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Single Case

Infantile Appendicitis: A Deceptive Challenge with Disastrous Consequences

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Abstract
Acute appendicitis (AA) in neonates and infants is an infrequent event. In day-to-day practice, death due to AA is hardly ever reported to a coroner or a medical examiner. Here, we report on an 8-month-old infant assigned to the medical examiner as the death occurred within 10 days of a surgical procedure. The cause of death was undetermined. Autopsy revealed gross and histologic features of AA. A postmortem review of the medical records showed signs and symptoms consistent with AA. On the other hand, a recent history of upper respiratory tract infection followed by clinical diagnosis and treatment by a community pediatrician probably blindsided the hospital physicians. This case illustrates the challenges of AA in infancy. The literature review revealed that a misdiagnosis of AA is more likely to occur on several occasions. They include patients who present "atypically," patients who are not thoroughly examined, patients receiving antipyretic or analgesic medication and discharged, those diagnosed as having gastroenteritis, and patients who do not receive an appropriate discharge or follow-up instructions.

Precis of the Article: In this article, we emphasize the challenge of the diagnosis of acute appendicitis in infancy. In our opinion, emergency physicians should consider atypical presentations of acute appendicitis and avoid a discharge diagnosis of gastroenteritis unless the patient meets strict diagnostic criteria.

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Introduction

Acute appendicitis (AA) is expected in the surgical emergency unit. It has a lifetime risk between 5 and 10% with a slightly male predominance [1]. Its surgical management is very successful. Usually, it has a minimal hospital stay time, with minimum complications, and the mortality is between 1 and 3% [2]. AA is common in pediatric emergency departments (EDs) but rarely encountered in neonatal departments. It is seldom considered a differential diagnosis in children under 3 years [3, 4]. Emergency surgical interventions, antibiotic prophylaxis, and other management criteria have lessened the death following an appendectomy. However, urgent surgery is warranted for AA. Delayed presentation, diagnosis, or surgical intervention may lead to severe consequences, especially following perforation of the appendix [5, 6].

Despite advances in modern diagnostic tools, advanced surgical techniques, and antibiotics, some neonatal and infantile cases are missed even today in high-income countries. A complete autopsy with ancillary investigations would, in most cases, detect the underlying diseases and help the clinicians to educate themselves.

Case Report

An 8-month-old female child was presented to a tertiary Children's Hospital Emergency Department with persistent fever for 5 days, constant inconsolable crying, refusal of feeds, and reduced urine output. The infant was taken to a Community Pediatrician 6 weeks before presenting to the hospital for fever and cough. The pediatrician diagnosed an upper respiratory infection with potential pneumonia. As a result, the child received amoxicillin, a penicillin antibiotic used to treat many different types of infection, and albuterol, a bronchodilator that relaxes muscles in the airways. On the eighth-day follow-up visit, the pediatrician advised the caregiver to continue the bronchodilator and prescribed beclomethasone dipropionate (two puffs two times a day for 20 days). One week after completing the steroids, the infant decompensated and displayed shortness of breath. However, she reduced oral intake, decreased urination, and cried inconsolably 3 days later. She was again taken to the same pediatrician, who prescribed clavulanic acid 2 days later.

The ED physician noted nontoxic vital signs, oxygen saturation of 100%, congestion, flat fontanelle, flexible neck, and transmitted upper airway sounds at the hospital admission. The abdomen was tender. There were no abnormal bowel sounds. Initial laboratory investigations showed a white blood cell count of 16.1 (6–17.5) 10^{-9}/L, C-reactive protein 240 (<8.0) mg/L, serum sodium, potassium, and chloride of 130.0, 6.0, and 95 mmol/L, respectively. Hemoglobin was 165 g/100 mL of blood, and platelets were 1,050 10^{-9}/L. During the physical examination at the ward, the infant underwent lumbar puncture, chest and abdominal X-rays and ultrasounds, and blood and urine culture. She was on broad-spectrum antibiotics, and the cultures were negative. Ultrasound and x rays showed pleural and peritoneal effusions, maximum fluid collection in the right iliac fossa area (5.9 cm in diameter), and tissue edema, all thought to be due to capillary leak syndrome. A nasopharyngeal swab demonstrated the Parainfluenza 3 Virus. The working diagnosis was a viral respiratory infection. In the middle of the first day in the ward, the infant had a cardiac arrest. She was successfully resuscitated after 30 min of cardiopulmonary resuscitation. The following day, she developed abdominal and lower extremity compartment syndrome. An open laparotomy decompressed the abdomen on the second day of admission. There was a highly edematous abdominal wall with minimal bleeding, pressure builds up in the abdominal cavity relieved by surgery, and healthy bowel with no ischemia. Sadly, she died on the third day after admission to the ward.

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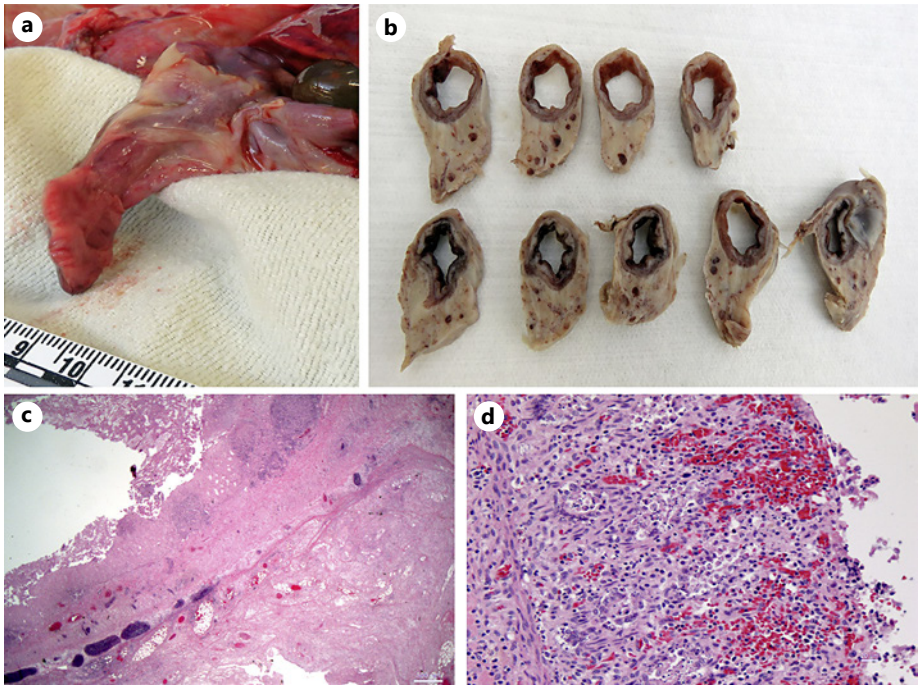

Fig. 1. a Gross examination of the appendix showing the redness on the surface. **b** Cross sections of the formalin fixed appendix showing remarkable thickening of the wall. **c**, **d** Low- and high-power magnification of the appendix showing extensive necrosis (**c**, ×50, hematoxylin and eosin staining) and acute (neutrophilic) inflammation on the serosa (**d**, ×400, hematoxylin and eosin staining).

This infant was the 11th baby of a young mother, who had no prenatal care, smoked cannabis and tobacco, and consumed methamphetamine and alcohol during pregnancy. The baby was born at 38 weeks of gestation. She stayed in the hospital for a day due to a heart murmur that proved functional. She had an episode of cyanosis and hypotonia and a choking spell in her second and third months of life, respectively. The infant was not well cared for by her biological mother and developed global developmental delay due to lack of stimulation and contact. Therefore, she was given to a foster mother at 33 weeks of age and was doing well. In this case, the death occurred within 10 days of a surgical procedure, and there was no cause of death. Therefore, the death was reported to the medical examiner, and a medicolegal death investigation was commenced.

At autopsy, the body was a female infant consistent with 8 months of age. There were no congenital abnormalities. There were no inflicted external or internal injuries. The skeletal survey was negative for recent and old fractures. There was generalized edema of the body consistent with the observed weight of 13.5 kg compared to admission weight of 8.47 kg 3 days before death. The anterior abdominal wall was found opened with a midline supra and infra umbilical surgical incision. The loops of the bowel were covered with a secured plastic sheet. There were bilateral pleural effusions. Esophagus, stomach, small intestine, and colon were viable and healthy. The appendix was located at the retrocecal area. There was swelling, inflammation, and pus-covering serosa (Fig. 1a). Part of the pelvic mesocolon and colon was in contact with the appendix. There was inflammation and pus-covering serosa. The lungs disclose edema and patchy hemorrhage of the lower lobes. The heart and brain were unremarkable. Liver and kidneys showed congestion, while the other organs were normal. Microscopic examination showed acute inflammation of the appendix with focal necrosis, polymorph nucleates (neutrophilic) infiltration in the appendix wall, and fibrin on the surface (Fig. 1b–d).

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Acute inflammatory changes were also seen on the pelvic mesocolon and colon. After the comprehensive death investigation, the cause of death was septicemia due to AA. The misdiagnosis was presented at the monthly morbidity and mortality rounds of the hospital where the infant died. Morbidity and mortality rounds harbor a confidential clause and aim to identify missteps and improve clinical care. The conclusion of the death investigation permitted the case presentation for education purposes to minimize such occurrences in the future.

Discussion

The appendix is an elongated diverticulum arising from the inferior surface of the cecum [7]. The clear pathogenesis of appendicitis is still unclear, but obstruction of the lumen of the appendix is the leading hypothesis for appendicitis [8]. This obstruction may be due to various reasons, including lymphoid hyperplasia, fecaliths, parasites, etc. Lymphoid hyperplasia is commonly seen in children and young adults, and it may be secondary to viral infection [1]. There was no hyperplasia of the lymphoid tissue at the histological examination of the appendix. Notably, a fibrinous exudate does not mean a perforation. In our case, the appendix was grossed in multiple slices, and numerous histological levels were performed to avoid missing a perforation. Though appendicitis is seen in all ages, a higher incidence is reported between 10 and 19 years. The literature review indicates that misdiagnosis approaches nearly 100% in children younger than 2 years [9]. Common symptoms of AA in this age are vomiting, pain, fever, and diarrhea [10]. However, respiratory tract infection and shortness of breath may be seen at the clinical presentation and may elicit a delay in diagnosis. In infancy, the misdiagnosis is not rare, and local sepsis and complication, like in our patient, are inevitable [3, 11]. Laboratory investigation and image studies are commonly indicated to establish the diagnosis of AA. High white blood cell counts and C-reactive protein levels are good indicators for diagnosing appendicitis, especially if abdominal tenderness is present, but they may not be specific in infancy [12].

In the setting of AA, an abdominal ultrasound may show enlargement, distension, and obstruction of the appendix, high echogenicity, thick bowel loops, diminished bowel peristalsis, and pericecal and vesical free fluid. Despite some fluid collection was detected in our case, the rarity of AA in this age group-oriented the clinical team to opt-out a repeated ultrasound and computed tomography scan [13]. The initial misdiagnosis of appendicitis is associated with striking clinical pictures and complications in subsequent presentations. It is evident that reliable history and clinical examination are vital for an accurate AA diagnosis, but such setting may be quite challenging in young children [14, 15].

A similar scenario was also seen in our case. Our patient disclosed some red flags that could have alerted the clinicians not to rule out AA of an infant on a careful review of the hospital records. Some features could have alerted the physician to suspect appendicitis on ultrasound examination. They may include constant inconsolable crying, abdominal tenderness, fever, and maximal fluid accumulation in the right lower quadrant of the abdomen. The outcome would have probably been different had this been diagnosed on the first day. Such cases of misdiagnosis of appendicitis may easily end up in future litigation. Independently from the patient's age, the subsequent profile should be implemented to avoid a missed diagnosis of AA. The profile may include no "classic" signs or symptoms of AA, pain but no nausea or vomiting, absence of pelvic examination, administration of pain medication followed by discharge from the ED, diagnosis of gastroenteritis, and no specific documentation on the ED chart to return for follow-up examination within 12 h.

In conclusion, we emphasize that ED physicians should consider atypical presentations of AA in any age group. Our case highlights that appendicitis remains a differential diagnosis

when the treatment does not single out the working diagnosis, especially among infants. It also highlights the importance of an autopsy or coroner/medical examiner examination to minimize such events in the future.

Acknowledgment

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Statement of Ethics

An ethics approval is not required. This is a medicolegal case and has been released by the Medical Examiner's Office following closure of the investigation. According to the Law, the publication needs to be anonymous. This retrospective review of patient data did not require ethical approval in accordance with provincial/state and national guidelines. Written informed consent was obtained from the Deputy Chief Medical Examiner for publication of the details of the medical case and any accompanying images.

Conflict of Interest Statement

The senior author (Consolato M. Sergi) has been involved in receiving honoraria, giving expert testimony, and receiving grants and royalties (Springer, Elsevier, and Nova publishers).

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Author Contributions

All authors (Thambirajah Balachandra, Amal N. Vadysinghe, Consolato M. Sergi) contributed to the draft, collection of illustrative material, and final approval of the manuscript.

Data Availability Statement

Data are contained within the article. No new data were created or analyzed in this study. Data sharing is not applicable to this article.

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