An Uncommon Complication of a Common Disease: Pneumatosis Intestinalis in an Infant with Kawasaki Disease

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Kawasaki disease is the leading cause of acquired heart disease among children who are under the age of 5 years and living in developed countries. The etiology of this disease is unknown, and a prompt, multi-disciplinary workup and diagnosis is essential for minimizing complications in this multisystem vasculitis. Development of coronary artery abnormalities is the hallmark representing morbidity and mortality associated with the disease [1]. Apart from the diagnostic criteria, other multi-systemic clinical signs and laboratory findings have been well-established in association with Kawasaki disease. Common gastrointestinal manifestations include abdominal pain and distention, vomiting, diarrhea, and hepatobiliary dysfunction.

We present a case of a 7-month-old child diagnosed with typical Kawasaki disease who developed acute abdominal distention during the course of the disease, with pneumatosis intestinalis.

Pneumatosis intestinalis is a radiological sign characterized by the presence of gas cysts on the bowel wall. Since no clear etiology has been advocated, management ranges from mere conservative observation to surgical intervention based on the underlying cause and clinical presentation.

PATIENT DESCRIPTION

A 7-month-old male infant presented to our hospital with a 4-day history of high fever, irritability, vomiting, and diarrhea as well as a diffuse erythematous rash. His past medical history including pregnancy, delivery, and postnatal period was unremarkable. The child was otherwise healthy, appropriately developed, and immunized. His past medical history was positive for several events of wheezing during infancy, which were treated with inhaled corticosteroids.

On presentation to the emergency department, he was irritable and uncooperative. Crying-induced stridor was noted. His temperature was 38.5°C, heart rate 199 beats per minute, and blood pressure 111/69 mmHg. Physical examination demonstrated a diffuse maculopapular rash, non-purulent conjunctival erythema, redness of the lips, and a hyperemic pharynx and a palpable cervical lymph node. Signs of mild dehydration including prolonged capillary refill and dry mucous membranes were present. Heart sounds were dual without any audible murmurs. Examination of the lungs and abdomen was unremarkable. Neurological examination was normal, with the exception of irritability.

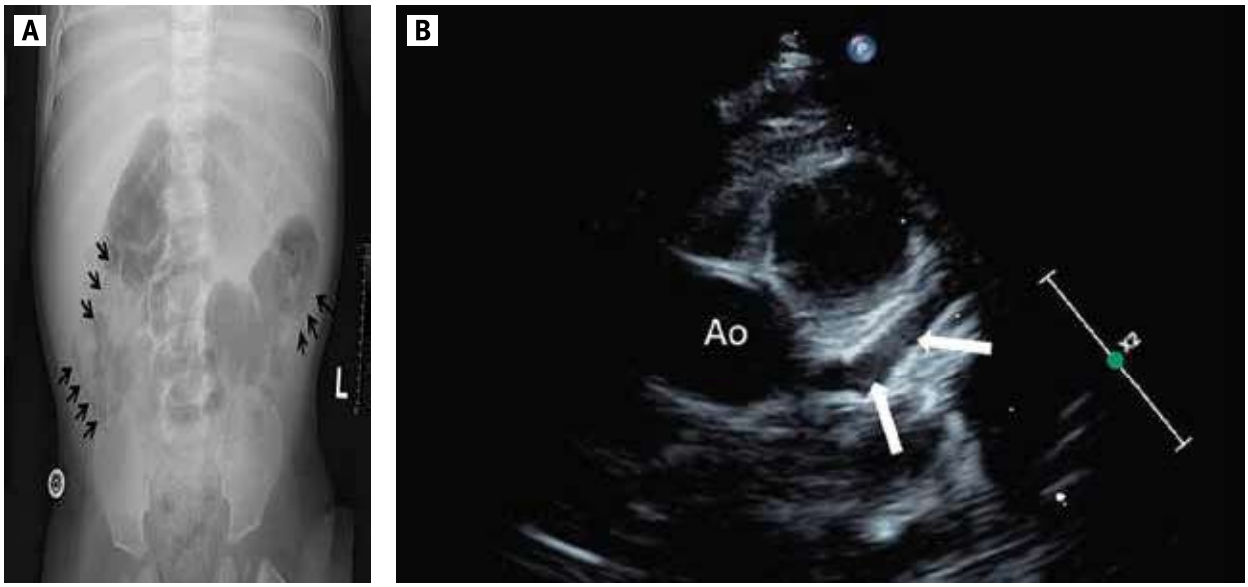
Initial laboratory studies demonstrated thrombocytosis (526,000/mm^3), a normal white blood cell count (9200/mm^3), and normal hemoglobin levels (10.7 g/dl). Further laboratory findings included elevated gamma-glutmyltransferase (110 U/L), elevated alanine aminotransferase (87 U/L), eunatremia (135 mmol/L), mild hypoalbuminemia (3.5 g/dl), and significantly raised C-reactive protein (CRP; 173 mg/L). Urinalysis showed mild proteinuria (2+) and a trace of leukocytes. Blood, urine, and stool cultures were negative.

As Kawasaki disease was suspected, a transthoracic echocardiogram (TTE) was performed. The test was consistent with mild dilatation of the right coronary artery (RCA; Z score 3), with no involvement of the left main coronary artery (LMCA) or left anterior descending artery (LAD). No pericardial effusion was noted.

Due to the clinical signs and laboratory findings, a diagnosis of Kawasaki disease was made. Initial management included administration of intravenous immunoglobulin (IVIG; 2 g/kg in a single infusion) in addition to high-dose acetylsalicylic acid therapy (80 mg/kg/day) and H2 blocker, with clinical improvement and lower degree of fever. On the third day of admission, the patient was increasingly restless.

Physical examination revealed a distended but non-tender abdomen with normal bowel sounds. No blood or mucous were present on rectal examination. An abdominal X-ray showed pneumatosis intestinalis involving both the right and left sides of the colon [Figure 1A]. The patient was managed conservatively. Clinical improvement was notable over the following 2 days with a subsequent abdominal radiograph which demonstrated a near-complete resolution of intramural bowel gas. During his admission, the patient was afebrile and developed desquamation signs.

Figure 1. Abdominal **[A]** radiograph obtained 3 days after hospital admission and **[B]** echocardiography image from a 7-month-old male infant diagnose with Kawasaki disease
[A] Pneumatosis intestinalis seen in the upper left and lower right colon (arrows)
[B] Parasternal short axis imaging plane showing a dilated left main coronary artery (arrows)



Overall, his condition continued to improve with regression of abnormal liver function enzymes and CRP. The thrombocyte count gradually rose up to 707,000/mm^3. Repeated echocardiograms did not show any changes in his coronary arteries and he was discharged 6 days post-admission.

Two weeks following his discharge, during a follow-up visit at the cardiology clinic, the patient was afebrile but still irritable. The echocardiogram demonstrated progressive dilations in the coronary vessels [Figure 1B], RCA was moderately dilated (Z score 8–9). LMCA and LAD were mildly dilated (Z score 3.5 and 4.8, respectively). Laboratory findings included thrombocytosis (900,000/ mm^3) and an elevated CRP (86 mg/L).The patient was then re-admitted and treated with another course of IVIG (2 g/kg in a single infusion). Four days later, he was discharged with dual antiplatelet therapy (acetylsalicylic acid and clopidogrel) after an uneventful stay.

Repeated echocardiograms conducted 1, 2, 4, and 8 weeks after discharge demonstrated improvement in all coronary artery dilations. RCA (Z score 3.6), LMCA, and LAD were found to be in normal range; therefore, clopidogrel treatment was stopped.

COMMENT

Kawasaki disease is a systemic, medium-sized vessel vasculitis most commonly seen in children. Classic diagnostic criteria include at least 4 days of fever along with at least four of the following: enlarged cervical lymph nodes, polymorphous exanthema, changes in the extremities, non-purulent bilateral conjunctivitis, and erythema of oral mucosa. Patients with prolonged fever who do not fulfill all the listed criteria at presentation (≥ 2 criteria) would be considered for the diagnosis of atypical Kawasaki disease. Furthermore, a myriad of clinical and laboratory characteristics feature Kawasaki disease including the gastrointestinal tract. Common findings consist of diarrhea, vomiting, abdominal pain, hepatitis, cholestasis, and gallbladder hydrops. Other rare gastrointestinal manifestations include bowel obstruction, paralytic ileus, jaundice, pancreatitis, colitis, ischemic bowel, and colon edema [1].

In this article, we described a 7-month-old male infant who presented to our hospital with the classic presentation of Kawasaki disease in the acute phase with the subsequent development of abdominal distension and pneumatosis intestinalis on X-ray. To the best of our knowledge, this is the first documented case of such a complication.

Pneumatosis intestinalis refers to the presence of intramural gas within the small or large intestine and is most commonly seen on plain a X-ray or computed tomography (CT) scan.

Minority of cases are primary pneumatosis intestinalis (15% of cases) which is mostly a benign condition that may be clinically unnoticed for several years. However, secondary pneumatosis intestinalis (85% of cases), has been linked to a wide variety of clinical conditions. In the neonatal period, the majority of cases are secondary to necrotizing enterocolitis (NEC) which is a serious condition with high mortality rates in the neonatal period. Nevertheless, after the neonatal period, pneumatosis intestinalis can be secondary to bone marrow transplantation, congenital heart disease, noninfectious

colitis, intestinal motility disorders, infections, chronic lung diseases and more. As so, provision of therapy varies according to the underlying cause, additional signs and clinical judgment [2].

So far, gastrointestinal involvement in Kawasaki disease patients has been described mainly in small scale retrospective series and case reports. While gastrointestinal symptoms are well-known in Kawasaki disease patients, they do not comprise the diagnostic criteria. In one study [3], it was shown that at least one gastrointestinal symptom (e.g., vomiting, diarrhea, or abdominal pain) was present in approximately 60% of the patients. In another study [4], 4.5% (n=10) of Kawasaki disease patients, were admitted to the surgical unit for acute abdomen. Nine of them had an atypical presentation of Kawasaki disease, including symptoms such as abdominal pain, abdominal distension, vomiting, hepatomegaly or jaundice and eventually underwent surgical intervention. In 2002, a case report in New Zealand described a fatal late-onset NEC in a term infant with multi-organ arteritis as exhibited by post mortem evaluation. Kawasaki disease was proposed as a possible etiology in this case [5].

CONCLUSIONS

We present a case of an infant with Kawasaki disease and pneumatosis intestinalis, which resolved with conservative treatment. Pediatricians should be aware of this possible complication and have a high index of suspicion of the various gastrointestinal manifestations in Kawasaki disease. Conservative treatment may be successful and lead to resolution without the need for surgery.

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Capsule

Safety profile of autologous macrophage therapy for liver cirrhosis

Therapies to reduce liver fibrosis and stimulate organ regeneration are urgently needed. **Moroni** et al. conducted a first-in-human, phase 1 dose-escalation trial of autologous macrophage therapy in nine adults with cirrhosis and a Model for End-Stage Liver Disease (MELD) score of 10–16 (ISRCTN 10368050). Groups of three participants received a single peripheral infusion of 10^7, 10^8, or up to 10^9 cells. Leukapheresis and macrophage infusion were well tolerated with no transfusion reactions, dose-limiting toxicities or macrophage activation syndrome. All participants were alive and transplant-free at one year, with only one clinical event recorded, the occurrence of minimal ascites. The primary outcomes of safety and feasibility were met. This study informs and provides a rationale for efficacy studies in cirrhosis and other fibrotic diseases.

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Capsule

FPR1 is the plague receptor on host immune cells

The causative agent of plague, *Yersinia pestis*, uses a type III secretion system to selectively destroy immune cells in humans, thus enabling *Y. pestis* to reproduce in the bloodstream and be transmitted to new hosts through fleabites. The host factors that are responsible for the selective destruction of immune cells by plague bacteria are unknown. **Osei-Owusu** et al. showed that LcrV, the needle cap protein of the *Y. pestis* type III secretion system, binds to the *N*-formylpeptide receptor (FPR1) on human immune cells to promote the translocation of bacterial effectors. Plague infection in mice is characterized by high mortality; however, *Fpr1*-deficient mice have increased survival and antibody responses that are protective against plague. The authors identified *FPR1R190W* as a candidate resistance allele in humans that protects neutrophils from destruction by the *Y. pestis* type III secretion system. Thus, FPR1 is a plague receptor on immune cells in both humans and mice, and its absence or mutation provides protection against *Y. pestis*. Furthermore, plague selection of *FPR1* alleles appears to have shaped human immune responses towards other infectious diseases and malignant neoplasms.

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