 days, characterized by passage of clots and deviation from her regular menstrual pattern. The patient is deaf and mute since birth. Her initial investigations showed HB – 4.5G/DL, PLATELET – 18,000, TLC – 57,000, PCV – 11.2. Upon general examination, the patient had elevated jugular vein pressure, bilateral pedal oedema (Grade 4), and a pale appearance. Multiple palpable lymph nodes were noted in the right supraclavicular, left jugular, and right femoral. A cardiovascular examination revealed a bounding pulse, normal heart sounds (S1 and S2), and an ejection systolic murmur that resembled a hemic murmur. The peripheral smear revealed anis poikilocytosis, the presence of nucleated RBCs, and significantly elevated blasts with characteristics consistent with acute Leukemia. Ultrasonography of the belly and pelvis indicated splenomegaly and minor free fluid in the Douglas pouch, while a chest X-ray showed cardiomegaly. The clinical laboratory confirmed the diagnosis of acute myeloid Leukemia (AML). The RegiSCAR developed diagnostic criteria for DRESS in Table 1. The patient was initially treated with Piperacillin tazobactam 4.5g IV but suffered an adverse response after injection, thus her antibiotic was changed to Meropenem 1 g IV once daily. The patient developed hypotension (90/60 mmHg), tachycardia (104/min), Edema, lymphadenopathy, a total blood count abnormality, and sepsis. It implies a drug reaction with eosinophilia and systemic symptoms. She received intravenous hydration while having her blood pressure and peripheral venous pressure closely monitored. The laboratory test results (together with the usual range of values) are provided in Table 2. The patient was then referred to the infectious illness clinic. The patient received all aseptic treatments while being kept in isolation. In accordance with the advice of infectious diseases clinic both antibiotics were immediately discontinued, Ceftriaxone was given as an alternative, and she was treated with vitamin supplementation (Inj. Eldervit, Folic acid, Vitamin K), antiemetics, PPI, and blood transfusions, including 1 pint of Single Donor Platelets and 2 pints of Packed Red Blood Cells. The patient got pancytopenia and sepsis after using meropenem and piperacillin tazobactam. Patient was discharged in good condition.

3. DISCUSSION

DRESS may account for 10% of adverse drug reactions in Asian countries[4]. An understanding of the pathogenesis of DRESS is still lacking. Genetic polymorphisms and the activation of human herpesviruses, including HHV 6/7, Epstein-Barr virus, and Cytomegalovirus, have been associated to the pathogenesis of DRESS, according to study. Diverse organ systems, including the circulatory, lymphatic, and digestive systems particularly the liver can be included in DRESS[6]. The 75% of DRESS patients showed lymph node involvement, which manifested as either localised or extensive lymphadenopathy. Increases in the number and percentage of leukocytes and eosinophils are the main indicators of haematological involvement[4]. When severe systemic symptoms occur, anaphylaxis a rapid, systemic allergic reaction often triggered by foods, medications, or insect stings presents significant therapeutic challenges[7]. Anaphylaxis is caused by the degranulation of mast cells and basophils, which releases histamine and other inflammatory mediators into the systemic circulation, resulting in widespread vasodilation, increased vascular permeability and a resulting reduction in blood pressure[7]. There aren't any official diagnostic guidelines for DRESS. This instance was evaluated using the RegiSCAR European Registry of Serious Cutaneous Adverse Reactions (SCAR). In this case, the patient met the diagnostic criteria for DRESS, which refers to specific treatment.[4] On the basis of the degree of visceral organ involvement, a treatment strategy should also be created[8]. First, you should stop taking sensitising drugs. Patients with mild-to-moderate disease should also get supportive care and topical glucocorticoids[4]. Men made up 59% of those who had pancytopenia while using meropenem, with 38% being above the age of 60. The cross-reactivity of TAZ/PIPC and Meropenem with carbapenems had been estimated to be 50% likely to occur in penicillin-allergic people[3,6]. Previous studies indicate that pancytopenia and sepsis caused by meropenem are fatal[2]. Sepsis and pancytopenia are two rare, potentially fatal adverse effects of piperacillin tazobactam and meropenem that we found in our patient.

Table 2: Laboratory results

TEST	RESULT	NORMAL RANGE
Haemoglobin	3.4g/dl	12-16g/dl
Neutrophil	04 %	40-80%
Lymphocytes	14, Blast- 80 %	20.0 - 40.0%
Monocytes	1%	2-10%
Platelet count	16 $\times 10^3$ /µL	150 - 410$\times 10^3$ /µL

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International normalized ratio	1.28	0.8-1.2
Prothrombin time	15.4 sec	6-12 sec
White blood cells	70.2 $\times 10^3$ /µL	4.0 - 11.0$\times 10^3$ /µL
Red blood cells	0.95$\times 10^6$ /µL	3.8 - 4.8$\times 10^6$ /µL
Mean corpuscular haemoglobin concentration (MCHC)	30.9 %	31.5 – 34.5 %
Mean corpuscular haemoglobin (MCH)	35.8 pg	27.0 - 32.0 pg
Mean corpuscular volume (MCV)	115.6 fL	83-101fL
Creatinine serum	0.52 mg/dL	0.6-1.1 mg/dL
Protein total, serum	5.07 g/dl	6.4 - 8.3 g/dl
Albumin	3.43 g/dl	3.5-5.2 g/dl

4. CONCLUSION

As the administration of piperacillin tazobactam and meropenem increases, it seems that patients should be informed of these two rare but deadly adverse effects. Clinicians should also examine the significant adverse effects indicated in this report. To further comprehend and assess the role of haematology in the response to DRESS, more research should be conducted.

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The patient consented to the publication of her case for educational purposes.

Conflict of interest:

The study was conducted without any financial or commercial ties that might be seen as a potential conflict of interest, according to the authors.

Ethics statement:

The study involving human volunteers did not require an ethical assessment or permission, as per local laws and institutional requirements. To take part in this study, the patients/participants provided written informed consent. The dissemination of any potentially identifying information used in this study was approved by the subject in writing.

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