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Case Report

Fatal systemic reactions, concurrent of anaphylaxis and systemic toxic reactions to hymenoptera-sting

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ABSTRACT

Hymenoptera-sting can cause localized and systemic reactions (SR). SRs such as anaphylaxis and systemic toxic reactions (STR). It is estimated to occur in 3% of adults and can be life-threatening. Diagnosis is based on clinical manifestations, previous of allergic history, IgE-mediated confirmation and the offending insect identification. Anaphylaxis patients should immediately receive adrenaline intramuscularly, emergency medical attention and other supporting treatment. We report a 36-year-old man with fatal SRs, concurrent of anaphylaxis and systemic toxic reaction due to multiple hymenoptera-stings.

Keywords: Hymenoptera-sting, Anaphylaxis reaction, Systemic toxic reaction, Organ failure

INTRODUCTION

Hymenoptera-sting may result in a wide range of clinical spectra, including localized and SR. The common type of SR are anaphylaxis and STR included rhabdomyolysis, hemolysis, renal and hepatic dysfunction also cerebral disturbances. The diagnosis was based on clinical manifestation and treated symptomatically.[1-7] The immediate and optimal management prevents SR to be fatal.[8-12]

We reports a case of fatal SRs to multiple hymenoptera stings (Concurrent of anaphylaxis and STR).

The patient's family member specifically provided written informed consent for the publication and any accompanying images. The study procedure was approved by ethical committee of hospital with register number: 18/RSU/Litbang/2020. The study was conducted in accordance with declaration of Helsinki.

CASE REPORT

A 36-year-old man, one hour earlier was stung by hymenoptera in a large-numbers on all over his body while he was climbing a tree. He came to emergency department (ED) with shortness of breath and swellings predominantly round the eyes. He had a history of bronchial asthma, but no history of other chronic diseases. History of alcohol consumption and drug or food allergies were denied. Blood pressure (BP) was 100/70 mmHg, pulse rate (PR) 92 (beats/min), tachypnea (30 times/min), axillary temperature 36.7^{O}C, and oxygen saturation (SpO_2) 94% on room air. The diagnosis was anaphylaxis due to hymenoptera-stings. He was given adrenaline 0.3 mL IM, 4 litres per minute of O_2 non-rebreathing mask and normal saline 500 mL infusion. Dipenhydramine 10 mg inj. IM added with 200 mg hydrocortisone inj IV. The shortness of breath got worse. There were muscle pain and dark-red colored urine, he looked restless and disoriented.

He was observed in the intensive care unit (ICU). BP was 90/70 mmHg, mild tachycardia (110 beats/min), tachypnea (32 times/min), fever (xaillary temperature 37.6^{O}C), and oxygen saturation 93% on room air. On the skin found multiple vulnus ictum with a diameter of±0.1 cm, discrete distribution of the upper and lower extremities, abdominal and thorax. Hyperpigmented macules, multiple, round in shape, measuring±0.2 cm observed. There were rales on lungs. Total IgE serum level was significantly increased. Other laboratory results; leukocytosis (36.64x10^3/µL, 94.31%) with dominant of neutrophils. Transaminitis was also found, accompanied by an increase in blood urea nitrogen and creatinine serum, hyponatremia, while blood gas analysis metabolic acidosis. On urine analysis found red cells 10-15/hpf (0-1/hpf) (Table 1). Decreased of conscious due to hypoxic encephalopathy, metabolic encephalopathy or electrolyte inbalance.

The diagnosis was anaphylaxis concurrent and STR (rhabdomyolysis, hemolysis, renal and hepatic dysfunction also cerebral disturbances). There was also found pneumonitis followed by acute respiratory distress syndrome (ARDS). An endotracheal tube was placed on the patient because the patient had apnea. The treatment was continued with hydration; normal saline infusion, 5 % dextrose, Ringer's lactate alternately and aminofusine to keep urine production over 25 mL/h. Empiric antibiotic, 1 g meropenem inj. IV (each 8 hours), 3% Nacl 500 cc, 15 l/min of O_2 non-rebreathing mask, 100 mg hydrocortisone inj. IV (each 12 hours) and 10 mg dipenhydramine inj. IM (each 8 hours). Chest X-ray showed consolidation in lower zone of left lung (Figure 1A).

Meanwhile, on repeated chest X-ray, there was increasing consolidation in the lower zones of the right and left lungs (Figure 1B). On 2nd day of admission in ICU, patient was re-examined BGA and electrolyte, the results were severe metabolic acidosis, with a blood pH of 6.85 (Table 2).

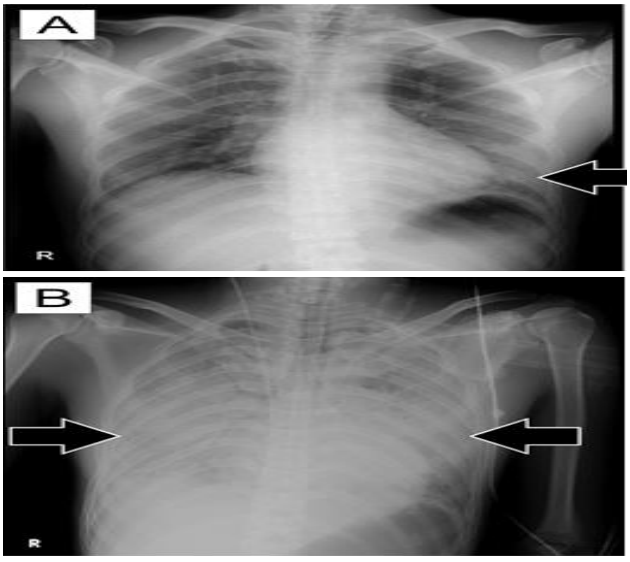

Figure 1 (A and B): Chest x-ray of initial admission and day two of treatment.

The therapy was added by sodium bicarbonate, an endotracheal tube was placed because he had apnea. During the close-observation, there were no significantly treatment response and the patient died.

Table 1: Laboratory results.

Laboratory data	First day (21/7/20)	Reference range
Leukocyte (10^9/L)	38,850	4.100-11.000
Haemoglobin (g/dL)	15.97	13.5-17.5
Platelet (/mcL)	141,000	150,000-440,000
ALT (IU/L)	13,972	11.00-33.00
AST (IU/L)	2,333.2	11.00-50.00
Total bilirubin (mg/dL)	1.76	0.3-1.3
Direct bilirubin (mg/dL)	0.45	0-0.3
Indirect bilirubin (mg/dL)	1.31	
HBsAg	Non-reactive	Non-reactive
Anti HCV	Non-reactive	Non-reactive
Ureum nitrogen (mg/dL)	90.7	8.00-23.00
Creatinin serum (mg/dL)	2.8	0.70-1.20
Total IgE (IU/mL)	467	< 87
Urinalysis		
Protein	+++	Negative
Red cells	10-15/hpf	0-1/hpf

ALT: alanine aminotransferase; AST: aspartate aminotransferase; IgE: Immunoglobuline (E); hpf: high power field.

Table 2: The blood gas analysis and electrolyt results.

Laboratory data	Day-1 (21/7/20)	Day-2 (22/7/20)	Reference range
pH	7.33	6.85	7.35-7.45
pCO_2	25.8	100.2	35-45
pO_2	81.1	48.5	80-100
BEecf	-12.9	-16.4	-2-2
HCO_3^-	13.2	17.3	22-26
SO2c	95.4	52.8	95-100
TCO_2	14	20.3	24-30
Serum K^+ (mEq/L)	4.42	4.62	3.50-5.10
Serum Na^+ (mEq/L)	109	129	136-145
Serum Cl^- (mEq/L)	87	92	94-110

DISCUSSION

Anaphylaxis is a severe and life-threatening systemic hypersensitivity reaction, is affects 1.2% to 3.5% of all people in their lives induced by hymenoptera-stings.[13] Interaction of allergens and IgE antibodies triggers the

release of mediators that can affect several target organs. Activation of mast cells and basophils will release mediators include histamine, tryptase, carboxypeptidase A, proteoglycans. Histamine stimulates vasodilation and increases vascular permeability, heart rate, cardiac contraction. Prostaglandin D2 is a bronchoconstrictor, pulmonary and coronary vasoconstrictor and peripheral vasodilator. Leukotrienes cause bronchoconstriction, increase vascular permeability. PAF is a strong bronchoconstrictor and it increases vascular permeability.[14,15] The clinical manifestations of anaphylaxis can occur within seconds of exposure to the antigen. Severe upper airway obstruction with angioedema can cause asphyxia while lower airway obstruction is caused by bronchospasm. Cardiovascular manifestation is hypotension caused by massive fluid shifts to the extravascular space. Gastrointestinal symptoms may include nausea, vomiting, diarrhea, and abdominal pain.[16]

Current expert consensus has defined anaphylaxis.[17] The diagnosis is based on; Acute onset with involvement of skin, mucosal tissue and at least one of the following: a) respiratory compromise and b) reduced blood pressure or symptoms of end-organ dysfunction, two or more of the following; skin/mucosal symptoms and signs, respiratory compromise and/or gastrointestinal symptoms and reduced blood pressure after a known allergen exposure.[18]

Clinically, anaphylaxis involves at least two organ systems or sudden changes in vital signs.[19,20]

The patient was complaint shortness of breath and generalied swellings predominantly round the eyes in a few minutes after the stung. Fully alert, BP was 100/70 mmHg, PR 92 x/min, respiratory rate 30 x/min, axillary temperature 36.7^{O}C, and oxygen saturation (SpO_2) 94% of room air. Leukocytosis (absolute 36.64x10^3/µL, 94.31%) with dominant of neutrophils, high level of total IgE (467 IU/mL). The clinical and laboratory finding suggested anaphylaxis.

He was given intramuscular 1:1000 (1 mg/ml) adrenaline injection at a dose of 0.01 mg/kg (0.01 mL/kg) body weight into the lateral thigh, oxygen supplement, a large volume of fluid. may leak from the patients circulation during an anaphylaxis and closed monitor. Although the role of glucocorticoids in anaphylaxis is lack of evidence but in the clinical practise, these agents continue to be used routinely.[17,21-24,25] He was treated with 200 mg hydrocortisone IV, dipenhydramine 10 mg IM, 4 litres per minute of O_2 non-rebreathing mask, but the condition was progessed be worsen (multi organ dysfunction).

Finally, the patient was diagnosed with anaphylaxis concurrent with STR and was given treatment (by continuing the acute management of anaphylaxis added with symptomatically treatment) in the ICU.

Envenomation cause of STR (Multi-organ dysfunction/ failure) due to hymenoptera-sting.

STR of hymenoptera venom as a part of SR are generally seen in stings amounting to >50.[7] The number of lethal stings is estimated at 500 stings and mortality is due to direct systemic effects of venom. Age, body weight, number of stings, and individual characteristics (immune status, comorbidities, and previous sensitization) determine the severity.[26] Hymenoptera venom contains of several active components; phospholipase A2 (PLA2), hyaluronidase, melittin, and apamine which can cause skin necrosis at the sting site and rhabdomyolysis will cause kidney failure.[27] PLA2 triggers release arachidonic acid from lipids in cell membranes, which triggers ecosanoids production. Hyaluronidase breaks down chondroitin and hyaluronic acid in connective tissue. Low molecular weight components contribute to toxic effect; apamin (neurotoxin), mast cell degranulating peptides and histamine. This substance plays a role in lysing red blood cells, leukocytes, platelets, and damaging vascular endothelium. The severe STR include rhabdomyolysis, hemolysis, renal dysfunction, hepatic dysfunction and cerebral disturbances.

The comparison between the literature review and the case are: [2,8-12,26,28] Muscle pain, dark-red colored urine due to multiple insect-stings is associated with rhabdomyolysis. These clinical manifestations support by urine analysis found red cells 10-15/hpf (0-1/hpf), is suggested rhabdomyolysis.

Indirect hyperbilirubiaemia; total bilirubin 1.76 mg/dL, direct bilirubin 0.45 mg/dL, indirect bilirubin 1.31 mg/dL) are suggested hemolysis.

Mejía-Vélez reported that 7 out of 43 patients who developed acute renal failure (ARF) due to multiple wasp stings. It shows that renal function did not improve and the patients died, emphasizing the importance of determining the severity of renal impairment and early treatment for renal dysfunction. The hematuria occurs in the first 24 hours. Hypotension, intravascular hemolysis, myoglobinuria and direct toxic effect of massive quantity of venom associated with ARF. In this case, ureum nitrogen 90.7 mg/dL, creatinine serum 2.8 mg/dL are suggested ARF.

Liver complications may be affected by direct toxicity of venom, autoimmune reactions and cause toxin-induced anaphylactic shock. In this case was found the elevation of transaminases (ALT 13,972 IU/L, AST 2,333.2 IU/L), are suggested hepatotoxic effect

Hypoxemia, metabolic acidosis and electrolyte inbalance may cause hypoxic and metabolic encephalopathy. This case, severe metabolic acidosis: pH of 6.85, hypoxemia and hyponatremia are causing decreased of conscious. Chest X-ray showed consolidation in the lower zone of the left lung. Meanwhile, on a repeat chest X-ray was found that consolidation was increasing in the lower zone of the right and left lungs. Those suggested pneumonitis followed by acute respiratory distress syndrome (ARDS).

Finally, the diagnosis was anaphylaxis concurrent with severe STR due to massive hymenoptera-stings and pneumonitis followed by ARDS. The patient died on the second day of treatment. The cause of death was respiratory failure or cardiac arrest, multi-organ dysfunction.

CONCLUSIONS

The patients with a large number of hymenoptera-stings should seek medical care as early as possible. Physicians should be well aware of these complications, an explore actively to exclude anaphylaxis, the involvement of kidney, liver and other essential organs. The previous of allergic history are the risk factors for an unfavorable outcome of anaphylaxis and can develop worse due to severe STR. This case study shows the multiple hymenoptera-stings patient need prompt and appropriate therapy and close monitoring.

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REFERENCES

1. Unal D. Hymenoptera venom anaphylaxis. J Immunol Clin Res. 2018;5(1):1047.
2. Cichocka-Jarosz E. Hymenoptera venom allergy in humans. Folia Me Cracov. 2012;52(3-4):43-60.
3. Betten DP, Richardson WH, Tong TC. Massive honey bee envenomation-induced rhabdomyolysis in an adolescent. Pediatrics. 2006;117(1):231-5.
4. Fonteque JH, Mendes RP, Souza AF. Systemic toxic reaction due to multiple honeybee stings in equine: Case report. Arquivo Brasileiro de Medicina Veterinária e Zootecnia. 2018;70:767-72.
5. Ou WF, Huang WH, Chiu HF, Mao YC, Wen MC, Chen CH et al. Clinical manifestation of multiple wasp stings with details of whole transcriptome analysis: Two case reports. Medicine (Baltimore). 2021;100(4):e24492.
6. Ittyachen AM, Abdulla S, Anwarsha RF. Multi-organ dysfunction secondary to severe wasp envenomation. Int J Emerg Med. 2015;8:6.
7. Daher EF, Silva Junior GB, Bezerra GP, dkk. Acute renal failure after massive honeybee stings. Rev Inst Med Trop São Paulo. 2003;45(1):45-50.
8. Bilò MB, Tontini C, Martini M, Corsi A, Agolini S, Antonicelli L. Clinical aspects of hymenoptera venom allergy and venom immunotherapy. Eur Ann Allergy Clin Immunol. 2019;51(6):244-58.
9. Fehr D, Micaletto S, Moehr T, Schmid-Grendelmeier P. Risk factors for severe systemic sting reactions in wasp (Vespula spp.) and honeybee (Apis mellifera) venom allergic patients. Clin Transl Allergy. 2019;9:54.
10. Stoevesandt J, Sturm GJ, Bonadonna P, Oude Elberink JNG, Trautmann A. Risk factors and indicators of severe systemic insect sting reactions. Allergy. 2020;75(3):535-45.
11. Prado M, Quirós D, Lomonte B. Mortality due to Hymenoptera stings in Costa Rica, 1985-2006. Rev Panam Salud Publica. 2009;25(5):389-93.
12. Pramanik S, Banerjee S. Wasp stings with multisystem dysfunction. Indian Pediatr. 2007;44(10):788-90.
13. Przybilla B, Ruëff F. Insect stings: clinical features and management. Dtsch Arztebl Int. 2012;109(13):238-48.
14. Yao X, Wang J, Liu B. A case report of anaphylactic shock induced by cisatracurium. Arch Clin Med Case Rep. 2019;3(5):285-8.
15. Peavy R, Metcalfe D. Understanding the mechanisms of anaphylaxis. Curr Opin Allergy Clin Immunol. 2008;8(4):310-5.
16. Sreevastava L, Tarneja S. Anaphylactic reaction: An overview. MJAFI. 2003;59:53-6.
17. Jimenez-Rodriguez TW, Garcia-Neuer M, Alenazy LA, Castells M. Anaphylaxis in the 21st century: phenotypes, endotypes, and biomarkers. J Asthma Allergy. 2018;11:121-42.
18. imons FE, Ardusso LR, Bilò MB, Dimov V, Ebisawa M, El-Gamal YM et al. World Allergy Organization. 2012 Update: World Allergy Organization Guidelines for the assessment and management of anaphylaxis. Curr Opin Allergy Clin Immunol. 2012;12(4):389-99.
19. Sampson HA, Muñoz-Furlong A, Campbell RL, Adkinson NF Jr, Bock SA, Branum A et al. Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol. 2006;117(2):391-7.
20. Muraro A, Roberts G, Worm M, Bilò MB, Brockow K, Fernández Rivas M et al. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy. 2014;69(8):1026-45.
21. Dodd A, Hughes A, Sargant N, Whyte AF, Soar J, Turner PJ. Evidence update for the treatment of anaphylaxis. Resuscitation. 2021;163:86-96.
22. Shaker MS, Wallace DV, Golden DBK, et al. Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis. J Allergy Clin Immunol. 2020;145(4):1082-123.
23. Ribeiro, Maria Luiza Kraft Köhler, Chong, Herberto José and Rosario, Nelson AugustoDiagnosis and treatment of anaphylaxis: there is an urgent need to implement the use of guidelines. Einstein (São Paulo). 2017;15:500-6.

24. Brown SG, Mullins RJ, Gold MS. Anaphylaxis: diagnosis and management. Med J Aust. 2006;185(5):283-9.
25. Radhakrishnan H. Acute kidney injury and rhabdomyolysis due to multiple wasp stings. Indian J Crit Care Med. 2014;18(7):470-2.
26. Toledo L, Moore D, Caixeta D. Multiple bee stings, multiple organs involved: a case report. Rev Soc Bras Med Trop. 2018;51(4):560-2.
27. Nandi M, Sarker S. Acute kidney injury following multiple wasp stings. Pediatr Nephrol. 2012;27:2315-7.
28. Mejía Vélez G. Acute renal failure due to multiple stings by Africanized bees. Report on 43 cases. Nefrologia. 2010;30(5):531-8.

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