Alpha-Gal: A Delayed Onset of Anaphylaxis and Uncovering the Cause

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CE Earn Up to 5.5 Hours. See page 591.

Contribution to Emergency Nursing Practice

- The current literature on alpha-gal delayed anaphylaxis indicates that it is increasing in incidence.
- This article contributes key factors and assessment findings relevant to delayed anaphylaxis.
- Key implications for emergency nursing practice found in this article include the importance of nurses' eliciting histories of tick bites and patients' dietary intake within the last 6 hours before presentation to emergency departments.

A 67-year-old man was driving his car down the expressway when he noticed that his hands were swollen, red, and extremely itchy. The patient was having difficulty breathing, swallowing, and talking, and his tongue was swollen. He pulled over at a rest stop, got out of his car, found 2 men working at the rest stop building, and asked for help. The patient was experiencing extreme itching and shaking. The 2 men sat him in a chair and called 911. The patient appeared to be very confused, and, as the paramedics arrived, the patient had a sudden loss of consciousness. The paramedics assessed airway, breathing, and circulation. The patient's blood pressure was 88/50, apical pulse was 150 per minute, and respirations were 32 per minute. The paramedics suspected acute anaphylaxis and started an intravenous line. Diphenhydramine, methylprednisolone, epinephrine, and 1 liter of normal saline were administered by paramedics. His oxygen saturation was 86%, and he was given oxygen at a rate of 4 liters per minute, which improved his oxygen saturation to 98%. The patient was immediately transferred to the emergency department. On the way to the hospital, he continued to drift in and out of consciousness and appeared very confused; his blood pressure was 76/40, apical pulse 148 per minute, and respirations 32 per minute. Upon arrival at the emergency department, the patient's condition remained critical, and he was confused and struggling to breathe. His blood pressure was 80/42 mm Hg, apical pulse 140 per minute and regular, temperature 37.3°C (99.2F) orally, respirations 30/minute and labored, and body mass index was 22.5 kg/m^2. The emergency nurse and physician suspected acute anaphylaxis and anaphylactic shock. He was immediately placed on a cardiac monitor and continuous oxygen at 4 liters per minute. His oxygen saturation on 4 liters per minute via nasal cannula was 98%. He was treated aggressively in the emergency department for anaphylactic shock with fluids, epinephrine, diphenhydramine, methylprednisolone, and albuterol nebulizers. Over the course of 2 hours, the patient was stabilized with supportive care, and his blood pressure rose to 110/84, apical pulse 96 per minute, and respirations at 22 per minute. The patient was then transferred to the intensive care unit (ICU) for further monitoring and care. The ICU nurse and physician continued supportive care. The ICU nurse talked at length with the patient about the events that preceded his symptoms. The nurse started to suspect the patient might have had an alpha-1,3-galactose (alpha-gal) reaction, and blood work was ordered.

The patient's past medical history provided valuable information leading to his diagnosis and included multiple tick bites, ehrlichiosis, and Rocky Mountain spotted fever. He had no past surgical history. He was unaware of any food allergies. The patient reported that he was a vegetarian since the age of 20; although he consumed milk and egg products, he did not consume mammalian or nonmammalian meat.

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The patient also reported that he did not smoke or consume illegal drugs and typically drank a glass of wine twice each week. He ran, rock climbed, and hiked regularly. A review of the patient's systems showed shortness of breath, difficulty breathing, wheezing, generalized hives, tachycardia, dizziness, syncope, abdominal pain, nausea, and vomiting. No fever, chills, sore throat, chest pain, or diarrhea were reported. On examination, the patient was able to follow the conversation; answer questions; and was oriented to person, place, and time. His speech was clear and comprehension intact, as was his memory for recent and remote events. His visual fields were intact to direct confrontation. Funduscopic examination demonstrated no evidence of hemorrhage, and disc margins were sharp and clear. He had no jugular vein distention or carotid bruits. His cardiovascular examination revealed his heart rate was tachycardic, with a regular rhythm. His heart sounds were normal without gallop, friction rub, or murmur, and he had intact distal dorsalis pedis and posterior tibial pulses, bilaterally. His breath sounds were equal bilaterally, with no rales or rhonchi. However, he did have faint expiratory wheezes throughout. His abdomen was soft and nontender, with normoactive bowel sounds in all 4 quadrants, with no hepatosplenomegaly.

Anaphylaxis is an acute medical emergency that is potentially fatal.[2] A recent study conducted in the United States reported the cumulative prevalence of 5.1% if the criterion for a diagnosis of anaphylaxis was involvement of 2 or more systems, together with respiratory or cardiovascular involvement.[3] Recently, a novel immunoglobulin E (IgE) antibody response was found between the oligosaccharide galactose-alpha-1,3-galactose (alpha-gal) and a mammalian oligosaccharide epitope (mammalian meat protein) and has been found to have been responsible for acute and delayed anaphylaxis.[4-6] Immediate anaphylaxis was first noted with intravenous cetuximab.[4] Cetuximab has been approved to treat colorectal cancer that has metastasized and squamous cell carcinoma of the head and neck that is local or advanced or recurrent or metastatic.[1] Delayed anaphylaxis was first documented 3 to 6 hours after ingestion of mammalian meat protein.[4] More recently, a link has been found between alpha-gal and mammalian antivenom used to treat snake bites.[7] There has been evidence that tick bites are the cause of antibody response to alpha-gal.[4]

The signs and symptoms of acute anaphylaxis versus delayed anaphylaxis are similar. A careful review of the patient's past medical history and a medication and dietary history can give the nurse and physician clues as to the underlying mechanism of the resultant anaphylaxis. Typical anaphylaxis is characterized by immediate reaction. In contrast, anaphylaxis to mammalian meat is characterized by a delayed reaction that can occur from 2 to 5 hours after consumption. However, the reaction is no less serious or life threatening than typical anaphylaxis.[4]

The signs and symptoms of acute anaphylaxis are also no different from delayed anaphylaxis to mammalian meat except in the timing. Symptoms can include intensive generalized itching and flushing of the skin, hives anywhere on the body, a sense of impending doom, swelling of the throat and mouth, difficulty swallowing or speaking, tachycardia, wheezing, abdominal pain, nausea and vomiting, sudden weakness, hypotension, collapse, and unconsciousness.[1]

Anaphylaxis can be defined as a multisystem allergic reaction that can include shock and airway compromise.[2] Onset of anaphylaxis to stings or allergen injections is usually rapid: 70% begin in less than 20 minutes and 90% in less than 40 minutes.[3] Food anaphylaxis may or may not have a slower onset or slow progression. Rapid onset is associated with greater severity. Acute or delayed anaphylaxis both involve multiple systems and many times manifest as hypotension, shock, and airway compromise.[3,8-12] Patients will often have gastrointestinal symptoms, including nausea and vomiting, when they are having allergic reactions to food.

Secondary to his age and loss of consciousness, initial emergency department laboratory tests for this patient included a troponin level, complete blood count with differential, comprehensive metabolic panel, and urinalysis. A 12-lead electrocardiogram (ECG) and a chest x-ray were completed. The patient was stabilized and transferred to the ICU for continued monitoring of his cardiac and respiratory status to rule out myocardial infarction and conduct sequential troponin levels, 12-lead ECGs, and cardiology consultation. All results of laboratory tests, ECGs, and x-ray were within normal limits. A cardiologist was consulted, and myocardial infarction was ruled out.

There was a high suspicion of an alpha-gal delayed anaphylaxis reaction secondary to the patient's past medical history of tick bites and contracting ehrlichiosis and Rocky Mountain spotted fever. The following day, his tests for allergy to mammalian meat, including his alpha-gal IgE, were 13.80 KU/L (range ≤0.35), beef was 9.69 KU/L (range ≤0.35), mutton 4.79 KU/L (range ≤0.35), and pork 7.10 KU/L (range ≤0.35). The patient recalled eating breakfast that morning at a restaurant. He ordered eggs, and, as he began eating, he noticed sausage in them, at which point he stopped eating. His episode of anaphylaxis occurred 3 hours after the accidental ingestion of mammalian meat. His history of a tick bite, accidental ingestion of mammalian meat, and delayed anaphylaxis with high levels of alpha-gal, beef, pork, and mutton led to his diagnosis of alpha-gal. The patient had an uneventful stay in the ICU and was discharged home 2 days later.

The important takeaway is that acute anaphylaxis and delayed anaphylaxis are not always apparent on presentation. Nurses can conduct careful reviews of patients' past medical histories including tick-borne illnesses, medications, and dietary intake in the previous 6 hours. Emergency nurses are well trained to treat and manage acute anaphylaxis. However, delayed anaphylaxis to mammalian meat is a fairly new diagnosis, and emergency nurses are in unique positions to make the differentiation of acute versus delayed anaphylaxis. The majority of patients who present to emergency departments with anaphylaxis are discharged after observation with a diagnosis of idiopathic anaphylaxis but are never aware of its cause. In this patient, the history of tick bites with resultant ehrlichiosis and Rocky Mountain spotted fever, and the accidental ingestion of sausage, provided cues to his diagnosis. The patient is under the care of an allergist and carries diphenhydramine and an epinephrine pen with him wherever he goes.

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