

Intestinal Perforation Following Treatment of Viral Croup: A Consequence of Disease or Intervention?

Ragavan Siddahrthan^{1*}, Avraham Schlager² and Matthew Clifton³¹Department of Surgery, Oregon Health and Science University, USA²Department of Surgery, Akron Children's Hospital, USA³Department of Surgery, Emory University, USA

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*Corresponding author

Ragavan Siddahrthan, Department of Surgery, Oregon Health and Science University, USA, Tel: 224-406-0592; Email: Ragasid@gmail.com

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Abstract

We present two cases of intestinal perforation following admission and treatment for croup. The details of the respective hospital courses are discussed with a focus on potential etiologies of the intestinal demise. To our knowledge, these represent the only reported cases of viral croup progressing to intestinal perforation.

Croup or laryngotracheo-bronchitis is an infection of the upper respiratory tract most commonly affecting young children. This inflammatory process causes a classic barking cough and low grade fevers. It can be caused by myriad viruses with Parainfluenza 1 and 3 being the most common. Although generally self-limited, in its most severe form croup can cause severe respiratory distress requiring hospitalization. Current treatment of severe croup includes oral or intravenous steroids, racemic epinephrine, heliox and occasionally, intubation [1]. In general croup does not involve the gastrointestinal tract. We report two patients with severe croup requiring intubation that developed intestinal ischemia and subsequent perforation. To our knowledge, these are the only reported cases in the literature of croup and associated intestinal ischemia.

Case Report

Case 1

A two year old male with no past medical history was diagnosed with croup at an outside hospital. He was treated with oral steroids but continued to have progressive respiratory deterioration and was transferred to our institution. On arrival, the patient's oxygen saturation was 49%. He was administered racemic epinephrine 3 times and placed on 8L oxygen with heliox via a non-rebreather mask. Chest x-ray demonstrated increased interstitial markings suspicious for pneumonia and the patient was started empirically on a third generation cephalosporin. Blood cultures were negative but viral assay demonstrated Metapneumovirus. Despite continued respiratory support the patient required intubation and was transferred to the ICU. Repeat blood cultures were negative for bacteria but an endotracheal culture grew rare clusters of *S. aureus*. On hospital day seven the patient developed increasing abdominal distention. An abdominal x-ray demonstrated pneumatosis intestinalis. The patient was managed conservatively with broadened antibiotic coverage and nasogastric decompression. An abdominal ultrasound demonstrated large volume ascites. A peritoneal catheter was inserted and 7,200 mL of serosanguinous fluid drained over the ensuing three days. Fluid sampled from the initial drain had rare growth of *Enterococcus faecalis*.

Eventually the drain became dislodged but the patient's abdomen became less distended so reinsertion was not attempted. On hospital day 16 the patient developed mild abdominal wall erythema and again became distended. Labs showed a lactate of 0.8 mmol/L, the WBC count was 7080 cells/uL and the C-Reactive Protein (CRP) ranged from 11.7-23.2 mg/dL. A repeat ultrasound demonstrated an undrained intra-abdominal collection. A new catheter was placed which drained succusentericus. An exploratory laparotomy was performed, revealing a liter of stool spillage and necrotic intestine in the distal small bowel and ascending colon with normal intestinal rotation. Histologic assessment of the intestine demonstrated transmural ischemic hemorrhagic necrosis of the small intestine and ascending colon with multiple perforations. The specimen was sent to the Center for Disease Control (CDC) for evaluation for immunohistochemical assessment which tested negative for viral infection.

Case 2

A seven month male was diagnosed with croup by his primary care provider and treated as an outpatient with oral corticosteroids. Four days later the patient had progressive respiratory distress and was evaluated at an outside hospital and administered two doses of racemic epinephrine before transfer to our institution. He received an additional dose of racemic epinephrine upon arrival

but continued to deteriorate with worsening respiratory distress and stridor. The patient was admitted to the ICU and subsequently intubated. On admission, the patient's blood cultures were negative but his viral assays were positive for Parainfluenza and Rhinovirus. On hospital day five, the patient's WBC became elevated to 20,210 cells/uL and he was started empirically on a third generation cephalosporin. Cultures were redrawn and the endotracheal cultures demonstrated *S. aureus* but the blood cultures were once again negative. On hospital day 8 the patient developed distention and an abdominal x-ray demonstrated pneumatosis intestinalis. An NG tube was placed and antibiotic coverage was broadened. He became increasingly distended and an abdominal x-ray on hospital day 10 revealed pneumoperitoneum. The patient was taken to the operating room for an exploratory laparotomy which revealed patchy gangrenous necrosis of the splenic flexure, descending and sigmoid colon. Post-operative histological assessment revealed transmural necrotizing colitis with multiple perforations. Peritoneal fluid cultured during the operation was cultured and had rare growth of *Pseudomonas aeruginosa*.

Discussion

To our knowledge, this is the first description of pediatric croup with respiratory failure with associated intestinal ischemia and perforation. Potential etiologies include both the inciting viruses as well as the subsequent pharmacologic intervention. There are no reports in the medical literature of a causal relationship between croup and its inciting viruses with bowel ischemia. The fact that these two cases had different inciting viruses makes a viral etiology for intestinal ischemia and perforation somewhat less likely.

An infectious etiology beyond the initial viral infection is plausible. The presence of *S. aureus* in the endotracheal tube could be a sign of *S. aureus* bacteraemia which has been associated with embolic small bowel perforations, though the lack of positive blood cultures makes this mechanism unlikely [2]. *Pseudomonas* septicemia has also been associated with bowel perforations. A case report from 1995 highlights two patients with septic shock from a *Pseudomonas* diarrheal illness [3]. Both of these patients had positive blood cultures as well as eschar gangrenous lesions. One of our patients had *Pseudomonas* growth from peritoneal fluid drained during surgery but never had blood cultures or physical manifestations of *Pseudomonas* sepsis. Descriptions of pneumonia associated with intestinal perforations exist in the literature [4]. In these cases the patients had significant co-morbidities (ventilator dependence, hypotonia and neurologic deficits) as well as positive blood cultures with more significant signs of sepsis including elevated lactate and WBC counts greater than 40,000 cells/uL. For our patients, sepsis and subsequent septic shock could explain a hypo perfused state and account for the perforations. Both of our patients were in critical condition requiring ICU monitoring, vasopressors and fluid boluses. However, one patient's lactate remained near normal levels and both patients' blood cultures remained negative throughout the hospital stay. Sepsis, though a plausible etiology, cannot conclusively explain the intestinal perforations in our patients.

An alternative explanation for the intestinal ischemia may relate to the common therapeutic intervention that the patients received while in the ICU which includes racemic epinephrine, antibiotics and heliox treatment. Racemic epinephrine has become standard of care in the treatment of respiratory distress in croup. It has proven to have

fewer systemic effects than IV epinephrine, but systemic effects are still possible. Ischemia due to racemic epinephrine is a documented side effect. In theory, the systemic effects of racemic epinephrine could have caused vasoconstriction of the splanchnic blood supply leading to bowel ischemia. A case from 1999 highlights a pediatric patient who experienced a myocardial infarction after racemic epinephrine administration for severe croup symptoms [5]. In addition, the use of IV epinephrine for respiratory distress has been shown to cause intestinal ischemia. A case report from 2001 highlights a healthy patient with severe asthma that required high doses of IV epinephrine. These high doses of epinephrine resulted in bowel infarction that was identified on hospital day 2 when an abdominal x-ray showed pneumatosis [6]. One caveat of this mechanism is that in our patients, the pneumatosis developed several days after the administration of the racemic epinephrine.

Antibiotics would seem to be an unlikely cause of the bowel ischemia in this case. Although antibiotics could theoretically lead to *Clostridium difficile* colitis which could progress to megacolon, intestinal ischemia and perforation, these patients did not have diarrhea, the predominate symptom of *C-difficile* colitis [7]. Nevertheless, as stool samples were never sent for PCR analysis, *C.difficile* colitis cannot be definitively excluded.

Heliox is used in respiratory distress because it improves gas exchange in the lungs through improved laminar flow. In several studies heliox has been shown to improve perfusion during a stroke in animal models, though the mechanism was not clearly identifiable. Heliox also appears to help in cardiac ischemia though again the mechanism is not entirely clear [8]. We could not identify any evidence that large doses of heliox cause intestinal ischemia.

In conclusion, though the exact cause of intestinal necrosis could not definitively be deduced from these two cases, an association between patients being treated for severe croup and subsequent intestinal perforation has been demonstrated. Since intestinal ischemia may be caused by the therapeutic interventions necessary to treat croup, a high index of suspicion along with serial abdominal exams and x-rays should be included in the management to mitigate the morbidity of this complication.

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