Can this be happening? Anaphylaxis in the newborn

Jeffrey Frame, MD1 J.W. Sparks, MD2 Ravi Bhaldia, MD3

1. Clinical Fellow, Boston Children's Hospital, Boston, MA contact: jeffrey.frame@childrens.harvard.edu
2. Associate in Perioperative Anesthesia, Boston Children's Hospital and Instructor in Anesthesia, Harvard Medical School, Boston, MA
3. Resident Physician, Department of Anesthesiology, Beth Israel Deaconess Medical Center, Boston, MA

Case Presentation

A full term, thriving 3 week old with no significant prenatal or perinatal medical issues presented for elective resection of her sacrococcygeal teratoma.

Course

The patient underwent an uncomplicated inhalation induction with nitrous oxide and sevoflurane. Mask ventilation was easy with baseline lung compliance of 4-6 ml/cm H₂O. Inhalational agent was rapidly decreased after noting relative hypotension prior to IV placement. Once IV access was obtained, she received a dose of rocuronium (1 mg/kg). Approximately 1 minute later mask ventilation became increasingly difficult, with decreasing lung compliance and SpO₂ values, and relative hypotension. An ETT was placed and Ephedrine (0.5mg) administered without clinical improvement. A rash on her abdomen was noted. A preliminary diagnosis of a drug reaction was considered. Following IV epinephrine (1 mcg/kg), she had brisk improvement in respiratory and hemodynamic status, with a slow resolution of skin discoloration. She received one additional dose of epinephrine (0.5 mcg/kg) for apparent recurrence. The operative case was cancelled. She was given adjunct medication treatment and observed for an additional 75 minutes prior to extubation, which occurred without incident.

Two days later, she returned to the OR and received an IV induction with propofol and vecuronium. Mild generalized cutaneous erythema was noted after induction without hemodynamic or respiratory compromise. General anesthesia was maintained with a balanced technique, and it was noted that the patient displayed erythema after administration of morphine as well as a brief episode of brachycardia at the conclusion of the case. She was safely extubated and had an uneventful recovery.

Discussion of Event

Diagnosis of medication reactions is difficult under general anesthesia but is suggested by hypotension, brachycardia, and cutaneous eruption. Neonates are less likely to develop medication reactions. Risk factors for anaphylaxis in the neonate are not well understood, but include mastocytosis, atopy, asthma, and bronchiolitis. Mechanism of anaphylaxis may differ in neonates as compared to those with more mature immune systems.

Common Drug Reaction Manifestations under General Anesthesia

- **Pulmonary**: Wheezing, cyanosis, decreased lung compliance
- **Cardiovascular**: Hypotension, tachycardia, dysrhythmias
- **Cutaneous**: Erythema, flushing, urticaria, angioedema/swelling

Neonatal anaphylactic reactions have been infrequently described with causative agents including cephalaxine1, ceftriaxone2, cefazolin3, cefazidime4, vaccines5, and milk protein6. Neuromuscular blockers may have the highest incidence of anaphylaxis in the broader pediatric population. Severe reactions to atracurium have been reported in the neonate.7,8 While older pediatric patients having reactions to rocuronium9,10 have been reported, we are unaware of such a severe reaction being described in the neonate.

Treatment for anaphylaxis includes removal of the offending agent, ensuring adequate airway protection, IV fluids, epinephrine, and adjuncts such as H₁ and H₂ antagonists, bronchodilators, and corticosteroids.

References


Discussion of Event: Differential Diagnosis

- **Pulmonary**: Aspiration, foreign body, bronchial mainstem or esophageal intubation, gastric insufflation
- **Cardiovascular**: Dysrhythmias, return of fetal circulation, unrecognized congenital heart disease, vasovagal reaction
- **Immuneologic**: Mastocytosis, hereditary angioedema, serum sickness, idiopathic urticaria, carcinoid tumor
- **Medication**: Inadequate anesthesia, medication overdose

Definitive diagnosis remains elusive in adults and is particularly challenging in infants with immature immune systems. Two commonly obtained lab tests are histamine and tryptase. Histamine has a short half life, and must be drawn within approximately 20 minutes. Serum beta-trypaetase (mature tryptase), also a marker of mast cell activation, remains measurable for several hours.

Anaphylaxis has significant clinical cross-over with other reactions11 and mastocytosis12, and these may easily be mistaken for one another. Baseline levels of alpha and beta-trypaetase should be obtained at a time remote to the event to rule out mastocytosis, in which an elevated alpha-trypaetase is anticipated at rest13.

Explanation for the patient’s clinical course remains uncertain, particularly without available confirming testing in this patient who was lost to follow up. The differential for this case includes mastocytosis & non-immune causes of histamine release, bronchoconstriction, aspiration, and recurrence of fetal circulation. Although extremely rare, consideration for drug reaction should be given to neonatal patients.