Case Report

Near Fatal Anaphylaxis Following Intravenous Co-amoxiclav in a Patient with Previous Tolerance

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Abstract

A severe allergic reaction to intravenous co-amoxiclav in a patient of chronic obstructive pulmonary disease who had previously tolerated oral and intravenous co-amoxiclav is being reported. Patient went into a cardio-respiratory arrest within a minute of receiving intravenous co-amoxiclav. Patient was revived with timely administration of epinephrine and mechanical ventilation. Prompt administration of epinephrine is the most important decision in the treatment of anaphylaxis. Other adjunctive treatment as histamine receptor antagonists and corticosteroids do not substitute for epinephrine. **[Indian J Chest Dis Allied Sci 2017;59:197-199]**

Key words: Anaphylaxis, Hypersensitivity, Co-amoxiclav, Penicillin allergy.

Introduction

With the increased consumption of co-amoxiclav, more patients have appeared with immediate hypersensitivity reactions with most studies indicating that amoxicillin was the inducer.[1] When a patient with no previous history of allergy or with previous tolerance to a particular beta-lactam antibiotic, is administered the antibiotic, one is not prepared for a near fatal anaphylactic reaction, and hence, this case alerts us to have our emergency measures in place for similar unexpected situations.

Case Report

A 67-year-old female patient with history of chronic obstructive pulmonary disease (COPD) with hypertension and diabetes mellitus came to the emergency department with COPD exacerbation. She was on tiotropium, formeterol with budesonide metered dose inhalers, oral theophylline, telmisartan and metformin. Patient was frequently hospitalised for COPD exacerbations and had received amoxicillin, co-amoxiclav orally and intravenously multiple times earlier without any allergic reactions and there was no history of any other allergic reactions in the past. On examination, the patient was febrile with a temperature: 37.8 ^{o}C, pulse rate: 120 per minute and regular, respiratory rate: 24 breaths/min and blood pressure: 150/70 mmHg. Oxygen saturation on pulse oximetry was 96%. Breath sounds were decreased bilaterally with few rhonchi. Cardiovascular examination was unremarkable, except for tachycardia.

Patient was treated with low flow oxygen at 2 liters per minute, nebulised salbutamol, ipravent and budecort, intravenous hydrocortisone hemisuccinate, deriphylline and co-amoxiclav. Patient complained of itching of the palm within seconds of administration of first dose of 1.2 g of co-amoxiclav and suddenly collapsed. Transient erythematous lesion appeared over the forehead. Pulse was 100 per minute and thready, and systolic blood pressure dropped to 90 mmHg. Immediately intramuscular epinephrine (0.5mL of 1:1000 [1mg/mL]), intravenous hydrocortisone 100mg and pheniramine maleate 22.75mg were administered. But patient's pulse dropped to 80/min and blood pressure was unrecordable. The dose of epinephrine was repeated and an additional intravenous line was secured and 0.9% normal saline was started. Patient was immediately intubated in the ward and transferred to intensive care unit and was put on mechanical ventilation with fraction of inspired oxygen (FiO_2) of 1. Ionotropic support was initiated. Patient improved and with favourable vital parameters was extubated after 24 hours. Patient was put on intravenous hydrocortisone, levofloxacin 500mg, theophylline, and nebulised medication for COPD in the ward and showed good clinical improvement.

Discussion

Co-amoxiclav is a combination of amoxicillin (beta-lactam antibiotic) with clavulanic acid to overcome beta-lactam resistance. Immunological responses to penicillin and other beta-lactam antibiotics are classified as 'immediate' which generally occur within minutes to an hour, and 'non-immediate' reactions

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which are non-immunoglobulin-E (IgE)-mediated and occur after 60 minutes to several days after administration of the last dose. Penicillin is estimated to cause 0.7% to 10% of all cases of anaphylaxis.[2]

A negative history of penicillin allergy in a patient does not guarantee safety from a hypersensitivity reaction, as our patient received both oral and injectable co-amoxiclav in the recent past. In a study of 151 fatalities due to penicillin allergy, 70% received penicillin previously without any reaction.[3]

There is an increased risk of anaphylactic reaction in patients who have been exposed to penicillin previously. It was observed that antibodies due to previous exposure to penicillin were present in the blood and tissues and in such cases even a minute dose may cause an explosive antigen antibody reaction. The effect of repeated exposure to penicillins presumbly accumulates, and hence, shows the highest frequency of anaphylactic reactions in previously exposed patients.[3]

The natural history of allergy to penicillins indicates that less than 80% of patients with an IgE-mediated penicillin allergy lose their sensitivity by 10 years after their reaction[4] but 1% to 16% of subjects may become resensitised after re-administration of a beta-lactam.[5] Old age combined with co-morbidities, such as cardiovascular disease and COPD is an important risk factor for severe anaphylaxis[6] and more likely to predispose to a fatal outcome because of a cardiovascular or respiratory comorbidity.[7] Beta-blockers and angiotensin converting enzyme (ACE) inhibitors increases the risk of severe anaphylaxis.[8] Our patient was elderly and had COPD, which served as risk factors for severe anaphylaxis.

Initial drug of choice in the management of anaphylaxis is epinephrine (adrenaline) which is given intramuscularly in the mid-antero-lateral aspect of the thigh in a dose of 0.01 mg/kg of 1:1,000 (1 mg/mL) solution, to a maximum of 0.5mg and to be repeated in 5-15 minutes, depending on the severity of anaphylaxis, control of symptoms and sustain or increase blood pressure. Most patients respond to 1 or 2 doses.[9] Intramuscular injection into the mid-antero-lateral aspect of the thigh is recommended as epinephrine has a vasodilator effect in skeletal muscle, that facilitates rapid absorption and prompt action in contrast to vasoconstrictor effects into subcutaneous tissue, which delays absorption and action all of those may be clinically relevant during anaphylaxis.[10]

Fatalities of anaphylaxis usually results from delayed or inadequate administration of adrenaline.[11] In a study of 164 patients with fatal anaphylaxis, the median time from initial symptom to cardio-respiratory arrest was five minutes in iatrogenic anaphylaxis.[12] In another study of anaphylaxis related fatalities,[13] only 25% of 92 individuals received adrenaline before cardiac arrest. Delayed injection of epinephrine might be one of several factors contributing to biphasic anaphylaxis, defined as symptom recurrence 1–72 hours (usually within 8 hours) after resolution of the initial symptoms, without ongoing or further exposure to the anaphylaxis trigger.[10]

Serious adverse effects, such as pulmonary oedema or hypertension potentially occur with overdose commonly after an intravenous bolus injection of epinephrine. In middle-aged or elderly patients who might have sub-clinical coronary artery disease and in patients with diagnosed coronary artery disease, potential cardiac effects of epinephrine should be weighed against the cardiac risks of untreated anaphylaxis.[14] There are no absolute contraindications to epinephrine use in anaphylaxis.[9] Glucocorticoids onset of action takes several hours and are not the sole drugs of choice in initial anaphylaxis treatment. These remain adjuvant drugs for anaphylaxis and these potentially prevent biphasic late phase reactions. Similarly H_1 and H_2 antihistamines are not initial and the sole drugs of choice in anaphylaxis although these decrease urticaria and itching.[9]

A skin test may be considered in parental administration of injectable beta-lactam antibiotic, especially penicillin even if the patient has received the antibiotic earlier and moreover in high risk patients despite a negative history for penicillin allergy which may not be always reliable.

Every centre or ward that administers injectable antibiotics should have a standard protocol for the management of hypersensitivity reactions and emergency drugs and equipment should be in place in case such a situation arise. Caution should be taken even in patients who do not give history of known previous allergy to the drug. Hypersensitivity reactions are unpredictable and can occur at any time, hence one should be prepared.

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