

# CASE CONFERENCE

## A CASE OF UNRECOGNIZED PREHOSPITAL ANAPHYLACTIC SHOCK

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### ABSTRACT

A case of prehospital anaphylactic shock that presented atypically, without a known exposure, is discussed. Anaphylaxis is a potentially life-threatening allergic reaction that requires prompt recognition and aggressive treatment. While there is little diagnostic dilemma in the recognition and management of "classic" presentations of anaphylaxis there is likely a need for further education of prehospital providers, as well as emergency physicians, on how to recognize atypical cases of anaphylaxis. These cases can be equally severe, with potentially fatal consequences if missed. The diagnosis and management of anaphylaxis are reviewed, as well as barriers that providers encounter in diagnosing uncommon presentations. **Key words:** anaphylaxis; emergency medical services; shock; epinephrine; prehospital

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### INTRODUCTION

Anaphylaxis is a potentially life-threatening, systemic, allergic reaction that requires both immediate recognition and aggressive treatment. The exact incidence and prevalence of anaphylaxis are difficult to determine because of the lack of recognition as well as the lack of uniformity in diagnostic criteria. However, some studies report a frequency ranging from 30 to 2,000 episodes per 100,000 persons, with a prevalence as high as 2%.<sup>1,2</sup> In a review of prehospital anaphylaxis by Kane and Cone, multiple state emergency medical

services (EMS) databases were queried regarding the proportion of EMS calls that involved allergic reactions or anaphylaxis. The authors concluded that approximately 0.4%–0.9% of all EMS runs are for an allergic reaction or anaphylaxis.<sup>3</sup> Death from anaphylaxis is fortunately an uncommon event, with one paper citing 150–200 deaths per year from food anaphylaxis alone, while two other studies reported death occurring in 0.65%–2% of patients who experience anaphylaxis, but reliable mortality data are challenging to quantify for the aforementioned reasons.<sup>4–6</sup>

Clinicians face several challenges when dealing with anaphylaxis. First, there is no universally accepted standard set of diagnostic criteria to define anaphylaxis, and no criteria have been prospectively validated. However, there are some working definitions used to aid in diagnosing anaphylaxis. The Canadian Pediatric Surveillance Program defines *anaphylaxis* as "a severe allergic reaction to any stimulus, having sudden onset and generally lasting less than 24 hours, involving one or more body systems and producing one or more symptoms such as hives, flushing, itching, angioedema, stridor, wheezing, shortness of breath, vomiting, diarrhea or shock."<sup>7</sup> The National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network developed the criteria shown in Table 1.<sup>8</sup> A second challenge is that anaphylaxis may present with varied and atypical features, which makes it easy for health care providers to overlook. In addition, it may also present without an exposure to a "classic" offending agent such as a bee sting or medication, and many times the patient will not have a known exposure to any substance, which further confuses the clinical picture. Lastly, there are no clinically useful laboratory markers or tests that can be used in the emergency setting to either rule in or rule out the diagnosis. Therefore, it is no surprise that anaphylaxis has been shown to be both underrecognized and undertreated by medical personnel.<sup>1,9–12</sup> We present a case of severe anaphylaxis that was not recognized in the field and discuss some issues related to making this difficult diagnosis.

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TABLE 1. Clinical Criteria for Diagnosing Anaphylaxis

*Anaphylaxis is highly likely when any one of the following three criteria is fulfilled:*

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (e.g., hives; pruritus; flushing; swollen lips, tongue, uvula)
- And at least **one** of the following
- a. Respiratory compromise (e.g., dyspnea, wheezing or bronchospasm, stridor, reduced peak flows, hypoxia)
  - b. Reduced blood pressure or associated symptoms of end-organ dysfunction (e.g., syncope, incontinence)
2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours):
    - a. Involvement of the skin or mucosal tissue (e.g., hives; itching; flushing; swollen lips; tongue; uvula)
    - b. Respiratory compromise
    - c. Reduced blood pressure or associated symptoms
    - d. Persistent gastrointestinal symptoms (e.g., crampy abdominal pain, vomiting)
  3. Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours):
    - a. Infants and children: low systolic blood pressure (dependent on age) or greater than 30% decrease in systolic blood pressure
    - b. Adults: systolic blood pressure of less than 90 mmHg or greater than 30% decrease from that person's baseline

Adapted from: Sampson HA, Munoz-Furlong A, Campbell RL, 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. *Ann Emerg Med.* 2006;47:373-80.

## CASE REPORT

### Prehospital Course

At 0908 hours, a 9-1-1 call was placed from the county jail requesting an ambulance for a "sick" inmate. An advanced life support (ALS) unit was dispatched, responded with red lights and siren, arrived at the jail in 6 minutes, and reported patient contact at 0919 hours. Upon arrival, EMS personnel found a 37-year-old white man seated in a chair in the county jail in the care of a nurse. The EMS personnel reported the patient to be very pale, diaphoretic, and complaining that he was unable to see anything. The nurse caring for the patient stated that she had witnessed an episode of unresponsiveness prior to EMS arrival that lasted approximately 40 seconds, during which time the patient's breathing appeared shallow and labored.

On initial assessment, the patient complained of diffuse abdominal pain as well as nausea and vomiting. The paramedic noted that it was difficult to get a complete history because of the patient's altered mental status. Past medical history was supplied by jail staff, who stated that the patient took lisinopril and hydrochlorothiazide (HCTZ) daily for high blood pressure. The patient was noted to be in handcuffs, had his feet shackled, and was wearing a full-body jumpsuit. Physical assessment revealed a systolic blood pressure of 80 mmHg, with weak radial pulses. The medic recorded that the airway was patent, lung sounds were present and clear bilaterally, there were normal heart sounds, and there was diffuse abdominal tenderness to palpation.

The crew began to administer oxygen to the patient by non-rebreather mask, inserted a 20-gauge peripheral intravenous (IV) needle, and began to administer lactated Ringer's solution at a wide-open rate. The patient was placed in a supine position and was moved to the cot, where the crew obtained a blood glucose level of 137 mg/dL. The patient was transferred to the ambulance and electrocardiography (ECG) was performed, which showed a normal sinus rhythm, and

EMS reported they could not obtain a pulse oximeter reading. After a 20-minute scene time (including extrication from the jail), the patient was transported nonemergently to the emergency department (ED). En route, despite repeated attempts, further blood pressure readings were unobtainable. However, EMS noted that the patient's color had improved with recumbency and receipt of oxygen and IV fluids (200 mL). Further history obtained during transport revealed that the patient was also experiencing some shortness of breath and had one episode of bowel incontinence en route to the hospital.

### Emergency Department Course

On arrival to the ED, the patient was noted by emergency physicians (EPs) to be cool, pale, and diaphoretic with mild cyanosis in the extremities and lips. The patient had no palpable radial pulses on the ambulance cot and was immediately placed in an ED bed. Police were asked to remove the patient's handcuffs and shackles and nursing staff completely disrobed the patient as he was still in his long-sleeved orange jumpsuit. Upon removal of the prison garments, it was apparent the patient had diffuse hives on his chest, back, and legs. The patient also had loose, nonbloody stool in his jumpsuit.

The ED staff were unable to record a blood pressure; they reported a heart rate of 125 beats/min, a respiratory rate of 24 breaths/min, and an oxygen saturation of 95% on high-flow oxygen. The patient was afebrile. Because of the hives, signs of hypoperfusion, and the inability to obtain a blood pressure, the patient was thought to be suffering from anaphylactic shock and was treated aggressively with epinephrine and IV fluids. In the ED the patient required seven doses of intramuscular (IM) epinephrine (each dose at 0.3 mg of 1:1,000 concentration), 125 mg of IV methylprednisolone, 50 mg of IV diphenhydramine, and 50 mg of IV ranitidine, as well as 5 liters of IV crystalloid (normal saline) through an 8-Fr introducer sheath in the

femoral vein. Initial blood work revealed a severe lactic acidosis, with a measured lactate level of 7.7 mmol/L, and acute renal failure.

The patient rapidly responded to epinephrine and IV fluids. His mental status completely cleared, tissue perfusion improved, and blood pressures were measured in the normal range, followed by resolution of the shortness of breath and hives. He continued to complain of diarrhea and abdominal cramping, so an abdominal computed tomography (CT) scan with IV contrast was performed and revealed evidence of "shock bowel" including diffuse bowel wall edema. The patient's ECG results and cardiac biomarkers were all within normal limits as well. A repeat lactic acid measurement (3.4 mmol/L) showed considerable improvement after resuscitation.

### Hospital Course

The patient was admitted to the intensive care unit with a diagnosis of anaphylactic shock. During the inpatient stay, further history revealed that the patient had taken a dose of ibuprofen the night prior to the event and noted that he had not taken his lisinopril in two days. After eating breakfast the next morning, he stated that he had developed severe abdominal cramping, nausea, and vomiting, and then became dizzy and noted tingling and numbness in his extremities, at which time 9-1-1 was called.

The patient was discharged after a three-day hospital stay with complete resolution of symptoms. It was ultimately thought that the anaphylactic shock was caused by an unknown agent, but the patient was advised to avoid angiotensin-converting enzyme (ACE) inhibitors, angiotensin-receptor blockers, and all nonsteroidal anti-inflammatory drugs (NSAIDs) for the remainder of his life. He was discharged with an epinephrine auto-injector (EpiPen, Mylan Inc., Canonsburg, PA) and told to keep it with him at all times.

### DISCUSSION

This case demonstrates how easily anaphylaxis and even anaphylactic shock can be missed. Several barriers may have contributed to the EMS crew's not recognizing anaphylaxis in this case, including the following: 1) lack of a "classic" presentation; 2) lack of a history of exposure to a specific allergen (and inability to obtain an optimal history because of the shock state); and 3) lack of visible signs of anaphylaxis (though signs of hypoperfusion were present).

This patient presented with symptoms mainly reflecting hypoperfusion and gastrointestinal (GI) system involvement, including abdominal pain, nausea, vomiting, and stool incontinence. This presentation may be contrary to what many health care

providers view as "classic" anaphylaxis, which frequently presents with one or more of the following: urticaria, pruritus, angioedema, and wheezing.<sup>8,13</sup> However, in a 2004 study of 1,149 patients presenting to an ED with allergic reactions, Brown noted that the presence of GI complaints was a marker for severity. Specifically, he found incontinence, along with confusion, and syncope to be strongly associated with hypotension and hypoxia; subsequently, those findings were used to define patients with severe allergic reactions. Nausea, vomiting, abdominal pain, wheezing, presyncope, chest/throat tightness, and stridor were used to define moderate reactions.<sup>14</sup> It is also worthwhile to note that GI findings are present in 25%–40% of patients experiencing anaphylaxis.<sup>13,15</sup> Upon review of this case, it is evident that the patient exhibited all of the signs of severe anaphylaxis and at least three findings that correspond to moderate reactions according to the clinical severity grading system developed by Brown.<sup>14</sup> Notably, dyspnea, wheezing, and upper airway angioedema can be absent in up to 45% of patients, making it even more difficult to diagnose.<sup>13</sup> Brown also reported a peculiar lack of the typical cutaneous findings as a marker of severity. Only 73% of patients experienced generalized hives, with even fewer demonstrating angioedema and/or itching.<sup>14</sup> However, similar studies have also noted that up to 20% of patients experiencing anaphylaxis may not have any cutaneous findings.<sup>8</sup> This seems contrary to the traditional view of anaphylaxis and may have made the diagnosis seem less likely to the EMS providers taking care of this patient.

This patient did not have an obvious trigger for anaphylaxis. The jail staff stated that the patient was taking lisinopril and HCTZ, though the patient denied having taken any lisinopril for two days. This may have misled the crew. The remainder of a more detailed exposure history was not obtained until the patient was resuscitated and interviewed by inpatient physicians who discovered the use of ibuprofen as well. The inpatient team was also able to gather a more thorough history regarding the timing of the event. Apparently, this occurred shortly after eating breakfast. It is impossible to know how the EMS crew would have used the further history if it had been available on scene or if it would have led EMS toward the diagnosis of anaphylaxis. Unfortunately, many patients will not have an inciting agent identified as a cause of their anaphylactic reaction. Emergency medical services are likely called for the sickest patients, and it is most difficult to get an adequate, much less optimal, history on these patients because of altered mental status, shock, respiratory distress, and other such conditions. Without a known history of exposure, many providers may be hesitant to aggressively treat anaphylaxis, particularly if they are unsure of the diagnosis. In the Brown study, 25% of anaphylaxis patients had no

TABLE 2. Summary of Medications Used in the Management of Anaphylaxis

Medication	Route	Dose (Adult)	Dose (Pediatric)	Frequency
Epinephrine (1:1,000)	IM	0.3–0.5 mg	0.01 mg/kg (max 0.5 mg)	q 5–20 minutes
Epinephrine (1:10,000)	IV	1–10 $\mu$ g/min infusion or slow push 0.1–0.5 mg	0.1–1 $\mu$ g/kg/min infusion or slow push 0.01 mg/kg (max 0.5 mg)	Titrated infusion or q 5–20 minutes
Diphenhydramine	IV/IM/PO	25–50 mg	1 mg/kg (max 50 mg)	q 4–6 hours
Ranitidine	IV/PO	50 mg	1 mg/kg IV/PO (max 50 mg)	q 6–8 hours
or				
Famotidine	IV/PO	20–40 mg	0.25 mg/kg IV (max 20 mg)*	q 12 hours
Crystalloid (NS or LR)	IV	1–2 L initially	20 mL/kg (initially)	As necessary
Steroids (methylprednisolone or prednisone)	IV/PO	125 mg IV (methylprednisolone) or 60 mg PO (prednisone)	1–2 mg/kg IV	q 6 hours or q 24 hours
Glucagon	IV/IM	5–15 $\mu$ g/min infusion or 1–2 mg IV slow push or 1–2 mg IM	5–15 $\mu$ g/min infusion or 20–30 $\mu$ g/kg IV slow push	Titrated infusion or q 5 minutes

\*No data on patients <1 years old.

IM = intramuscularly; IV = intravenously; LR = lactated Ringer's (solution); max = maximum; NS = normal saline; PO = orally; q = every.

identifiable cause for their reactions.<sup>14</sup> Two other reviews of patients who suffered from anaphylaxis also reported unexpectedly high rates of "idiopathic" anaphylaxis. Kemp et al. reviewed 266 anaphylaxis cases and found that 37% of patients had no known cause for their reaction.<sup>16</sup> Webb and Lieberman reviewed 601 anaphylaxis cases and discovered that an impressive 59% had "idiopathic" causes.<sup>17</sup>

The crew did not note any visible signs of anaphylaxis on the patient, particularly urticarial lesions (hives). The patient was incarcerated and was restrained in handcuffs, leg shackles, and a long-sleeved, full-length prison jumpsuit. This made exposure of the patient (i.e., lifting up the patient's shirt to look at the torso) more challenging. This step in assessment was omitted by the prehospital providers, which potentially caused the crew to miss a useful piece of evidence, in this case, hives. Performing this additional maneuver might have led them to the correct diagnosis and allowed the appropriate treatment to have been initiated in the out-of-hospital setting. This is a tremendous lesson in the importance of gaining adequate exposure to ill-appearing patients, especially if there is no obvious identifiable cause for their illness. As stated above, though, the absence of hives cannot be used to rule out anaphylaxis.

Immediate management of anaphylaxis, as in all resuscitations, begins with addressing the adequacy of airway, breathing, and circulation. Simple maneuvers that all clinicians, including basic life support (BLS) providers, can do are to place the patient in the recumbent position, which has been shown to improve outcomes, as well as to begin administration of high-flow oxygen.<sup>18,19</sup> However, the mainstay of treatment for anaphylaxis is administration of epinephrine. While there have been no prospective, randomized trials per-

formed on emergency patients who present with anaphylaxis in order to evaluate various dosing regimens or various routes of administration of epinephrine, it appears the optimal route for first-line treatment with epinephrine is IM (particularly, in the lateral thigh). These recommendations were based on studies done on both pediatric and adult subjects who had a history of anaphylaxis, were given epinephrine either subcutaneously (SC) or IM, and had plasma epinephrine levels measured. These studies revealed that there were higher concentrations of epinephrine present, as well as a faster onset of peak concentrations, when epinephrine was given via the IM route in the lateral thigh.<sup>20,21</sup> The typical adult dose of epinephrine is 0.3–0.5 mg of the 1:1,000 concentration administered IM and 0.01 mg/kg (maximum of 0.5 mg) for pediatric patients. This dose can be repeated as needed every 5–20 minutes depending on patient response. Intravenous epinephrine can also be given for patients in profound shock, either as a first-line therapy or when IM therapy has failed. Intravenous epinephrine should be given, using the 1:10,000 concentration, at doses of 1–10  $\mu$ g/min as an infusion titrated to effect or slow IV push of 0.1–0.5 mg (0.01 mg/kg pediatric dose) of the 1:10,000 solution, for those who have refractory anaphylaxis or those who have inadequate response to IM therapy.<sup>8,10,22–26</sup> Paramedics whose scope of practice includes IV epinephrine for anaphylaxis need extensive education about indications and contraindications as well as specific discussion of different concentrations available for use.<sup>27</sup>

Second-line therapies for anaphylaxis (after epinephrine administration) include administration of large volumes of IV crystalloid; H<sub>1</sub> and H<sub>2</sub> (histamine) receptor antagonists, which when given together (parenterally) have been shown to reduce

urticaria in acute allergic reactions<sup>28,29</sup>; and corticosteroids at doses of 125 mg of IV methylprednisolone or 60 mg of oral prednisone, which ideally help to prevent any prolonged reaction and/or recurrence in the immediate postresuscitation period. Steroids are crucial, in an albeit imperfect attempt, in preventing the classic “biphasic” reanaphylaxis that can occur after initial therapy, sometimes up to 24 hours later.<sup>30</sup> Glucagon has also been shown to be potentially useful, when given as an IV infusion at a dose of 5–15  $\mu\text{g}/\text{min}$  or 1–2 mg slow IV push, for patients with refractory anaphylaxis, especially for those patients who are taking beta-blockers and/or ACE inhibitors. Glucagon has inotropic and chronotropic effects that are independent of the beta-receptors and also stimulates endogenous catecholamine release.<sup>13,22,31</sup>

Ultimately, the patient in our case report received multiple doses of IM epinephrine, along with IV steroids, H<sub>1</sub> and H<sub>2</sub> receptor antagonists, and large volumes of crystalloid IV solutions, upon arrival to the ED.<sup>8,13,24</sup> Without the classic finding of urticaria, discovered on disrobing the patient, it is unclear how rapidly the EPs would have diagnosed anaphylaxis and initiated specific treatment.

## CONCLUSION

This case demonstrates the many challenges that health care providers face in diagnosing anaphylaxis that presents atypically. There is little diagnostic dilemma when a patient presents after an obvious exposure to an allergen, and then suddenly develops hives, angioedema, pruritus, throat tightness, and wheezing. However, the real challenge is the rapid identification and initiation of aggressive therapy for patients who have atypical presentations of anaphylaxis. While the findings may be atypical, the condition itself is no less potentially life-threatening.

This case also underscores the need for EMS educators and medical directors to assess the educational level of their EMS providers so they can address any potential knowledge gaps in the recognition of anaphylaxis, particularly with regard to atypical presentations. For example, it is likely that many EMS providers, as well as physicians, are unaware that GI signs and symptoms such as nausea, vomiting, abdominal pain, diarrhea, and incontinence have been reported to be associated with moderate to severe anaphylactic reactions.<sup>14</sup>

The fact that the patient did not have any visible cutaneous signs of allergic reaction during assessment by EMS, had no readily identifiable exposure to a typical allergen, had altered mental status, and had a preponderance of GI symptoms made this diagnosis difficult in the prehospital setting. Patients suffering from anaphylaxis may not present with what many providers believe to be “typical” or common findings. Health

care providers should always consider anaphylaxis in the differential diagnosis for patients presenting with sudden onset of GI symptoms accompanied by unexplained shock with or without obvious cutaneous findings.

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