

Anaphylaxis: Lesson Learned from Five Cases

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ABSTRACT

Anaphylaxis is a severe hypersensitivity reaction. Its clinical manifestations vary, affecting several organs at once. Skin symptom is the most frequent manifestation; however, diagnosis of anaphylaxis will only be established when involving one or both vital organs, which are cardiovascular and respiratory system. Other symptom, such as that involving central nervous system or gastrointestinal tract, may accompany. We present five cases of anaphylaxis which vary in onset of symptoms, allergen, degree of severity, therapeutic response and clinical manifestation. Anaphylactic reaction to drugs in these cases is mainly manifested as anaphylactic shock and reaction to food allergen causing obstruction of respiratory tract. Four anaphylactic events occurred at home and only one occurred in a hospital, thus education on anaphylaxis to general community is very important, especially for the patients and their families. Prompt medical assistance in patients with anaphylactic symptoms determines their therapeutic response. Skin test prior to administration of cephalosporin does not give negative predictive value toward anaphylactic event.

Key words: anaphylaxis, allergen, epinephrine, skin test.

INTRODUCTION

Anaphylaxis is a form of severe systemic hypersensitivity reactions, which may put a patient in a life threatening situation.¹ Recently, anaphylactic events were reportedly increasing.²⁻⁴ An English report showed that anaphylactic event occurred in 1 of 5800 in-patients,⁵ 13250 patients were admitted due to anaphylaxis in 1992-2000,⁴ and 214 deaths occurred due to anaphylaxis during the same period.⁶ These data have shown that though rare, anaphylaxis may cause death, thus resulted in certain impacts, not only to the patients and their families, but also to the health care workers and doctors, especially in medicolegal aspect.

This writing will present 5 anaphylaxis cases with various medical aspects, from which we will be able to learn and gain benefit from these cases.

CASE ILLUSTRATION

Case 1

A male, 65 years old, was unconscious when he was brought to the hospital. Twenty minutes before, due to toothache, the patient had amoxycillin 500 mg, mefenamic acid 500 mg, and dexamethasone 0.5 mg at the same time. About one to two minutes after, the patient complained that all his body was itchy; he felt nauseated and vomited, was sweating, and finally was unconscious. He was immediately brought to the nearest hospital. According to his family, he never had asthma or allergy to certain drugs.

Physical examination revealed that the patient was in soporous condition, was sweating, non-palpable pulse, and non-measurable blood pressure. Respiratory rate was 28x/min, heart beat 132x/min, no gallop, wheezing was noticed from both sides of the lungs, no wet ronchi, unpalpable liver nor spleen, and pale extremities. In the emergency unit, the patient was put in supine position. He was given 5 L/min O₂, epinephrine shot 0.3 mL IM in lateral femur, load of 1-1.5 L of NaCL 0.9% IV, and 1 ampoule of dexamethasone.

For the next ten minutes, the blood pressure was measured at 50 mmHg with palpation and pulse was

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weak at 120x/min. He was given a second shot of 0.3 mL epinephrine IM, 1 mL of diphenhydramine, and 1 ampoule of ranitidine IV. In the twentieth minute, his blood pressure was 70/50 mmHg, pulse was 108x/min, and he was somnolence and had positive contact. The patient was given IV dopamine 5-10 µg/kgBW/min and was sent to the ward after his blood pressure reached 90-70 mmHg, pulse 96x/min, and apathy consciousness. The next day, the patient was sent home with blood pressure of 130/80 mmHg, pulse 80x/min, full consciousness, and normal activity. He was given cetirizine 10 mg/day and methyl-prednisolone 16 mg/day for 3 days, and was advised to have follow up care at the allergy clinic in the hospital.

Case 2

A 32-year-old male came with a complaint that one hour after taking griseofulvin 125 mg, he felt that his whole body was itchy and red. He felt nauseated and vomitted for about 5 times. He was sleepy and was asleep for about an hour. When he woke up, his face was swollen and he immediately went to the hospital. He never had any allergy to drug, previously. In the ER, he was fully conscious (compos mentis), pulse was weak at 120x/min, blood pressure was 85/60 mmHg, respiratory rate 16x/min, warm, reddish skin, no wheezing and no cold extremity. He was given injection of epinephrine 0.3 mL IM, flush of NaCl 0.9% 1 L IV, 1 ampoule of dexamethasone, 1 mL diphenhydramine, and 1 ampoule of ranitidine. After 20 minutes, his blood pressure was 100/70 mmHg, pulse 96x/min, and the patient felt better. He was observed for 2 hours in the ER before transported to the ward for further observation. When he was sent home the next day, his blood pressure was 130/80 mmHg, pulse 76x/min, no more reddish nor itchy skin, and was given cetirizine 10 mg/day and methyl-prednisolone 16 mg/day for 3 days.

Case 3

A male, 15 years old, was treated for typhoid fever. It was decided to give him ceftriaxone after negative skin test. Two hours after an IV bolus of ceftriaxone, the patient vomitted. There was no other complaint or symptom afterward. The second ceftriaxone was given slowly through IV drip. After an hour, the patient was shivering severely. His blood pressure was 150/90 mmHg, and pulse was 140/min. To overcome the condition, he was given 5 mg (1 ampoule) of dexamethasone, however, his blood pressure kept falling to 90/60 mmHg and pulse was 140/min. Subcutaneous epinephrine 0.3 mL was given, along with IV flush of ringer lactate. After ten minutes, blood pressure was 80/40 mmHg and pulse was still at 140/min. Blood pressure was improving after he received the fourth epinephrine shot, dobutamine 10

µg/kgBW/min, Hemacell and methyl-prednisolone 125 mg IV. After an hour, his blood pressure was 130/80 mmHg and pulse 100/min.

Case 4

A 14-year-old male, overweight with 50 kg of body weight, was admitted to the ER with complaint of small reddish bumps, and itchy on his skin along with sore throat. He had felt it 30 minutes prior to his arrival at the hospital. One-and-a-half hour before, he had eaten peanuts. About a year and two months before, he had experienced allergic reaction to peanut, consisted of pruritus and urticaria. When he was admitted in the ER, the patient was still conscious, though looking weak, sweating and had breathing trouble. His blood pressure was 100/70 mmHg; heart rate 120x/min, regular and sufficient; respiratory rate was 28x/min. At the time, he was immediately diagnosed as having anaphylactic reaction with laryngeal edema. He was lying in supine position, and was given oxygen 4 L/min, epinephrine (1:1000) 0.3 mL IM in the deltoid, methyl-prednisolone 62.5 mg IV, diphenhydramine 25 mg IM in gluteal region, and was given IV NaCl 0.9% 20 drops/min. After ten minutes, his condition worsened, and the patient became restless and cyanotic. Blood pressure dropped to 90/60 mmHg; heart rate became 132x/min, regular but weak; respiratory rate was 36x/min accompanied by stridor. The patient was given a second shot of epinephrine (1:1000) 0.3 mL IM in deltoid, and then was taken to Intensive Care Unit for immediate intubation or tracheostomy procedure. However, five minutes later the patient was apneic and died of respiratory failure.

Case 5

A doctor, 37-year-old male, came to the ER with complaint of the occurrence of reddish bumps, and itch in his skin and breathing trouble, twenty minutes after he had eaten shrimp. Previously, the patient also had history of seafood allergy manifested as reddish bump and itch in his skin. When he was admitted to ER, the patient was conscious, had breathing difficulties, no wheezing, but stridor could be heard. Blood pressure was 110/70 mmHg, heart rate 104 x/min, sufficient and regular; respiratory rate was 28x/min. The patient was diagnosed as having anaphylactic reaction with laryngeal edema. He was laid down, given oxygen 6L/min, epinephrine injection (1:1000) 0.3 mL IM in the deltoid, methylprednisolone 250 mg IV, diphenhydramine 25 mg IM in the gluteal, and NaCl 0.9% IV 20 drops/min. After an hour of observation, the patient began stabilizing, and was then transferred to intensive care unit for further observation, before he was finally sent home two days later.

DISCUSSION

Of all five cases of anaphylaxis presented, four cases had occurred at home and one case had occurred in a hospital ward. In these case series, the triggers of anaphylaxis were food and drugs. In the literature, other triggers have been reported such as, latex,⁷ insect bite,^{8,9} physical activity,¹⁰ up to unknown causes or idiopathic.¹¹

Case 1 is an example of very severe case of anaphylaxis,^{12,13} involving several vital organs or organ systems such as the heart (shock, tachycardia), lungs (wheezing), brain (sopor), gastrointestinal tract (nausea, vomit) and the skin (pruritus, erythema). Gastrointestinal symptoms and loss of consciousness usually occur in very severe anaphylaxis.¹² Even though allergen or the drug was administered orally, the symptoms appeared very fast (2 minutes), and this is a sign of severe anaphylaxis. Pumphrey reported cases of anaphylaxis that died because of drugs whose symptoms were usually under 5 minutes.¹⁴ Of all the drugs that often cause anaphylaxis, beta-lactam (penicillin, ampicillin, amoxycillin) is the most frequent.¹⁵ Skin symptoms and signs (pruritus, erythema, urticaria, angioedema) are important symptoms and signs in diagnosis of anaphylaxis because 80-90% of cases of anaphylaxis are accompanied by skin symptoms.^{16,17} Consequently, the 2nd anaphylaxis consensus has concluded that clinical diagnosis of anaphylaxis (first criterion) is established when there are a skin symptoms (pruritus, erythema, urticaria, or edema of the lips, tongue, or uvula), accompanied with at least one of respiratory symptoms (breathing difficulties, stridor, wheezing, bronchospasm, hypoxemia) and decrease of blood pressure or related with organ dysfunction (hypotonia or collapse, fainting or incontinence). Rapid and extensive fluid administration is very important, considering that in severe anaphylactic shock about 35% of body fluid escape from the blood vessels in less than 10 minutes,¹⁸ making it urgent to improve fluid depletion. From therapeutic point of view, this case had received adequate treatment, beginning from the point of transporting patient to the nearest hospital to the accuracy of treatment, hence the patient was salvageable.

Case 2, however, was less complicated than the first case, though the patient had also experienced anaphylactic shock. Drowsiness and, consequently, sleep were possibly the sign of hypotension. The symptoms appeared much slower but the criteria of anaphylaxis had been fulfilled. This case is being presented to emphasize that anaphylactic symptoms may occur very slowly. This case of anaphylaxis needed one-day observation in order to anticipate biphasic reaction, which

is the reappearance of anaphylaxis symptoms 6-8 hours after the initial symptoms.^{19,20}

The third case emphasizes a few things regarding anaphylaxis. First, skin test to ceftriaxone does not have predictive value toward anaphylactic event,²¹ as proven in this example that even though the skin test result was negative, in reality the patient underwent severe anaphylaxis. It is an important point because frequently in daily practice, physicians usually perform skin test prior to administration of IV antibiotics. Only penicillin has reliable skin test result, albeit the use of specific antigen to penicillin, major and minor determinant antigen.²² Allergic reaction to certain drugs are determined by its metabolite, which for most drug is still unknown, including cephalosporine. Therefore, skin test usually performed in clinics and hospitals may actually be considered as provocative test, which means that that positive result suggest that the antibiotic should not be administered, and negative result may allow antibiotic administration but predictive value of anaphylactic reaction cannot be ascertained. Subsequently, the physician in charge must be vigilant of possible imminent anaphylactic reaction. Secondly, it was a severe case of anaphylaxis. The patient had lost consciousness, starting from delirium from initial symptoms to somnolence when blood pressure had reached 80/40 mmHg and back to *compos mentis* after blood pressure reached 120/70 mmHg although his heart rate was still at 120x/min. Four subcutaneous injection of epinephrine 0.3 mL within 10-15 minutes interval, infusion of dobutamine, and administration of Hemacell colloid to overcome his condition, after the previous load of lactate ringer failed to improve the patient's condition. The administration of subcutaneous injection of epinephrine must be noted because recent studies have shown that intramuscular administration in lateral femur produced more rapid and higher concentration in comparison to subcutaneous administration.²³ Thus, it is advised to administer epinephrine intramuscularly in cases of anaphylaxis.

The fourth and fifth cases had anaphylactic reaction with laryngeal edema associated with food allergy. Case 4 was anaphylactic reaction with repeated trigger and was late to be admitted to the hospital. Such a condition would result in delayed treatment including epinephrine administration and would be fatal. Peanut has been reported as trigger to anaphylaxis and is the most frequent cause of food allergy aside from seafood or especially shrimp.^{24,25} The report also stated that anaphylaxis with food as etiology is usually preceded with previous milder allergic reaction. Most fatal cases

of food anaphylactic reaction occur in younger age (<30 years) in comparison to insect bite (56 years) or drug (61 years).¹⁴ Death in anaphylactic reaction due to food is generally caused by obstruction of upper and lower respiratory tract, while it is due to anaphylaxis shock in drug.⁶ In contrast to case 4, even though the case was similar, patient in case 5 was immediately admitted to the hospital and received prompt treatment— injection of epinephrine and intravenous injection of high-dose corticosteroid—preventing fatal outcome. The patient was discharged in stable condition or restored health after two days of treatment. In both cases, none of the patients was given aggressive fluid replacement therapy because the patients did not undergo shock.

Other learnt lesson from all five cases was that many anaphylactic events occur at home. This presents a challenge for health or educational institution to inform the public through mass media or lectures regarding the danger of anaphylaxis in the community and the importance of prompt treatment. Because of its swift reaction course, the availability of ready-to-use epinephrine injection (EpiPen) is essential to patients who have had anaphylactic reaction. Education is not only for the patients and their family, but also important for health care workers, including doctors, to recognize early symptoms of anaphylactic reaction, and if possible to provide prompt and accurate treatment. The authority, in this case Badan Pengawasan Obat dan Makanan (National Agency of Drug and Food Control), should oblige food industry to put composition of substances contained in a processed food in the label. This is important so that patients with previous anaphylaxis who are allergic to certain substances can read and avoid the allergen or etiology of anaphylaxis.

CONCLUSION

It is important to re-emphasize that the main treatment for anaphylaxis is epinephrine or adrenaline not corticosteroids nor antihistamines. Corticosteroids and antihistamines, whose binding receptors are either H1—such as diphenhydramine—or H2—such as cimetidine or ranitidine—are only second line therapy in the management of anaphylaxis. Physicians should provide epinephrine in their practice—with careful watch on its expiry date. The sooner epinephrine is administered, the better the response, as suggested by the UK anaphylaxis resuscitation team.

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