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A CASE REPORT ON PIPERACILLIN AND TAZOBACTAM INDUCED ANAPHYLACTIC REACTION INCLUDING SEIZURES IN PATIENT OF URINARY TRACT INFECTION

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Abstract: **Anaphylaxis is a rapid-onset, multisystem hypersensitivity reaction with potentially fatal outcome. Clinically, anaphylaxis most frequent manifestations are cutaneous. Type A anaphylactic Hypersensitivity reaction is immediate type of reaction that occurs due to release of IgE antibodies and mediators that cause various lesions.**

A 26 year old female Patient who was a known case of seizure disorder was presented with chief complaints of burning micturition and abdominal pain due to urinary tract infection and lower urinary tract symptoms. Injection tazomac was started to treat Urinary Tract Infection but after Ist dose patient developed Sudden fall in BP, tachycardia, weak thready pulse, seizures, altered sensorium, angioedema, eye edema, pedal edema as hypersensitivity reaction therefore injection was immediately stopped and specific treatment of adrenaline, dopamine, levocetirizine, pheniramine, lorazepam and phenytoin was started to treat symptoms. Patient was shifted to ICU, ECG was done, which suggest ECG changes, trop – I was done which was suggest Acute Ischemic Changes, cardiology reference was done. The Patient was well treated and discharged in satisfactory conditions, and was adviced allow up in cardiology OPD.

Allergic reactions to antibiotics may occur in the form of immediate or delayed hypersensitivity. Immediate reactions are usually immunoglobulin (IgE-mediated whereas non-immediate or delayed-type hypersensitivity reactions are usually non-IgE or T-cell mediated. Healthcare professionals should keep the record of medication history that to which drug patient is allergic so that it can be avoided in future and in case of any ADR it should be reported.

Keywords: **Lower urinary tract symptoms(LUTS), Tazomac(Piperacillin+ Tazobactam), Adverse drug Reaction (ADR).**

1. INTRODUCTION

Uriedopencillin class of antibiotics are also named as antipseudomonal penicillins. Among these class of drugs piperacillin is more potent and pose superior action against *Klebshiella* and is effective in neutropenic/ immune compromised patients having serious gram-negative infections and in burns.1 Pharmacokinetics of Piperacillin matches with Tazobactum, which is used in severe infections like peritonitis, pelvic/ urinary/respiratory infections. However, this combination is not effective against piperacillin-resistant Pseudomonas. A dose of 4-12 g/day is required for mild infections and in case of severe infections a higher dose is required (12-24g/day). The combination of Piperacillin-Tazobactum was effective against a range of gram-positive and and gram negative bacterial infections[1,2].

A recent systematic study review stated that there are variety of adverse drug reactions has been reported with the piperacillin-tazobactam, and the reactions are hemolytic anemia, bone marrow suppression, diseases such as neutropenia and thrombocytopenia, type 1 hypersensitivity and acute delirium[3,4] A array of adverse reactions can precipitate within minutes after the hours of exposure to a drug which are of type 'A' or "Augmented' in nature and usually have a low mortality. Others pencillin class of drugs are not readily predictable due to high mortality risk (Type 'B' or 'Bizarre')[5].

Anaphylaxis is a rapid-onset, multisystem hypersensitivity reaction with potentially fatal outcome.Clinically, anaphylaxis most frequent manifestations are cutaneous; however, respiratory, cardiovascular, gastrointestinal, and other symptoms may also occur . Drug-induced anaphylaxis (DIA) hypersensitivity mechanism is mainly an IgE-mediated response, but others have been characterized . Penicillin was in the past DIA most frequent cause, but was recently surpassed by amoxicillin[6].Healthcare professionals (HCP) are exposed to a large number of substances that act as allergens and/or irritants. These allergenic substances were known to cause contact dermatitis, but nowadays a wide spectrum of clinical manifestations like asthma,rhinitis, conjunctivitis and anaphylaxis is also included[7].

2. CASE REPORT

A 26 year old female was admitted to the Hospital with complaints of abdominal pain since 5 months with left sided flank and burning micturition . Patient also had a history of Lower urinary tract symptoms and increased frequency of urine. Recent episode of left sided abdominal flank was sudden in onset with moderate intensity and partially relieved on its own. Laboratory tests revealed that patient was infected with urine with bacteriurea, Increased Pus cells (52-60) in urine and she had low haemoglobin count (8.8g/dl). Based on laboratory investigations and differential diagnosis patient was diagnosed with Acute Abdominal Pain with LUTS. Patient urine was send for the culture sensitivity and meanwhile injection Tazomac (Piperacillin + Tazobactam) was started but on ist dose. Patient developed sudden fall in BP, tachycardia, weak thread pulse, seizures, altered sensorium, angio edema, eye edema, pedal edema.

Prompt, management of patient was done in the line of anaphylactic shock that is first of all injection Tazomac was stopped and injection adrenaline and injection dopamine was given to prevent anaphylactic shock , IV fluids were rushed and all other medications were stopped.

Patient was immediately shifted to ICU where Adrenaline infusion were started along with IV fluids. After about 1 hour Patient's Systolic BP was reached 90 mmHg.

Injection lorazepam and injection phenytoin were started to treat seizures, injection levocetirizine and pheniramine were started to prevent allergic reactions due anaphylaxis. Injection Hydrocortisone was started to reduce angioedema, pedal edema and eye edema and pain. After 24 hours ADR was tapered and BP was maintained to 110/60 mmHg. Angioedema , pedal edema and eye edema was reduced after 48 hours therefore her adrenaline was stopped and BP was maintained to 100/70 mmHg.

ECG & trop – I which was suggestive of Acute Ischemic Changes was adviced by cardiologist. Patient was discharged in satisfactory condition. She was adviced to follow up in cardiology OPD after 5 days.

3. DISCUSSION

Hypersensitivity is defined a body's abnormal or exaggerated immune response with the onset of ADR's. Type I Anaphylactic hypersensitivity is defined as any ADR or type of immune response which develop rapidly in response to the allergen or antigen to which person is previously exposed (anaphylaxis is an antonym of prophylaxis). This type of reaction is occurred with 15-30mintues after the exposure of allergen. Type I reaction is mediated by *IgE type of Antibodie against any Antigen*[8].

Allergic reactions in respose to any Antigen may occur in the form of immediate or delayed hypersensitivity reaction. Immediate hypersensitivity reactions are usually immunoglobulin (Ig)-E-mediated whereas non-immediate or delayed-type of hypersensitivity reactions are usually T-cell mediated[9].

(1) During the *first contact, host react with antigen, and sensitization occurs.* After first contact with antigen, B lymphocytes which are circulating get activated and differentiate to form IgE-secreting plasma cells. IgE type of antibodies which are so formed are now bind to the Fc receptors which are present on the surface of mast cells and basophils, which are the main effector cells of type I reaction.

(2) During the second contact with the same antigen, IgE antibodies which are present on the surface of mast cells-basophils are so firmly bound to Fc receptors that it causes cell damage, in a series of---- lysis of cell membrane, which leads to influx of sodium and water which leads to *degranulation* of mast cells-basophils.

(3) These granules contains inflammatory mediator — Histamine, Serotonin, Vasoactive intestinal peptide (VIP), chemotactic factors of anaphylaxis for neutrophils and eosinophils, leukotrienes B4 and D4, prostaglandins (thromboxane A2, prostaglandin D2 and E2) and platelet activating factor. The effects of these agents are:

- increased vascular permeability;
- smooth muscle contraction;
- early vasoconstriction followed by vasodilatation;
- shock;
- increased gastric secretion;
- increased nasal and lacrimal secretions; and
- Increased migration of eosinophils and neutrophils at the site of local injury as well as their rise in blood (eosinophilia and neutrophilia).
- Seizures[9]

In this Particular case Patient Developed developed Sudden fall in BP, Tachycardia, weak thready pulse, seizures, Altered Sensorium, Angioedema, eye edema, peddle edema after piperacillin and tazobactam combination administration therefore to treat ADR the offending drug was immediately stopped and treatment of adrenaline, dopamine, levocitrazine, pheniramine, lorazepam and phenytoin.

Piperacillin shares the beta-lactam ring with ampicillin, amoxicillin and cloxacillin and so these antibiotics must be avoided in this patient. The sensitization found to cefuroxime may represent a co-sensitization also due to exposure, or might be associated to beta-lactams cross-reactivity[10].

5. CONCLUSION

The presented ADR was type A anaphylactic type of hypersensitivity reaction to drug. The patient was allergic to drug and developed various symptoms as already described in piperacillin and tazobactam study and was well treated. Healthcare professionals should keep the record of medication history that to which drug patient is allergic so that it can be avoided in future and in case of any ADR it should be reported.

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