Grade IV anaphylaxis resistant to epinephrine in a healthy child presenting for elective scalp lesion removal under general anesthesia

Michael Yim[1] MD, MPH and John Liu[2] MD
[1]*University of California, Davis Medical Center Department of Anesthesiology and Pain Medicine*
[2]*Shriners Hospitals for Children-Northern California Department of Anesthesiology*

Introduction

Anaphylaxis is a life-threatening IgE mediated reaction that requires prompt diagnosis and treatment and is characterized by severity classification from I (cutaneous-mucous signs such as erythema/urticaria with or without angioedema) to IV (cardiac arrest) (1). Though rare, medications that can cause anaphylaxis include neuromuscular blocking agents and antibiotics(2).

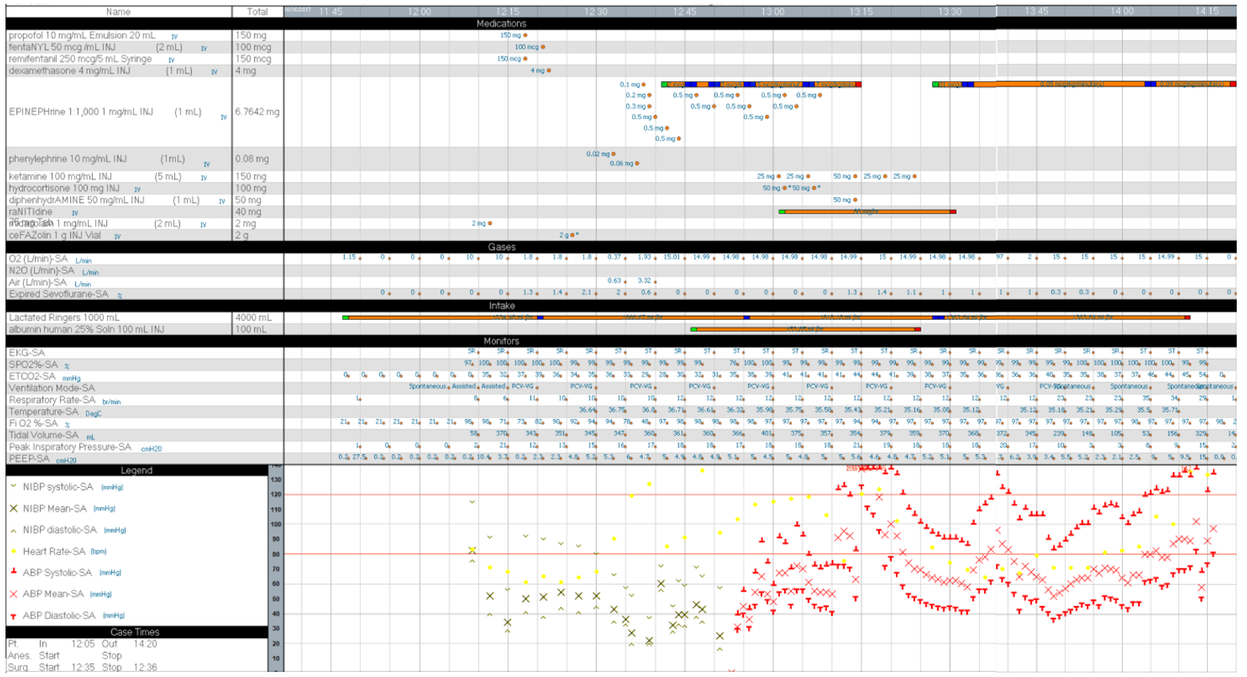
Anaphylaxis Grading System

World Allergy Organization Subcutaneous Immunotherapy Systemic Reaction Grading System (see text)				
Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Symptom(s)/ sign(s) of one organ system present[1] **Cutaneous** Generalized pruritus, urticaria, flushing or sensation of heat or warmth[1] **or** Angioedema (not laryngeal, tongue or uvular) **or** **Upper respiratory** Rhinitis (e.g., sneezing, rhinorrhea, nasal pruritus and/or nasal congestion) **or** Throat-clearing (itchy throat) **or** Cough perceived to come from the upper airway, not the lung, larynx, or trachea **or** **Conjunctival** Conjunctival erythema, pruritus or tearing **Other** Nausea, metallic taste, or headache	***Symptom(s)/ sign(s) of more than one organ system present*** **or** **Lower respiratory** Asthma: cough, wheezing, shortness of breath (e.g., less than 40% PEF or FEV1 drop, responding to an inhaled bronchodilator) **or** **Gastrointestinal** Abdominal cramps, vomiting, or diarrhea **or** **Other** Uterine cramps	**Lower respiratory** Asthma (e.g., 40% PEF or FEV1 drop, NOT responding to an inhaled bronchodilator) **or** **Upper respiratory** Laryngeal, uvula or tongue edema with or without stridor	**Lower or Upper respiratory** Respiratory failure with or without loss of consciousness **or** **Cardiovascular** Hypotension with or without loss of consciousness	Death
Patients may also have a feeling of impending doom, especially in grades 2, 3, or 4. **Note:** children with anaphylaxis seldom convey a sense of impending doom and their behavior changes may be a sign of anaphylaxis, e.g., becoming very quiet or irritable and cranky.				

From the American Academy of Allergy Asthma and Immunology
https://www.aaaai.org/practice-resources/tools-and-technology/immunotherapy-forms/immunotherapy-systemic-reaction-treatment-and-grad

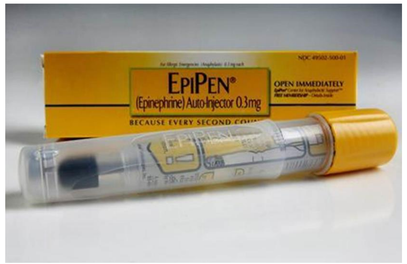
Case

We describe a case of Grade IV anaphylaxis in a healthy 11 year old female that presented for surgical resection of a superficial scalp lesion under general anesthesia. The patient received midazolam and fentanyl premedication, followed by propofol and remifentanil for induction and was uneventfully intubated. Dexamethasone and cefazolin were administered and within minutes the patient became tachycardic and progressively hypotensive to 50/20. During this sharp decline in cardiac performance intravenous fluids and phenylephrine boluses were given without improvement. Differential diagnosis considerations included anaphylaxis, hypovolemia, pneumothorax, pulmonary/air embolism, and other causes of tamponade physiology. Epinephrine (100mcg followed by 300mcg) was given without effect and an OR code was called to recruit additional resources. Pulse oximetry and ETCO2 became untraceable and chest compressions were initiated. Anesthetic gases were turned off, 600mcg of epinephrine was given and return of spontaneous circulation was achieved within 1 minute. An epinephrine infusion was started, and arterial and central venous access were obtained. With the epinephrine infusion at maximum dose, episodes of severe hypotension persisted requiring additional code dose epinephrine boluses every 2-3 minutes for 30 minutes before hemodynamics stabilized. During this period hydrocortisone, diphenhydramine, ranitidine, and ketamine were administered for presumed anaphylaxis. Serum tryptase was elevated to 15.3 at 1 hour (normal <13) and 20.6 at 4 hours. There were no mucocutaneous signs or rash visible. The patient did not exhibit any signs of bronchospasm and ventilation was adequate throughout the case. After vital signs stabilized a leak test was positive with the tracheal cuff deflated. The patient was extubated and transported to the pediatric intensive care unit and had full neurologic recovery in the postoperative period.



Discussion

To our knowledge, this is the first reported pediatric case of grade IV anaphylaxis under general anesthesia initially resistant to multiple code-doses of epinephrine. This report shows that early diagnosis and aggressive treatment with repeated administrations of epinephrine in suspected anaphylaxis can be life-saving. Although most cases of anaphylaxis respond to 1mcg/kg boluses of epinephrine and low dose epinephrine infusion, grade IV anaphylaxis presents with sudden cardiovascular collapse requiring astounding amounts of epinephrine. In community settings, these cases do not respond to EpiPen administration and are sometimes mistaken for EpiPen failure instead of inadequate epinephrine dosing.



Conclusion

Anaphylaxis is a life-threatening condition that requires early, repeated and sometimes astounding amounts of epinephrine administration to achieve the best possible outcome.

References

1. Anesthesiology 2009; 111:1141-50
2. Anesthesiology 2005; 102:897-903