Hong Kong College of Physicians
Case report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least EIGHT Weeks before the date of Interim Assessment

Name of candidate (print and sign):
Hospital and Unit: Specialty:
Name of supervisor (print and sign):
Date(s) and place (hospital) of patient encounter: 1/12/2019
Date of report submission: 11/9/2022

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: A case of piperacillin-tazobactam anaphylaxis

Case history:

A 57-year-old male patient was admitted for high fever and chills for one day on 1 Dec 2019. He had increased sputum or shortness of breath. He had no abdominal pain, nausea, vomiting or diarrhea. He had no symptoms suggestive of urinary tract infection. He had no headache or photophobia. His medical history included nasopharyngeal carcinoma (NPC) with radiotherapy done in 1999, post-radiation hypothyroidism, adrenal insufficiency, dysphagia, vocal cord palsy, and bilateral temporal lobe necrosis on magnetic resonance imaging of the brain. He had ischemic stroke in 2013 and intracranial hemorrhage in 2019 with residual left sided hemiparesis. He was found to have mild stenosis of his bilateral carotid arteries by carotid Doppler ultrasound. He also had hypertension and hyperlipidemia. In recent 2 years, he had frequent hospitalizations due to recurrent aspiration pneumonia. He started feeding via nasogastric tube. His usual medications included hydrocortisone, thyroxine, amlodipine, famotidine, simvastatin, tramadol, paracetamol and lactulose. He had known allergy to amoxicillin-clavulanate and meropenem, both presented as rash and itchiness after the two antibiotics.

On examination, his temperature was 40.1 ℃, blood pressure was 122/83 mmHg, heart rate was 114 bpm, respiratory rate was 18 bpm, and oxygen saturation was 94% breathing ambient air. He was conscious and oriented. He appeared agitated and

diaphoretic. The jugular venous pressure was not elevated. There were no carotid bruits. The lungs had fair air entry on auscultation. Auscultation of the heart showed normal first and second heart sounds (S1 and S2) without any heart murmur. The abdomen was soft and non-tender. The legs were warm to touch and the calves were soft. The skin of face and neck appeared erythematous due to fever, however no rash were presented. Initial investigations showed a mild leukocytosis with elevated neutrophils. His routine blood tests otherwise were unremarkable. His chest X-Ray was clear.

In view of recent hospitalizations of recurrent aspiration pneumonia, empirical intravenous (IV) piperacillin-tazobactam was started for possible pneumonia. Hydrocortisone 20mg bd was also given orally for stress cover. After piperacillin-tazobactam infusion for 10-20ml only, patient suddenly developed severe hypotension and desaturation. The blood pressure was down to 57/32 mmHg. The pulse rate was 116 bpm. The oxygen saturation was down to 85% on ambient air. Patient was agitated and distressed. He complained of generalized itchiness over his body. There was no obvious skin rash, despite that his skin remained erythematous similar to the time of admission. Chest auscultation showed increased sputum sound without any stridor or wheeze. His abdomen was soft and non-tender.

The patient was treated as anaphylaxis to piperacillin-tazobactam. Piperacillin-tazobactam infusion was stopped immediately. He was given intramuscular (IM) adrenaline 1:1000 0.1mg and IV hydrocortisone 200mg immediately. He received aggressive fluid resuscitation with gelofusine and dopamine infusion for circulatory support. His hemodynamics were stabilized afterwards. Patient was given IV steroid and chlorpheniramine. His antibiotics was switched to levofloxacin.

Patient’s medical records were reviewed carefully. In the past he tolerated piperacillin-tazobactam without allergic reactions. However during his last hospitalization a couple of weeks ago, the patient developed significant hypotension after piperacillin-tazobactam use. His blood pressure dropped from 125/68 mmHg to 40/20 mmHg 20 minutes after IV piperacillin-tazobactam infusion. He was given IM adrenaline 1:1000 0.5mg, followed by dopamine and IV fluid resuscitation. However, since there were no itchiness or skin rash, the cause of hypotension was later believed to be multi-factorial, including septic shock, postural hypotension or autonomic dysfunction in view of his underlying histories of NPC. Unfortunately, tryptase was not check at that time. He later completed a course of IV piperacillin-tazobactam for seven days without allergic reaction.

During this hospitalization, tryptase level taken immediately after the event was elevated (25.3 ug/L, normal range 0-11.4 ug/L). A repeated test 24 hour later was 7.56 ug/L. The significant elevation of tryptase level immediately after the event was suggestive of piperacillin-tazobactam anaphylaxis. Although no rash was presented at the time of presentation, patient did developed urticaria rash predominantly over four limbs and abdomen three days later after the event.

Discussion and literature review:

Allergic drug reaction is a hypersensitivity reaction with an underlying immunological mechanism. It is typically classified into 4 types: 1) type I, mediated by drug-specific IgE antibodies; 2) type II, mediated by IgG and IgM antibodies, 3) type III, mediated by immune complexes; and 4) type IV, mediated by T-cells [1]. Clinically, allergic drug reactions can be classified as immediate and non-immediate reactions [2]. Immediate allergic reactions typically occur within 1-6 h after culprit drug administration, which include urticaria, angioedema, conjunctivitis, rhinitis, bronchospasm, gastrointestinal symptoms and most importantly anaphylaxis. Non-immediate allergic reactions may occur at any time after culprit drug administration, which include delayed urticaria, skin eruptions, vasculitis, toxic epidermal necrolysis, Stevens–Johnson syndrome (SJS), and drug reaction with eosinophilia and systemic symptoms (DRESS) [2].

Anaphylaxis is an acute and life-threatening clinical syndrome [3]. It is often characterized by a group of severe clinical problems: 1) rapid circulatory compromise (hypotension, tachycardia, hypotension associated symptoms e.g. confusion and syncope); 2) respiratory compromise (pharyngeal or laryngeal edema, bronchospasm, tachypnea); 3) severe gastrointestinal symptoms (e.g. repeated vomiting, severe crampy abdominal pain), and / or 4) skin and mucocutaneous involvement (urticarial, flushing, pruritus, angioedema). Skin and mucocutaneous involvement are usually present but may be subtle or even absent.

Differential diagnoses of anaphylaxis include vasovagal reactions, asthma attacks, foreign body aspiration, pulmonary embolism, myocardial infarction and / or

arrhythmia, hereditary angioedema [4]. Measurement of serial serum tryptase level can help differentiate anaphylaxis from other diagnosis. Acute elevation of serum tryptase indicates degranulation of mast cells, either due to an IgE-mediated or non-IgE-mediated mechanism. Tryptase levels start to rise in serum within minutes of anaphylaxis, peak in 0.5-1 hour, and then gradually returns to normal over the next 5-24 hours [5]. The elevation of tryptase level has good of specificity (89–100%) although fair sensitivity (64%) for diagnosis of anaphylaxis [6]. Moreover, the level of tryptase has correlation with the severity of anaphylactic reaction. Therefore, blood sample for serum tryptase should be taken in a timely manner. In clinical setting, the first blood sample for tryptase should be sent within 4 hours after the onset of anaphylaxis, and a second blood sample for tryptase should be taken 24 hours after the anaphylaxis event.

However, the identification and determination of drug allergy can be clinically challenging. As mentioned above, many clinical conditions may well mimic the event of anaphylaxis. Skin allergic reactions, including urticaria, maculopapular rash, itchiness, and angioedema, sometimes could be subtle. In our case, other possible causes for hypotension further complicated the picture, including septic shock, adrenal insufficiency, and carotid body or sinus dysfunction. The event developed suddenly after the initiation of pipercillin-tazobactam infusion. Patient also developed itchiness and rash during the event. These favour anaphylaxis over septic shock. Patient had been put on stress dose hydrocortisone since admission, therefore adrenal insufficiency is less likely to be the cause of hypotension. Patient had bilateral internal carotid stenosis and further investigations for autonomic dysfunction should be arranged in outpatient setting. However, the elevation of tryptase level after the onset of the event is diagnostic of anaphylaxis.

This case has several learning points. Rapid recognition of allergic reaction and anaphylaxis is very important, and the clinical suspicion of anaphylaxis should always be high, even when use of the culprit drug appears uneventfully in the past. anaphylaxis should always be on the top of lists of differential diagnoses, even when multiple confounding causes and factors are existed. Acute management of anaphylaxis include immediate administration of IM adrenaline (1:1000) 0.01mg/kg without delay, aggressive resuscitation, followed by oral or IV anti-histamine, IV steroid use. A careful and complete allergy history review is need to determine the causal relationship. Finally, accurate documentation should be done to avoid re-exposure of the culprit medication in the future.

Tables and figures (where applicable) (no more than two figures)

Nil.

Reference (not more than 10)

1. Schnyder B, Pichler WJ. Mechanisms of drug-induced allergy. Mayo Clin Proc. 2009;84(3):268-272. doi:10.1016/S0025-6196(11)61145-2
2. Cernadas JR, Brockow K, Romano A, Aberer W, Torres MJ, Bircher A et al. General considerations on rapid desensitization for drug hypersensitivity - a consensus statement. Allergy 2010;65:1357–1366.
3. Turner PJ, Worm M, Ansotegui IJ, El-Gamal Y, Rivas MF, Fineman S, Geller M, Gonzalez-Estrada A, Greenberger PA, Tanno LK, Borges MS, Senna G, Sheikh A, Thong BY, Ebisawa M, Cardona V; WAO Anaphylaxis Committee. Time to revisit the definition and clinical criteria for anaphylaxis? World Allergy Organ J. 2019 Oct 31;12(10):100066. doi: 10.1016/j.waojou.2019.100066. PMID: 31719946; PMCID: PMC6838992.
4. Ellis AK, Day JH. Diagnosis and management of anaphylaxis. CMAJ. 2003 Aug 19;169(4):307-11. PMID: 12925426; PMCID: PMC180656.
5. Schwartz LB. Diagnostic value of tryptase in anaphylaxis and mastocytosis. Immunol Allergy Clin North Am. 2006 Aug;26(3):451-63. doi: 10.1016/j.iac.2006.05.010. PMID: 16931288.
6. National Clinical Guideline Centre (UK). Drug Allergy: Diagnosis and Management of Drug Allergy in Adults, Children and Young People. London: National Institute for Health and Care Excellence (UK); 2014 Sep. (NICE Clinical Guidelines, No. 183.) 7, Measuring serum tryptase after suspected anaphylaxis. Available from: https://www.ncbi.nlm.nih.gov/books/NBK274147/

No of words in Case History and Discussion (excluding references):_____1783_____

(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

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(signature of Trainee)

Endorsed by Supervisor *

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