

Anaphylaxis to Ceftriaxone – Evaluation of Two Cases

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Keywords

Anaphylaxis, ARDS, Ceftriaxone.

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ABSTRACT

Allergic reactions to beta-lactamase antibiotics are the most common cause of adverse drug reactions mediated by specific immunological mechanism. Anaphylaxis is diagnosed clinically. In two of our cases, patients developed acute respiratory distress syndrome (ARDS) secondary to anaphylaxis, which was however managed successfully without residual deficits.

INTRODUCTION

Ceftriaxone is a broad spectrum, third generation cephalosporin commonly used for treatment of wide range serious infections like bacterial meningitis, multidrug resistant typhoid, urinary tract infection, septicemia¹. Its bactericidal action is through inhibition of cell wall synthesis. The incidence of ceftriaxone induced hypersensitivity reaction is 1-3% however the incidence of anaphylaxis accounts to 0.1-0.0001% only². Features of anaphylaxis can range from mild skin lesions to fatal reactions like severe hypotension and bronchospasm³. Intraoperative antibiotic administration is a common practice and hence anaphylaxis can present as real challenge to anesthesiologists. Here we present two similar cases of ceftriaxone induced anaphylaxis in spite of negative intradermal skin testing.

CASE REPORT

Our first case, Piyari Sunar, 31 years old female who held from Dulegauda was brought to Emergency Department of Gandaki Medical College Teaching Hospital on July 23, 2015 A.D. with history of generalized body rash after ceftriaxone injection an hour back, for her fever in a nearby health post. Subsequently, she developed hemoptysis and became hypoxic. Her chest x-ray showed

bilateral pulmonary infiltrates and hence was diagnosed with acute respiratory distress syndrome (ARDS). In due course of time, she developed respiratory acidosis, multi-organ dysfunction involving her liver and kidneys.

However, with ARDS ventilator strategies, higher antibiotics and proper nursing care, she started improving and on August 1, 2015, her weaning was started. After 10 days of intensive limb physiotherapy and good nutrition, she was off ventilator support and finally was discharged on August 15, 2015 from the hospital with no residual deficit.

Our second case, 21 years old female Bipana Tamang, was posted for ureteroscopic lithotripsy (URSL) on March 1, 2017 A.D. for her right proximal ureteric calculus with mild hydroureteronephrosis. All her pre-operative investigations were within normal limits and hence she was planned for the procedure under spinal anesthesia. Pre-operative ceftriaxone test dose revealed negative intradermal test thus full dose antibiotic was given slowly through intravenous route. Monitors were attached which included electrocardiogram, non-invasive blood pressure and oxygen saturation probe. Spinal anesthesia was given with 0.5% bupivacaine 15 milligrams, after preloading (20 ml/kg) with normal saline. Spinal level was fixed at thoracic level 8 (T8) and there was no immediate hypotension or restlessness, no distinct cardiac or pulmonary abnormality. The entire

procedure was uneventful. However at the end of the procedure, patient developed dyspnea and restlessness. Acute pulmonary edema was suspected as her chest had diffuse creptitation. She was suspected to have developed allergic response to ceftriaxone and treatment was started in this line with steroids, antihistaminic and diuretics. Intra-operative chest x-ray showed diffuse infiltrates so the patient was managed in the line of acute respiratory distress syndrome (ARDS) with lung protective ventilator strategy. She improved clinically on third day and was extubated and discharged on eighth post-operative day. Hence, we concluded that this might have occurred due to the delayed anaphylactic response to ceftriaxone injection.

DISCUSSION

Anaphylaxis is an acute life threatening type I hypersensitivity reaction³. The signs and symptoms of anaphylaxis typically develop within few minutes of exposure to the offending agent but can occur as late as 72 hours post exposure⁴. Biphasic reactions which occur within one to 72 hours after the initial attack with an asymptomatic period of one to eight hours in between have been reported. This type of reactions are seen in 20% of total cases⁵. Anaphylaxis is usually but not always mediated by immunologic mechanism that results from sudden systemic release of mediators such as histamine, leukotrienes, prostaglandins from mast cells and basophils^{3,6}.

Rash is the most common clinical presentation¹ however its absence doesn't exclude the diagnosis of anaphylaxis⁷. It can present as acute life threatening reactions involving various systems however cardiovascular and respiratory compromise are of greatest concern to us as they are associated with fatalities³. The rapidity of occurrence of anaphylaxis signifies the severity of the process hence the more acute the onset of multisystem involvement, higher the chance of mortality⁴. The incidence of anaphylactic reactions during anesthesia has been reported to be 1:6000 to 1:20,000. Out of various agents implicated, antibiotics are responsible in 8.3% of cases⁸.

Ceftriaxone is widely used broad spectrum antibiotic. Severe allergic reactions due to ceftriaxone has been found to be around 1-3%^{1,6}. The diagnosis of anaphylactic drug reaction is based on the history of exposure to offending agent and clinical presentation. Intradermal skin test is sensitive, rapid and inexpensive however it is associated

with higher false positive and false negative results⁹. Intradermal drug test can be altered by prior ingestion of antihistamine drug, steroids, beta blockler or due to co-existing skin diseases like eczema. Cephalosporin skin test use native molecules but on intravenous administration, it undergoes degradation and generate unique haptens or neo-antigens thus skin test can be false negative as well¹⁰. Other methods for detection of allergic reactions are serum tryptase level and serum IgE level⁶. In both of our cases, the diagnosis was made on the basis of clinical presentation and history of exposure to the drug. Laboratory diagnosis was not made due to the unavailability of those tests in our hospital setup.

Vasodilation and leakage of plasma from capillaries due to increased permeability by prostanoids, leukotriens and kinins is the physiology behind acute cardiovascular collapse in anaphylaxis¹¹. Epinephrine inhibits the release of vasodilatory mediators from basophils and mast cells and hence improves cardiac output by increasing the vascular tone. With its action on beta receptors in respiratory bronchioles, epinephrine causes bronchodilation, decreases mucosal edema and airway resistance^{7,9}. Thus epinephrine and intravenous fluid support are the mainstay in management of anaphylaxis. Various other treatment modalities depends on the system involved in due course of time. The management of patient who present with anaphylaxis suddenly or later differ from one another. It can be self-limited and it is also possible that the patient presents to us when epinephrine is no longer required⁷.

Both of our patients presented to us with delayed symptoms and signs. It is nearly impossible to predict the kind of reactions of the insulting agent in humans. Diagnosis on the basis of history and skin testing can also be misleading as both false positive and negative reports exist pertaining to the fallacies in the technique or the material. Anaphylaxis to ceftriaxone is highly unpredictable ranging from simple rash to full blown cardiovascular collapse and death. In reviewing the literature, various deaths have been reported following ceftriaxone injection^{2,12,13}.

In conclusion, intradermal skin test is must in all the patients receiving any drug and after negative test, the drug is given as slow intravenous infusion to prevent sudden and dreadful cardiovascular collapse. Antibiotics are given within an hour of incision as prophylaxis to post-operative infection but it is wise to avoid the drug with the initiation of anesthesia there can be diagnostic delimita¹⁴. Those patients who survive anaphylaxis should be informed and

referred to an allergy specialist so that future mishaps can be prevented.

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