

Rare Event of Anaphylaxis Reaction in a Rabies Post-Exposure Prophylaxis Vaccine: A Case Report

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ABSTRACT

Background. One of the most fatal infectious illnesses, rabies can result in severe symptoms in humans and almost 100% fatality if patients don't receive prompt and sufficient PEP (Post Exposure Prophylaxis). Despite the rarity of allergic responses following rabies immunization, vaccines that protect against infectious illnesses can cause anaphylaxis. Determine if the patient will respond quickly to therapy, pass away in a matter of minutes, or recover on their own as a result of endogenous adrenaline, angiotensin II, and endothelin I secretion. The care of children suffering from anaphylactic shock will be the main topic of this case report.

Case Presentation. A six-year-old male patient was admitted to emergency department with shortness of breath, swelling of the whole face and body, gasping for air, and cyanosis of lips, hands, and feet. Previously, the patient was bitten by a dog on the front and right side of his neck 90 minutes prior. He was sent to the community health care facility and administered PEP immediately. It was administered in two ampules without any direct adverse reactions were seen in the following 30-minute observation. Neither previous illnesses nor allergies were reported by his parents.

When the patient arrived in emergency room, cyanosis was evident, and he was agitated. Airway was secured using head tilt and chin lift. Oxygen saturation was 60%, thus was given 10 liters/minutes oxygen. He was then given an intramuscular injection of 1:1000 0.3 mg epinephrine and fluid challenge of 300 cc ringer's lactate solution. Upon reassessing, his

vitals sign was not getting better. He had cardiac arrest, resuscitated, but to no avail.

Conclusion. During the treatment of rabies, anaphylaxis reactions were inevitable. Post procedure monitoring and emergency management of anaphylaxis reactions must always be prepared to prevent a fatal adverse reaction. Adequate preparation for both equipment and medical personnel is necessary to produce a better outcome.

Keywords: Anaphylaxis, Rabies, Post-Exposure Prophylaxis, Vaccine, Children, Case Report

INTRODUCTION

Anaphylaxis is a potentially fatal clinical phenomenon that develops when substantial amounts of inflammatory mediators are quickly produced from mast cells and basophils following allergen exposure in a formerly sensitized patient. This can set off a series of symptoms in the body that can ultimately result in shock. Anaphylactoid responses are similar to anaphylaxis, however they are not caused by IgE antibodies. They can be caused by anaphylatoxins like C3a or C5a, or by nonimmune mast cell degranulating substances. Since some disorders have skin reactions and systemic manifestations that resemble anaphylactic symptoms, these must be taken into consideration while making the differential diagnosis.^[1]

When it affects children, anaphylaxis can be idiopathic or anaphylactoid. Possible causes of anaphylaxis in children may include

foods, drugs, insulin, venoms, or latex. Anaphylaxis was reported in 41% of instances in a retrospective evaluation of 601 medical records, with food being the primary cause in 22% of cases, drugs in 11% of cases, and exercise in 5% of cases. [2,3]

Due to their interest to animals, lack of safety understanding, and unwillingness to disclose bites or scratches, children are more likely to be bitten by animals. They tend to be smaller in size and more prone to getting bitten on the face, head, and hand, which shortens the time the rabies virus incubation time. [4]

Incubation for rabies normally lasts between one and three months initially. However, depending on variables including the point of virus entry point and viral load, this can range from a week to a year. Patients may develop prodromal symptoms after being infected, including fever, nausea, headaches, and giddiness, along with paresthesia at the wound area. [4]

If a patient doesn't receive prompt and sufficient PEP, rabies can result in severe symptoms in humans and 100% fatality. Immunoglobulins and modern rabies vaccines are essential tools for preventing rabies virus infection. Although mild systemic reactions were occasionally observed, there were very few serious adverse effects (AEs) that required stopping or altering the immunization. [5]

The majority of reported adverse effects following rabies vaccine immunization are local responses such as discomfort at the injection area, swelling, erythema, and induration. Local responses are more frequent after receiving the Human Diploid Cell Culture Rabies Vaccine (HDCV) (60% to 89.5%) as opposed to the Purified Chick Embryo Cell Vaccine (PCECV) (11% to 57%), according to the US Centers for Disease Control and Prevention. The majority of local responses were modest and went away on their own within a few days. In contrast to 0% to 31% in PCECV, systemic responses such fever, headaches, dizziness, and gastrointestinal problems

were reported by 6.8% to 55.6% of HDCV users. According to the Vaccine Adverse Event Reporting System (VAERS) in the United States, there were 30 adverse events per 100,000 doses of PCECV given, with 3 severe events occurring for every 100,000 doses delivered. [4]

CASE PRESENTATION

A six-year-old male, 30 kg, was admitted to emergency department with shortness of breath, swelling of the whole face and body, gasping for air, and cyanosis of the lips, hands, and feet.

The patient was bitten by a dog on the front and right side of his neck 90 minutes prior. He was sent to the public health center (Pusat Kesehatan Masyarakat/ Puskesmas) immediately. His wound was thoroughly cleaned and he was administered PEP. The rabies vaccine was administered in 2 ampules without any direct adverse reactions were seen in the following 30-minute observation. Neither previous illnesses nor allergy was reported by his parents.

When the patient arrived in the emergency department, he was agitated and cyanotic. Vital sign was not detected using bedside monitor. Airway was secured using head tilt and chin lift. The patient had shortness of breath and had oxygen saturation of 60%. He was given 10 liters/minutes of oxygen. It was then followed by an intramuscular injection of 1:1000 0.3 mg epinephrine. Intravenous access then established shortly after. He was also given 300 cc of ringer's lactate solution for fluid challenge.

His vitals sign was not getting better. Respiratory rate was decreased to 10 x/minute, then further decreased to 8 x/minute carotid artery pulse was increased to 136 x/minute. Suction product was serous. Respiratory rate was further decreased to 8 x/minute, carotid artery pulse was 40 x/minutes.

The patient had a seizure for a few seconds, then he was apneic and had no pulse. Seven cycles of cardiopulmonary resuscitation, suction, endotracheal intubation, and three

times epinephrine injection 0.3 mg IV were performed, but patient showed total bilateral mydriatic pupils and flatlined ECG, hence patient was declared dead.

DISCUSSION

Many different exposures, including those to foods, medications, insulin, venoms, and latex, can cause anaphylaxis in children.^[2] The identification of symptoms and signs that appear suddenly following exposure to a known trigger is the basis for the diagnosis of anaphylaxis. Due to problems with under-recognition and under-treatment, infants, adolescents, and pregnant

adolescents may be especially susceptible to anaphylactic events.^[1]

The purpose of administering anti-rabies vaccine (VAR) is to strengthen the immune system in the body against the rabies virus. It is hoped that antibodies is formed and will neutralize the rabies virus. However, if the rabies virus has reached the central nervous system, VAR will no longer provide any benefit.^[6]

The following flowchart illustrates how the administration of VAR and anti-rabies serum (SAR) must be taken into consideration.^[6]

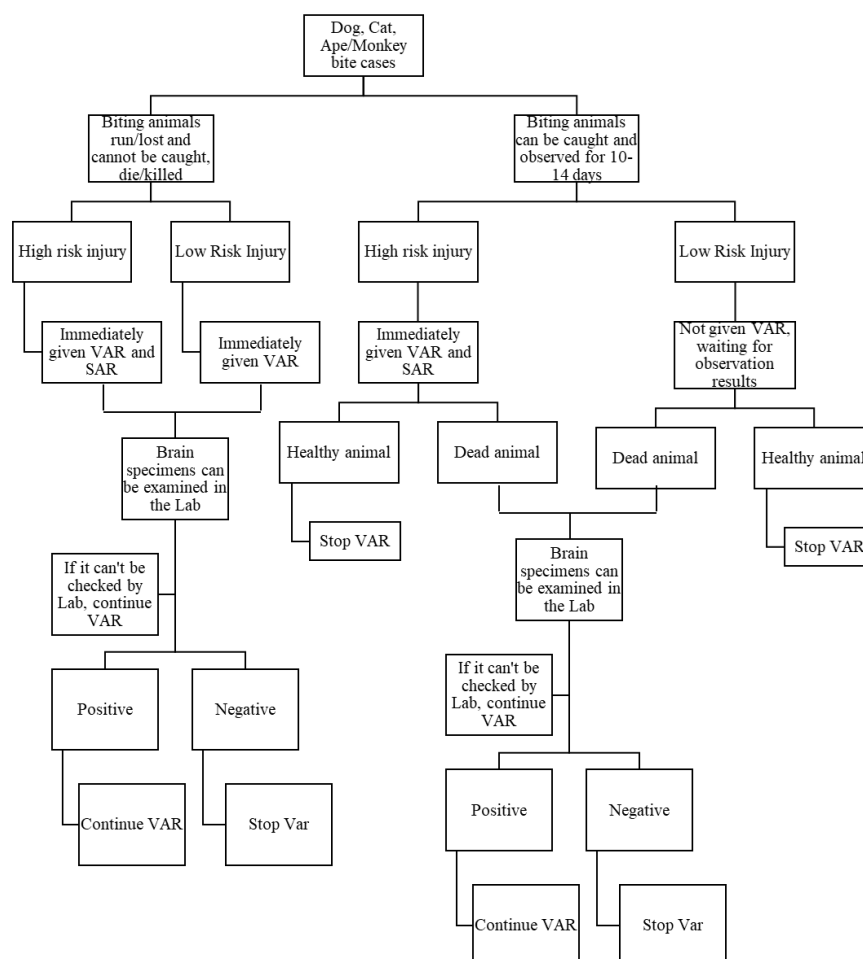


Figure 1. Management of Rabies Cases^[6]

High-risk wounds are licks/wounds on the mucosa, wounds above the shoulder area (neck, face, and head), wounds on fingers and toes, wounds in the genital area, wide/deep wounds, or multiple wounds. Low-risk injury is licks on open

skin or scratches/bites that cause blisters (excoriations) on the body, hands, and feet.^[6]

In this patient, the dog is capturable and in good health. So, we access patients in accordance with the WHO-defined category

of contact. In this case, the patient was scratched (5-10 mm) on the front and the right side of his neck without any bleeding. His parents sent him to the Labuan Bajo

Health Center. His level of exposure was classified as category III exposure according to World Health Organization Recommendation.

Table 1. Categorization of Exposure and Post-Exposure Prophylaxis (PEP)^[7]

Category	Categories of Exposure with Possible Animal	Post-Exposure Prophylaxis (PEP)
I	Animal licks on intact skin	Washing of contact skin areas, without PEP
II	Small bites of uncovered skin, minor scratches or bruises with no bleeding	Wound washing and administration of VAR
III	One or more transdermal bites or scratches, involving mucous membrane or animal licks on broken skin, direct contact with bats	Wound washing, administration of VAR and SAR

According to WHO, category III wounds must be cleaned, immediately immunized, and given rabies immunoglobulin. However, in this case, only an anti-rabies vaccination (VAR) was administered as rabies immunoglobulin (SAR) was not available at that moment.

According to Hay et al, when one of the three following conditions is met, anaphylaxis is most likely to occur:^[1]

1. Acute onset of illness that affects skin, mucosal tissue, or both; along with breathing difficulty or low blood pressure or symptoms of end-organ malfunction
2. Patient is exposed to a potential allergen and shows two or more of the following symptoms:
3. Two or more of the following that occurs rapidly after exposure to a likely allergen for that patient:
 - a. Affect skin-mucosal tissue
 - b. Breathing difficulty
 - c. Low blood pressure or associated symptoms such as hypotonia/collapse, syncope, incontinence)
 - d. Persistent gastrointestinal symptoms
4. Patient is exposed to a known allergen and have low blood pressure after exposure. The cut off is systolic blood pressure drop of at least 30% according to age.

This patient's condition manifested acutely within 90 minutes, including the skin and mucosal tissue and ultimately in widespread facial and body edema. The patient also has respiratory problems such as dyspnea and hypoxemia. Complaints were also

accompanied by a decrease in blood pressure as evidenced by not detecting the patient's blood pressure, thus confirming the diagnosis of anaphylaxis shock.

Based on the emergency treatment of anaphylaxis guideline, when clinical symptoms of an allergic reaction and typical signs of anaphylaxis have been found, airway should be established, high flow oxygen should be administered, monitoring of oxygen saturation with pulse oximetry, ECG, and blood pressure should be done. A maximum dose of 0.3 mg (0.3 mL) of intramuscularly administered adrenaline/epinephrine 1:1000, in the mid- anterolateral thigh, may be administered if no clinical improvement is observed after 5 minutes. Intravenous fluid challenge using crystalloid solution should also be initiated with a dose of 10 mL/kgBodyWeight. If shock persists after two injections of epinephrine IM, follow refractory anaphylaxis protocol. Should cardiac arrest occurs, follow advanced life support protocol.^[8]

Upon arrival in the emergency department, this patient's airway was secured using head tilt and chin lift. He was then 10 liters/minute of oxygen and 1:1000 0.3 mg IM epinephrine injection. He was also given 300 cc of ringer's solution. His condition deteriorated quickly; he had cardiac arrest. Seven cycles of cardiopulmonary resuscitation, suction, endotracheal intubation, and three times epinephrine injection 0.3 mg was done, but patient showed total bilateral mydriatic pupils and

flatlined ECG, hence patient was declared dead.

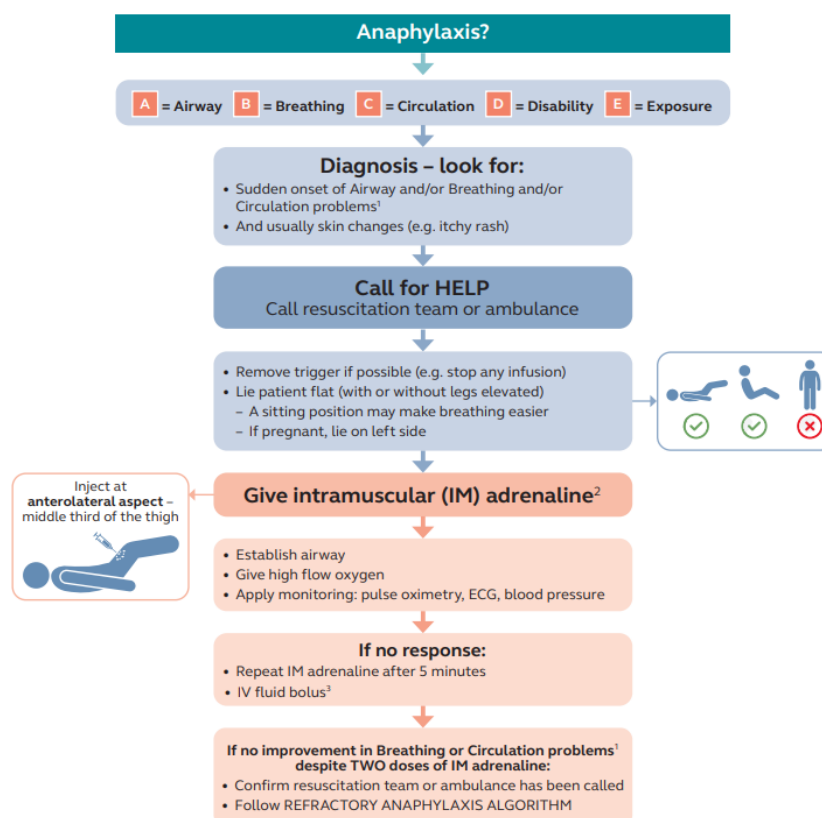


Figure 2. Treatment Guideline for Anaphylactic Shock⁸

CONCLUSION

Anaphylaxis is a potentially fatal clinical condition that develops when substantial amounts of inflammatory mediators are quickly released by mast cells and basophils following allergen exposure in a previously sensitized individual. Many different exposures, including meals, drugs, insulin, venom, and latex, can cause anaphylaxis in children. By far, food is the most frequent trigger. Anaphylaxis is diagnosed when symptoms and indications appear abruptly (a few minutes to a few hours) following exposure to a known or suspected cause.

Due to their interest to animals, lack of safety understanding, and unwillingness to disclose bites or scratches, children are more likely to be bitten by animals. If a patient doesn't receive prompt and sufficient PEP, rabies can result in severe symptoms in humans and 100% fatality. Immunoglobins and modern rabies vaccines are essential tools for preventing rabies virus infection. Although mild systemic

reactions were occasionally observed, there were very few serious adverse effects (AEs) that required stopping or altering the immunization.

During the treatment of rabies, sometimes anaphylaxis reactions were inevitable. Post procedure monitoring and emergency management of anaphylaxis reactions must always be prepared to prevent a fatal adverse reaction. Adequate preparation for both equipment and medical personnel is necessary to produce a better outcome.

Declaration by Authors

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