

Adenovirus-Associated Intussusception in a Child

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Abstract

Intestinal intussusception is one of the most common causes of acute abdominal emergencies in children under 2 years of age. We herein describe a case of adenovirus associated small intestinal intussusception in a 5-month-old boy. A brief review on triggers of intussusception in children is provided. Thorough gross and microscopic inspections of resected intussusception specimens are recommended to diagnose subtle predisposing triggers such as viral infections.

Keywords: Adenovirus, cytopathic effect, intussusception

INTRODUCTION

Intestinal intussusception is one of the most common causes of acute abdominal emergencies in children under 2 years of age, with a peak incidence between 5 and 9 months.^[1] A specific “pathologic lead point” can be identified as the cause of the intussusception in some instances. These may include lymphoid hyperplasia of the intestinal mucosa, Meckel's diverticula, intestinal duplication cysts, ectopic pancreatic tissue, hamartomatous lesions, and tumors. It is estimated that 90% of pediatric intussusception cases are “idiopathic” but likely associated with mucosal lymphoid hyperplasia/mesenteric lymphadenopathy that acts as the lead point.^[2] The latter observation raises the possibility of an underlying infectious etiology. This suspected association is supported by the frequently coincidental clinical history of recent or concurrent viral infections and the seasonal incidence pattern of intussusceptions.^[3]

Acute viral gastroenteritis caused by adenovirus, *rotavirus*, norovirus, and others have been implicated in intussusception cases, with adenovirus detected in the highest proportion.^[4,5] Adenovirus infections frequently display viral cytopathic effects and associated reactive changes, allowing for detection by the astute pathologist. Because of the clinical implications and severity of both intussusception and disseminated adenovirus infection, it is critical to recognize the potential infectious etiologies to ensure proper treatment. Herein, we describe a case of adenovirus-triggered intussusception in a child.

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CASE REPORT

A 5-month-old previously healthy boy presented with a 1 week history of cough and congestion, which progressed to decreased appetite, emesis, constipation, and lethargy. On physical examination, he was afebrile but appeared dehydrated with abdominal tenderness. An X-ray of the abdomen showed distended bowel loops, suggestive of small bowel obstruction. A subsequent ultrasound revealed an extensive ileocolic intussusception with small bowel telescoping through the colon to the level of the splenic flexure. There was a decreased flow to the area of intussusception with hyperemia of the adjacent mesentery. An exploratory laparotomy confirmed the intussusception, which was manually reduced, and a 12 cm congested segment of intussuscepted hemorrhagic bowel was resected at the level of the terminal ileum [Figure 1].

Histologic sections from the resected ileum revealed patchy areas of hemorrhagic necrosis within the mucosa and underlying prominent, hyperplastic lymphoid follicles [Figure 2]. Close microscopic examination showed patchy areas of smudgy viral inclusions within intestinal epithelial cells in proximity to areas of necrosis. IHC staining for adenovirus was positive confirming the diagnosis [Figure 3].

DISCUSSION

Intussusception is a common cause of intestinal obstruction in children under 2 years of age. The classic clinical presentation is the triad of intermittent abdominal pain, “currant jelly” stool (a mixture of blood and mucus), and a palpable abdominal mass. If the diagnosis is delayed, the risk of morbidity and mortality increases with potential complications including bowel ischemia and perforation. Intussusception triggers include infectious as well as noninfectious triggers.

Noninfectious triggers include Meckel’s diverticula, intestinal duplication cysts, ectopic pancreatic tissue, hamartomatous lesions, tumors as well as reaction to food antigenic proteins.^[3]

Infectious etiologies known to cause intussusception include bacterial infections, human herpesvirus 6,



Figure 1: Gross image of a bisected intussuscepted segment of ileum showing grossly evident lymphoid hyperplasia at the leading edge (arrow)

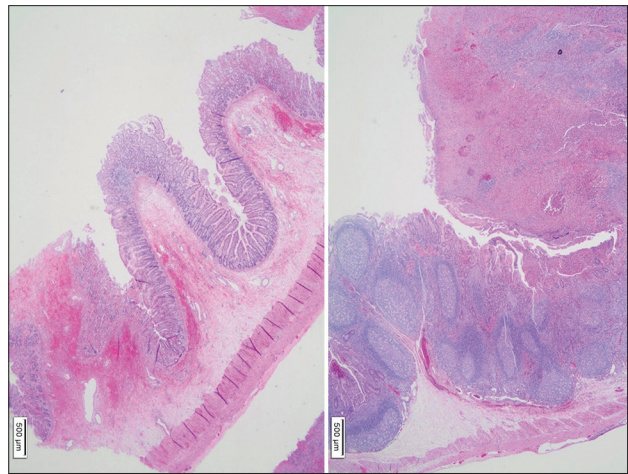


Figure 2: ileocolic resection with areas of hemorrhagic and necrotic mucosa, mixed inflammation, and prominent submucosal, hyperplastic lymphoid follicles

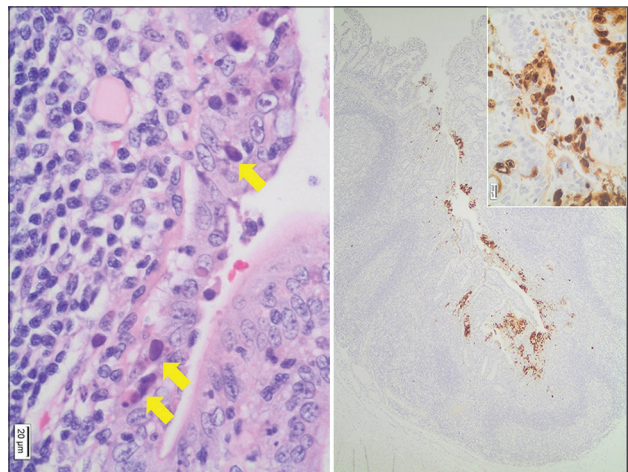


Figure 3: Left: H&E staining of intestinal mucosal epithelium showing smudgy, eosinophilic, intranuclear inclusions (arrows). Right: The infected cells show strong selective nuclear and cytoplasmic positivity for adenovirus by immunohistochemical staining.

rotavirus, enterovirus, cytomegalovirus, Epstein–Barr virus, and adenovirus. Adenovirus is the most common pathogen detected in intussusception specimens, comprising approximately 30% of cases.^[4,6,7]

The link between adenovirus as the etiology of intussusception was first reported in 1969 in Taiwan.^[8] Since then, investigating the etiology and role of viral infections in intussusceptions has been an area of interest, especially following the withdrawal of the *Rotavirus* tetravalent vaccine due to the risk of intussusception, which occurred in 1:10,000 recipients.^[4] Interestingly, subsequent studies have shown natural, environmental infections with wild-type *Rotavirus* does not pose an increased risk for intussusception.^[9]

Human adenoviruses received their name after isolation from adenoid tissue and have since been implicated in a wide range of diseases including upper respiratory infections, conjunctivitis, cystitis, gastroenteritis, and meningoencephalitis. The virus is also known to cause severe, disseminated disease in the immunosuppressed population. Montgomery and Popek describe a case of a child who died intraoperatively during resection of an adenovirus-associated intussusception and subsequently donated her liver; however, the recipient of the liver later succumbed to disseminated adenovirus infection.^[7] Conversely, the viral infection can be asymptomatic with subclinical lymphoid hyperplasia, which may act as a lead point for intussusception.

Adenoviruses are classified into seven species, A–G, and over 70 genotypes with multiple studies demonstrating species C to be the most commonly associated with intussusception.^[3,5,10,11] Quantitative viral detection of adenovirus in stool samples, most specifically species C, parallels the seasonal occurrence rate of intussusceptions, with an increased frequency in the winter in associations with upper respiratory tract infections and increased frequency in the spring and summer with associated gastroenteritis. This further suggests an infectious role in the development of intussusception.^[3,5]

Histologically, adenoviruses typically demonstrate viral cytopathic effects: smudged, glassy nuclei, eosinophilic intranuclear inclusions, and marginated chromatin without an increase in cell size. Although adenovirus causes cytopathic effects identifiable on H and E

stained slides, multiple studies have demonstrated these changes may be subtle and easily missed.^[12,13] Immunohistochemical staining for adenovirus improves the sensitivity of detection and can assist in deciphering the etiology of the intussusception. One of the most common histologic findings is submucosal lymphoid hyperplasia with germinal center formation, specifically located at the leading edge of the intussusception. Given this common finding, it is important to perform thorough gross inspection and careful microscopic examination to exclude underlying lesions, including Burkitt lymphoma, as a source of the lead point.

CONCLUSIONS

Pathologists need to be familiar with the common and less common causes of intussusceptions to aid in determining a possible underlying etiology. Meticulous gross pathologic and microscopic examinations are essential. Correlation with microbiologic studies, serologic viral titers, and immunohistochemical workup can be very helpful. Assessing the clinical history for a recent upper respiratory tract infection or other viral illness may provide important clues and help in reaching the appropriate diagnosis and initiating appropriate treatment timely.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Authors' contribution

All authors are involved in the clinical aspects of the reported material and drafting and final revision of the manuscript.

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Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

No prior approval is required at our institution for isolated case reports. Case history and samples are reported anonymously.

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