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Case Report

Biphasic anaphylaxis reaction in adult female: how to approach?

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ABSTRACT

Anaphylaxis is a severe allergic reaction, usually occurring one to two hours after exposure to an allergen, that can lead to death. Estimated lifetime prevalence of anaphylaxis is 1.6-5.1%, with global incidence between 50 to 112 episodes per 100.000 persons per year. Biphasic anaphylaxis is a form of recurrent anaphylaxis occurring between 1 to 72 hours after resolution of initial anaphylactic episode. Our case presents an 18-year-old female patient admitted to the emergency department (ED) with chief complaint of shortness of breath and swollen eyes after contact with caterpillar while gardening. General physical examination presented tachycardia, tachypnea, angioedema, urticaria. Localized lung examination presented bilateral wheezing. Patient fulfilled NIAID/FAAN criteria. Patient was administered 0.3 mg epinephrine intramuscular, diphenhydramine injection 10 mg, dexamethasone injection 5 mg, and observed in ED for 1 hour. Patient was then transferred to intensive care unit (ICU) and was in resolution. However, patient presented again with initial symptoms of dyspnea, swollen eyes, and itchiness while under observation. The objective of this paper is to present a rare case of biphasic anaphylaxis and further highlight the importance of awareness to occurrence of biphasic anaphylaxis.

Keywords: Anaphylactic reaction, Biphasic anaphylaxis, Allergy

INTRODUCTION

Anaphylaxis is an acute form of severe allergic reaction with symptoms comprising of multiple organ systems such as mucocutaneous, respiratory, and cardiovascular systems.[1,2] According to the World Allergy Organization, it has an estimated global incidence of 50 to 112 episodes per 100,000 persons per year, with incidence in pediatric population of 1 to 761 per 100,000 persons per year. Out of these data, there is also a recurrence of anaphylaxis in 26.5-54% of patients within the follow-up period of 1.5-25 years and it is also estimated that 1/20 of anaphylaxis cases require hospitalization.[1-3]

Biphasic anaphylaxis is recurrence of anaphylactic symptoms after complete resolution of initial symptoms within 1 to 72 hours, without the presence of allergen trigger. This reaction is estimated to occur in 20% of patients presenting with anaphylaxis.[3] Biphasic anaphylaxis is thought to be associated by medical history of asthma, prior anaphylaxis, treatment, and age. While this phenomenon is rare, awareness of biphasic anaphylaxis is key to proper and adequate management, and could further prevent progression of anaphylaxis to life-threatening conditions and even death.[4,5] It is also important to note potential risk factors and severity of condition to provide the needs of the patient, especially in the emergency unit.

Our case presents a patient with biphasic anaphylaxis while under observation and care within the emergency department, intensive care unit, and general inpatient ward.

CASE REPORT

An 18-year-old female patient presented to the emergency department with chief complaint of shortness of breath 10 minutes prior to admission. Shortness of breath was said to occur around 1 minute after the patient was gardening at home and caterpillar dust entered patient's nose. Patient also complained of itchiness and redness all over the body, and swollen eyes after the incident. Patient denied prior history of similar complaint, denied history of allergy to caterpillars or other insects. Patient confirms history of runny nose and sneezing in the morning, history of medication for symptoms was denied. History of food and drug allergy are denied, history of itchy and redness was denied, history of asthma was denied.

Vital signs showed blood pressure of 107/62 mmHg, heart rate of 82 times per minute, respiratory rate 22 times per minute, body temperature 36°C, oxygen saturation of 95%. Physical examination showed bilateral edema on eye palpebra and general urticaria. On lung examination, we found minimal wheezing on both fields, vesicular on both sides, no rales present. Laryngeal edema was not present. Further workup of laboratory examination was also conducted. Peripheral blood count presented white blood count 10.30, hemoglobin 11.2, hematocrit 34.3, mean corpuscular volume 70.9, mean corpuscular hemoglobin 23.1, platelets 256.

Patient was then admitted to the emergency department and given oxygen 3 liters per minute via nasal canula, normal saline 20 drops per minute, 0.3 mg intramuscular epinephrine injection, diphenhydramine 10 mg injection, and dexamethasone 5 mg injection. Patient was then monitored for observation for 1 hour. After observation for 1 hour, patient showed mild improvement however still complained of shortness of breath, general urticaria and palpebra edema are still present. Patient was then consulted to the Department of Internal Medicine and was administered intravenous fluid of dextrose 5% ½ normal saline 18 drops per minute, intravenous methyl-prednisolone 62.5 mg injection twice a day, and peroral loratadine tablet twice a day. Patient was also admitted to the intensive care unit (ICU) for further observation. After 24 hours in the ICU, patient denied complaint of shortness of breath and itchiness. Palpebra edema and general urticaria has improved. Oxygen saturation has also reached 95%. Patient was in stable condition so patient was advised to move to general inpatient ward.

Table 1: Patient's complete blood count (CBC) results at admission in the emergency department.

Examination	Results	Unit	Normal range
WBC	10.20	10^3/ul	4.0-10.0
Hb	11.2	g/dl	12.0-16.0
Hct	34.3	%	37.0-47.0
Platelets	256	10^3/ul	150-400

During second day of hospitalization, patient complaint of itchiness and shortness of breath. Upon physical examination, there were minimal wheals on both upper extremities, bilateral palpebral edema, no laryngeal edema found. There was no wheezing, but slight tachypnea. Vital signs showed blood pressure of 108/62 mmHg, heart rate of 80 times per minute, respiration rate of 22 times per minute, oxygen saturation of 95% on O_2 3 liters per minute on nasal canula. Patient was then further administered intravenous fluid of normal saline 18 drops per minute, intravenous methylprednisolone 62.5 mg injection twice a day, and peroral loratadine tablet twice a day, with additional pseudoephedrine tablet twice a day. Patient was put under close observation in case of any signs of recurrence. Patient's condition was observed to be improved, and patient was discharged the next day with peroral methylprednisolone tablet 8 mg twice a day, loratadine tablet 10 mg twice a day, and acetylcysteine tablet 200 mg thrice a day. Patient was discharged in a stable condition with no complications.

Table 2: Patient's vital signs throughout hospitalization.

Date	Time	Heart rate	Blood pressure	Oxygen saturation	Respiration rate
12/03/24	20.25	90	110/60	98% on O_2	24
	21.39	63	115/81	98% on O_2	22
	23.55	82	115/62	98% on O_2	22
13/03/24	00.59	70	113/63	99% on O_2	22
	01.59	68	118/74	98% on O_2	18
	10.00	90	107/60	98% on O_2	22
	11.30	63	110/63	100% on O_2	19
	18.30	79	104/61	97% on room air	20
14/03/24	00.00	80	108/62	98% on room air	20
	08.00	75	100/60	98% on room air	20

DISCUSSION

Anaphylaxis is defined as a severe, life-threatening systemic hypersensitivity reaction of rapid onset with potentially life-threatening airway, breathing, or circulatory problems, and is usually associated with skin and mucosal changes. There are two types of anaphylaxis reactions, namely immunoglobulin E (IgE) mediated and nonimmune mediated (direct activation). There is no

definite way to differentiate between the two as it is similar in clinical manifestations, however most cases are IgE mediated. When exposed to a particular allergen, antibodies will activate mast cells and basophils, causing degranulation and release of chemical and inflammatory mediators. In cases of nonimmune mediated anaphylaxis, there is a direct activation of mast cells, basophils, or complement.[1,2] Anaphylaxis can also be divided into its manifestation, namely biphasic and protracted anaphylaxis. Biphasic anaphylaxis is defined as the re-appearance of any anaphylactic symptom or new symptoms after resolution of primary reaction, without exposure of initial allergen. Initial anaphylactic reaction is usually followed by an asymptomatic period of 1 hour until up to 72 hours.[3] Protracted anaphylaxis is another atypical form of anaphylaxis, usually characterized by an anaphylactic reaction lasting until minimum of 5 hours without resolving completely.[5,6]

The reaction in our case could most likely be labeled as nonimmune mediated anaphylaxis, as the patient reported no previous history of allergy to causative agent. However, we did not perform a skin prick/intradermal test with suspected allergen to document IgE-mediated hypersensitivity, due to resource limitation.[1] There are several risk factors to biphasic anaphylaxis reaction which are history of anaphylaxis, unknown precipitant, symptoms of diarrhea, and wheezing.[7-9] Other risk factors also include history of asthma, pediatric patients ages between 6–9 years old, delay in admission to ER >90 minutes after onset, wide pulse pressure, treatment of initial reaction with more than 1 dose of epinephrine, and need of inhaled beta-agonist administration in the ER.[3] Another study stated that use of alpha and beta-adrenergic blockers and ACE inhibitors may exacerbate more severe anaphylactic episode. It is thought to be associated with defects in mediator degradation pathways. Further, is also upper respiratory infections and other acute current infections.[2,13] In this case, our patient has history of allergic rhinitis and currently has upper respiratory tract infection, being a predicted factor of biphasic anaphylaxis occurrence. History of previous anaphylactic reactions of allergy was denied, history of asthma in patient and in patient's family was also denied.

Our patient showed features of biphasic anaphylaxis within on the third day of hospitalization. In theory, biphasic anaphylaxis usually occurs within 1–8 hours of initial reaction, but there are reported cases occurring up to 72 hours.[3,5,9] Our patient showed signs of shortness of breath, itchiness, palpebral edema, and tachycardia. No signs of wheezing, hypotension, or shock. With that, it is recommended that all patients in the ER presenting with anaphylaxis must be observed until all signs and symptoms have resolved before being discharged.

We administered 0.3 mg of epinephrine injection intramuscularly, followed by injection of diphenhydramine 10 mg and dexamethasone 5 mg, with further administration of normal saline 20 drops/minute and oxygen via nasal cannula 3 liters/minute. Intravenous fluids and oxygen are vital especially in patients presenting with respiratory symptoms, decreased oxygen saturation, and hypotension. Distributive shock can occur, caused by vascular dilation as well as shift of intravascular fluid into extravascular space.[1] After observation for 1 hour, patient still showed mild symptoms, prompting us to administer a second dose of epinephrine 0.3 mg and methylprednisolone 125 mg bolus injection. Patient was observed for another hour and still showed minimal improvement; therefore, we administered another round of methylprednisolone injection with dose of 62.5 mg, loratadine 10 mg tablet, and intravenous dextrose 5% ½ normal saline 18 drops/minute. Patient was then admitted in the ICU. The treatment we have given is already in accordance to previous studies, in which patient is administered epinephrine in the case of anaphylactic reaction, where in this patient it is characterized with tachypnea, palpebral edema, and itching.[1-3] In this patient, we found respiratory problem and involvement of skin and mucosa. Epinephrine is first administered and functions as a nonselective adrenergic agonist that increases peripheral vascular resistance through vasoconstriction. It increases cardiac output, reverses bronchoconstriction and mucosal edema, as well as stabilizing production of mast cells and basophils. Methylprednisolone and dexamethasone as chosen corticosteroid is also administered in conjunction as it is thought to reduce incidence of biphasic reaction by inhibiting immune response. Antihistamine such as diphenhydramine and loratadine is also administered concomitantly with methylprednisolone to inhibit mast cells degranulation and inflammatory mediators. Due to its slower onset of action, it is administered after epinephrine. After administration of medication, our patient showed better outcome.[1,3,5] However, as tachypnea and itching still persist, we gave a second dose of corticosteroid namely methylprednisolone and also dextrose 5% ½ normal saline. In anaphylactic patients, glucagon can be administered. It has inotropic and chronotropic effects that may aid anaphylactic reaction. In this case, we used dextrose 5% ½ normal saline in replacement of glucagon due to unavailability at our center. After 24 hours in the ICU, patient was then transferred to general ward. In general ward, at third day of hospitalization, patient presented with shortness of breath, itchiness, and mild palpebral edema, indicating biphasic anaphylaxis. Patient also reported cough and runny nose. Patient's blood pressure was within normal limits, and respiratory rate increased minimally. With that, we further administered oxygen via nasal cannula 2 liters/minute, followed by methylprednisolone 62.5 mg injection, loratadine 10 mg tablet, and additional pseudoephedrine tablet. We found that the patient has signs of upper respiratory tract infections which are cough and runny nose. There are several potential risk factors of biphasic anaphylaxis, such as history of asthma, severe initial symptoms, delayed treatment, timing of epinephrine administration, number of epinephrine doses given, and delayed resolution of initial symptoms. Presence of upper respiratory tract infections can also be a contributing factor.[8-11] Our patient has some of these factors, namely

given more than 1 dose of epinephrine, delayed treatment, delayed resolution of initial symptoms, and presence of upper respiratory tract infection. Our patient was given 2 doses of epinephrine injection due to initial symptoms that haven't resolved with the first dose. Patient also had delayed treatment due to late arrival at the ER. Patient came to the ER 1 hour after onset, causing late administration of epinephrine. Patient also had delayed resolution of initial symptoms, in which symptoms did not resolve immediately. And last of all, patient also has signs of upper respiratory tract infection. Pseudoephedrine tablet was administered to combat runny nose. During follow up 24 hours after, patient's condition has improved drastically and patient was discharged in stable condition. Patient was discharged with loratadine tablet 10 mg twice a day, acetylcysteine tablet 200 mg thrice a day, and methylprednisolone tablet 8 mg twice a day for 3 days. Patient was also further educated on their condition, information about anaphylaxis, and things to consider in case of future anaphylactic attacks.

CONCLUSION

Anaphylaxis is a severe life-threatening condition that can cause high mortality. Various manifestations of anaphylaxis need to be diagnosed quickly and accurately to prevent complications in patients.

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