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Cefotaxime Induced Anaphylaxis Complicated with Massive Pulmonary Edema: An Intraoperative Hurricane

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Abstract
Antibiotics are second leading offending agent implicated in perioperative anaphylaxis. Here, we report a case of intraoperative anaphylaxis to Cefotaxime which presented as sudden cardiovascular collapse without apparent cutaneous signs. However, massive pulmonary edema became the prominent feature of this anaphylactic reaction. This again emphasises need for vigilance and promptness of anaesthesiologist towards occurrence of perioperative anaphylaxis and varied presentations.
Keywords: *Anaphylaxis, Pulmonary edema, Cefotaxime, Adrenaline.*

Introduction

Perioperative anaphylaxis is a rare but serious complication. Its incidence is reported variedly from 1 in 3500 to 1 in 25,000 anaesthetics with a mortality rate of 4% and 2% surviving with severe brain damage. In Indian survey, colloids followed by antibiotics are the commonest causes of anaphylactic reaction.[1]

Penicillin, Cephalosporin's and other beta lactamase antibiotics are the commonly used antibiotics during perioperative period. The reported incidence of anaphylactic reactions to penicillin is 1:1000,[2] but anaphylactic reactions are rare with cephalosporins (incidence-0.00 01% to 0.1%).[3]

Here, we are sharing a case of intra-operative anaphylactic reaction to Cefotaxime which presented as sudden cardiovascular collapse with prominent feature as pulmonary oedema which is a rare association.

Case Report

A 26 year male, ASA grade-I patient of fracture shaft right femur was posted for intramedullary nailing of right femur. His preanesthetic evaluation was unremarkable including no past history of any drug allergies or exposure to anaesthetics. Laboratory blood investigations including chest x-ray, electrocardiogram (ECG) were normal. Patient was receiving injection (Inj.) Cefotaxime 1gm TDS in ward since 4 days after negative 'Intradermal skin testing'.

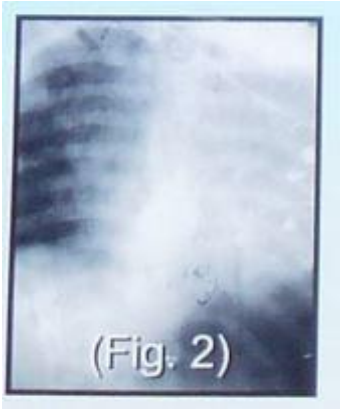
Before induction of anaesthesia, standard monitors were attached to patient. All hemodynamic parameters were within normal limits. Patient was preloaded with 500 ml Ringer's Lactate solution. Spinal anaesthesia was given with 3.5 ml of 0.5% Bupivacaine (H). After obtaining T8 segmental level of anaesthesia, patient was given left lateral position for surgery. Meanwhile he received 1ml (100mg) iv test dose of inj. Cefotaxime intravenously which showed no signs of sensitivity to Cefotaxime and after 10 minutes,

Inj. Cefotaxime 1 gm was given as slow intravenous (iv) infusion.

After 7-8 minutes of administration of loading dose (1 gm) of Cefotaxime, patient developed shivering and complaint of breathlessness. Monitor showed tachycardia (HR - 130/min), hypotension (SBP - 80 mm/Hg) and SpO_2 90%. Pulse was feeble and rapid. Inj. Mephenteramine 6mg iv stat was given. Auscultation of chest revealed bilateral crepts, more extensive on left side. Simultaneously, frothy secretions from nostrils and mouth were noted. Monitor showed HR -160/min, BP- 60/34 mmHg, Spo2 further dropped to76%. Sequence of clinical events and rapid presentation aroused the suspicion of anaphylaxis to Cefotaxime although there was absence of any obvious skin rash. Immediately patient was turned to supine position and given 100% O_2 on mask with Bain's circuit as he was breathing spontaneously, Inj. Adrenaline 5 ml (1:10,000) given intravenously, repeated after 10 minutes. Also, Inj. Adrenaline 1mg (1:1000) given intramuscularly. Simultaneously, intravenous infusion of Inj. Noradrenalin was initiated (2ug/kg/min) and further titrated as per arterial pressure. Also, inj. Pheniramine maleate (22.5mg), Hydrocortisone succinate (100mg), Dexamethasone (8mg), were administered intravenously. Blood pressure improved up to 90 mm/Hg. At interval of 10 minutes Inj. Furosemide 40 + 40 + 40 mg was administered, that resulted in improvement of oxygen saturation (SpO_2-92%). During resuscitation, surgery was stopped. As patient responded well to treatment within 45 mins, surgery restarted and completed by senior surgeon quickly within 15 min in semi lateral position.

At the end of surgery when patient was turned supine, he coughed out 500 ml of pink frothy secretions which improved SpO_2 up to 96%. Inj. Furosemide (IV) 40 + 40 mg was repeated again. Chest X- ray taken on operation theatre revealed extensive haziness more on left side than right. That may be due left lateral position during surgery. Pt. was conscious and oriented throughout the event and did not required tracheal intubation or mechanical ventilation. To rule out other differential diagnosis like pulmonary embolism and myocardial infarction blood sample for D-Dimer and CPK –MB was sent which were reported to be within normal limits. In post anaesthesia care unit, as patient became hemo-dynamically stable, inj. Noradrenaline drip was discontinued after 8 hours. Inj. Furosemide, Steroids & Oxygenation were continued till 72 hours.

On 6th week , with patient' s consent , intradermal allergy test was carried out for Bupivaccaine 0.5% (H) and Cefotaxime and (0.02 ml of 1: 10,000 dilution) with normal saline as control while keeping all resuscitative measures ready. Within 10 min, 5mm wheal of flare noticed only at Cefotaxime prick site and hence patient was labelled as hypersensitive to Cefotaxime .On 7th postoperative day, chest X-ray showed clear lung fields, however 2D-echo showed mild pulmonary hypertension. On 8th week, 2D-echo findings were normal.



Chest X-ray showing bilateral pulmonary edema, more extensive on left side (dependent side).

Discussion

Anaphylaxis is a severe, potentially life-threatening allergic reaction, can occur within seconds or minutes of exposure to allergen. It is IgE mediated, type I hypersensitivity reaction. Perioperative anaphylaxis rare but real challenge for anaesthesiologist because of various factors:

1. Too many drugs are administered within a short span of time. So, difficult to identify offending agent.

2. Since, patients are under drapes or general anaesthesia skin rash, urticaria, pruritis may be missed.
3. Hypotension, tachycardia may be confused with anaesthetic induced changes in vitals initially.

Causative agents implicated in intraoperative anaphylaxis in Indian survey are mainly colloids (22%), antibiotics (21%), muscle relaxant (15.4%), opioids (15.4%) etc.[1]

Amongst antibiotics, cephalosporins are commonly used antibiotics in perioperative period. First and second generation cephalosporins are known to cause more allergic reactions than third and fourth generation cephalosporins.[4] Reactions like pruritis, pain on injection with Cefotaxime varies from 1% to 10%. However, anaphylactic reaction are very rare <1%.[5] Cefotaxime, a third generation cephalosporin is most commonly used perioperative antibiotic since more than a decade in our hospital as it has broad spectrum activity against gram negative and gram positive bacteria.

Previous exposure to offending agent and sensitisation of immune system is required for occurrence of anaphylactic reaction. Average period of 5 -10 days is needed for sufficient antibody production from time of initial exposure.[5] Although, sensitisation was present in this case, latency period was short.

Anaphylaxis has varied clinical presentation but cardiovascular and respiratory involvements are of biggest concern especially to anaesthesiologists as they are the commonest cause of morbidity and mortality.[6] Presentation of anaphylaxis is usually acute and may progress very quickly resulting in rapid deterioration and sudden death. Symptoms may be sequential or simultaneous. Urticaria and angioedema are most frequent manifestations but may be delayed or even absent especially in rapidly progressing anaphylaxis [6] which happened in our case. Along with cardiovascular collapse there was rapid development of pulmonary oedema without any warning cutaneous signs. Pulmonary edema is not commonly associated with anaphylaxis but it is without precedent.[7] Increased capillary permeability is the hallmark of anaphylaxis which is attributed to histamine & PAF released by degranulation of mast cells. Leakage of fluid from capillaries into alveoli (air sacs) of lungs leads to development of pulmonary oedema.[8]

Epinephrine and IV fluids are mainstay of treatment as increased vascular permeability is characteristic of anaphylaxis. Intramuscular or subcutaneous epinephrine is recommended in a dose of 0.5 mg to 1mg of 1:1000 dilution and may be repeated every 10 min till blood pressure improves but in case of cardiovascular collapse as in this patient intravenous epinephrine 0.5 to 1mg (5 to 10 ml of 1:10,000) in divided doses like 0.1 mg /min may be required. Peadiatric dose depends on age of child. In an adult 2 to 4 L IV fluids is usually given in form of crystalloids or colloids. Since, our patient was complicated with massive pulmonary edema, we have to restrict fluid administration up to 1L over 1 hour. Rather we initiated infusion inj. Noradrenaline (2ug/kg/min) to treat profound hypotension. Secondary treatment includes antihistamines, bronchodilators and diuretics if required. Glucocoticoids are given to avoid biphasic anaphylaxis.[9]

Various differential diagnoses arise in an anaesthesiologist's mind in case of severe adverse event during intraoperative period which include vaso-vagal reaction, pulmonary embolism, myocardial dysfunction, negative pressure pulmonary edema. Simultaneous exposure to multiple offending agents intraoperatively renders the diagnosis confusing and hence the treatment. But sudden cardiovascular collapse followed by administration of Cefotaxime signalled the occurrence of anaphylaxis and further prompt response to treatment of anaphylaxis almost confirms the diagnosis. Raised serum Tryptase concentration of sample collected within 1-2hour helps to confirm the diagnosis. Value serum Tryptase more than 13.5nmol/l is considered significant. Other markers such as caboxypeptidase, histamine can also be evaluated

for further accuracy.[2,6] Since none of these tests for evaluation of markers were available in our setup, we confirmed our diagnosis by clinical presentation and by ruling out other differential diagnosis like absence of bradycardia rules out vasovagal reaction. Normal report of D-Dimer, postoperative Colour Doppler of both lower limbs, CPK –MB and 2 D ECHO preclude possibility of pulmonary embolism or myocardial dysfunction or infarction respectively. Since no deep sedation was given to patient, possibility of negative pressure pulmonary edema was ruled out.

Although, it is recommended to give 1 ml of antibiotic as test dose followed by slow iv infusion of rest of antibiotic but it could not benefit our patient. As per French society recommendations, skin allergy testing should be carried out after 5- 6 weeks of anaphylaxis.[10] As per the "Algorithm for the use of skin tests in the diagnosis of drug hypersensitivities" patient was educated about his hypersensitivity to Cefotaxime and warned to avoid the drug and other cephalosporins as cross reactivity may exists although rare. Also, adequate documentation of drug allergy was done.[11]

After reviewing various case reports of anaphylaxis, it is evident that neither thorough history taking about allergies nor skin testing was found to be useful to avert severe life threatening anaphylactic reaction. At the onset, anaphylactic reactions are usually diagnosed on clinical grounds . So, to conclude, in perioperative period considering exposure of patient to multiple offending agents, anaesthesiologists should always remain cognizant about of risk of perioperative anaphylaxis and its management.

References

1. Gandhi R, Sharma B, Sood J et al. Anaphylaxis during anesthesia : Indian scenario . IJA. 2017;61: 387-92
2. Amit G Bhagat, Kirti N Sarema. Intraoperative Anaphylaxis to Inj. Ceftriaxone: Here We GO Again…. IJA 2008; 52 (4): 462-466.
3. Kelkar PS, Li J. Cephalosporin allergy. N Engl J Med. 2001; 345: 804-9.
4. Patterson RA, Stankewics HA. Penicillin allergy [Updated 2019Apr23]. State Pearls [Internet]. Treasure Island(FL): State Pearls Publishing; 2019Jan-
5. Thirunavukkarasu AB, Vijayan S. Cefotaxime- induced near fatal anaphylaxis in a neonate: A case report and review of literature. Ind J Pharmacol.2011; 43(5):611-12.
6. Kumari A, Gupta R, Bajwa SJ. et al. A rare case of ceftriaxone induced anaphylaxis in anesthesia practice . Arch Med Health Sci.2015; 3:106-9
7. Tomar GS, Tiwari AK,Chawla S .Anaphylaxis related to fentanyl citrate .J Emerg Trauma Shock. 2012; 5(3): 257-61.
8. Reber LL, Hernandez, Galli SJ .The pathophysiolory of anaphylaxis. J Allergy Clin Immunol .2017; 140(2); 335-48.
9. Mali S, Jambure R. Anaphyllaxis management: Current concepts .Anesth, Essays Res 2012; 6(2) : 115 -23.
10. Aboul- Fotouh S , Maggdy YM ,Ali RM. A case report of systole after a test dose of ceftriaxone in an adult man . Ain-Shams J Anaesthesiol.2016 ; 9:617-19
11. Brockow K. Romano A. Blanca M. et al. General considerations for skin test peocedures in the diagnosis of drug hypersensitivity. Allergy. 2002; 57(1): 45-51.