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RESEARCH ARTICLE

A Case Series of Appendicitis and Pseudo-appendicitis in a Paediatric Intensive Care Unit

Kam L. Hon[1,*], Alexander K.C. Leung[2], Yan T.K. Lee[3], Stephanie Tsang[3], Karen K.Y. Leung[1], Wun F.A. Hui[1], Wing L. Cheung[1] and Wai Y.M. Leung[4]

[1]Department of Paediatrics and Adolescent Medicine, The Hong Kong Children's Hospital, Hong Kong, China; [2]Department of Pediatrics, The University of Calgary and The Alberta Children's Hospital, Calgary, Alberta, Canada T2M 0H5; [3]Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, China; [4]Department of Surgery, The Hong Kong Children's Hospital, Hong Kong, China

Abstract: ***Introduction*:** Appendicitis is a common childhood condition that can be diagnostically challenging. Severe cases may necessitate support in the critical or intensive care unit. These "critical appendicitis diagnoses" have rarely been described.

***Case Description*:** We retrospectively reviewed the Paediatric Intensive Care Unit (PICU) database of the Hong Kong Children's Hospital and identified cases of suspected and confirmed appendicitis. Clinical features, radiologic findings and final diagnosis of each case were summarized and reported in this case series. We review six anonymized cases of appendicitis managed in a PICU to illustrate the different age spectrum and clinical manifestations of the condition. Rupture of the inflamed appendix, peritonitis and pancreatitis were some of the complications encountered. Crohn's disease was found in one case as an underlying diagnosis. Also, one girl clinically diagnosed with appendicitis was found to be a case of ruptured hepatoblastoma with no appendicitis (*i.e.*, pseudo-appendicitis).

***Conclusion*:** Prompt diagnosis, surgical removal of the inflamed appendix, and use of appropriate antimicrobials when indicated are essential in reducing mortality and morbidity associated with severe appendicitis. Significant premorbid conditions such as acute myeloid leukemia, Mitochondrial Encephalopathy Lactic Acidosis Syndrome (MELAS), inflammatory bowel disease and complications may be present in patients needing intensive care as is illustrated in the present cases. Pseudo-appendicitis is an important differential diagnosis. Imaging is crucial and useful in establishing and confirming the diagnosis of appendicitis and pseudo-appendicitis in these PICU cases.

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1. INTRODUCTION

Acute appendicitis is a common childhood condition managed by emergency physicians and surgeons [1]. Diagnosis is often made clinically supplemented by Ultrasonography (USG) or Computed Tomography (CT) especially in complicated cases, and treatment is surgical with gratifying results. Herein, we present six anonymized consecutive cases of appendicitis managed in a Paediatric Intensive Care Unit (PICU) to illustrate the age spectrum and clinical manifestations of this condition. Prompt diagnosis, surgical removal of the inflamed appendix, and use of appropriate antimicrobials when indicated are essential to reduce the mortality and morbidity associated severe appendicitis. Rupture of the inflamed appendix, peritonitis, sepsis syndrome, and mutli-organ dysfunction are potential complications. In addition, we describe a girl clinically diagnosed with appendicitis but was found to be a case of ruptured hepatoblastoma with no appendicitis (*i.e.*, pseudo-appendicitis) (Table **1**).

2. METHODS (CASE DESCRIPTION)

We retrospective reviewed the PICU database of the Hong Kong Children's Hospital and identified cases of suspected and confirmed appendicitis. Clinical features, radiologic findings and final diagnosis of each case were summarized and reported in this case series (Table **1**).

3. CASE SERIES

3.1. Case 1

A 17-year-old boy presented to an emergency department with right lower quadrant abdominal pain for 2 days, associated with loose stool. His past health was unremarkable. Ur-

*Address correspondence to this author at the Department of Paediatrics and Adolescent Medicine, The Hong Kong Children's Hospital, Hong Kong, China; Tel: 852 35052982; Fax: 852 35127598; E-mail: ehon@hotmail.com

1875-6336/25 $65.00+.00

Table 1. Cases of appendicitis and pseudo-appendicitis managed in a PICU.

Patient	Past Health	Imaging Diagnosis	Complications
17-year-old male	Unremarkable	USG: confirmed diagnosis	Unremarkable, PICU for 1 day
12-year-old male	AML, chemotherapy	CT scan: confirmed diagnosis	Unremarkable, PICU for 2 days
1-year-old male	AML, chemotherapy	CT scan: confirmed diagnosis	Ischaemic bowel, peritonitis, fungal infection, pyelonephritis, palliative care, PICU for 14 days
6-year-old male	Unremarkable	USG, CT scan: confirmed diagnosis	Ileocolitis, subsequently diagnosed as Crohn's disease for 10 days
12-year-old male	ADHD	USG, CT scan: confirmed diagnosis	Ruptured appendicitis, peritonitis, superior mesenteric vein thrombosis, ARDS PICU for 6 days
16-year-old male	MELAS	CT scan: dilated appendix with distal appendicolith and thickened appendiceal wall.	Adhesive intestinal obstruction, pancreatitis PICU for 15 days
8-year-old female	Unremarkable	USG unremarkable; CT scan showed no appendicitis but abnormal liver. Pseudo-appendicitis	Ruptured hepatoblastoma

Abbreviations: ADHD: Attention Deficit Hyperactivity Disorder; MELAS: Mitochondrial Encephalopathy Lactic Acidosis Syndrome; AML: Acute Myeloid Leukaemia; ARDS: Acute Respiratory Distress Syndrome; USG: Ultrasound; CT: Computerized Tomography.

gent ultrasonography suggested acute appendicitis. Laparoscopic appendectomy was done, after which he was admitted to the PICU for monitoring for 1 day due to transient postoperative hemodynamic instability. When his condition stabilized, he was transferred back to the surgical ward.

3.2. Case 2

A 12-year-old boy presented with neutropenic fever (absolute neutrophil count <500 cells/µl), and right lower quadrant abdominal pain/tenderness for two days. The patient had acute myeloid leukemia with t (8, 21) translocation and was put on chemotherapy. A contrast CT suggested tip appendicitis. Empirical intravenous vancomycin and meropenem were given. In addition, red cell and platelet transfusion was given to correct the anemia and thrombocytopenia (lowest hemoglobulin 6 g/dL and platelet 20 x 10^9/L). Laparoscopic appendectomy was uneventful. Intraoperative findings confirmed distal-two-thirds appendicitis. He was transferred to the oncology ward for further management.

3.3. Case 3

A 1-year-old boy presented with neutropenic fever (absolute neutrophil count <500 cells/µl) with reduced appetite, abdominal discomfort, bilious vomiting, and diarrhea up to 10 times per day with occasional fresh blood and mucus for three days. He was newly diagnosed to have Acute Myeloid Leukemia (AML) and was on induction chemotherapy. CT abdomen showed inflammatory changes near the ileocecal valve and right hydronephrosis. The appendix could not be visualized. He was started on multiple antibiotics with antifungal coverage. Explorative laparotomy and appendectomy were done with intraoperative finding of ischemic bowel that warranted small bowel resection with stoma, and gangrenous appendicitis with appendicular abscess associated with peritonitis. Postoperatively, the patient suffered from a list of complications during his ICU stay: CT scan revealed other complications including right renal infarction and pyelonephritis, dilated small bowel and fluid collection at right lower abdomen. Five days later, his condition deteriorated further with signs of sepsis. Hence, a re-laparotomy was done to further assess the bowel status. Small bowel resection and caecectomy were performed to remove patches of ischemic bowel but the sepsis persisted. Pathology report showed dissemination of fungal infection. In the end, his parents opted for palliative care in the oncology ward after seeing their child in immense pain despite high dose analgesic. Further attempt to remove the gangrenous bowel would also render him dependent on total parenteral nutrition.

3.4. Case 4

A 6-year-old boy presented with a 2-week history of fever, decreased appetite, abdominal pain, bloody diarrhea, and oral ulcers. Upon admission, his blood tests showed a typical inflammatory bowel disease picture with microcytic anemia, neutrophilia, thrombocytosis, hypoalbuminemia, elevated C-reactive protein and Erythrocyte Sedimentation Rate (ESR), and elevated calprotectin. USG and CT abdomen showed appendicitis and ileocolitis. Laparoscopic appendectomy was performed. The child was then admitted to PICU for one day after surgery to correct electrolyte abnormalities. On postoperative day 6, he was admitted to PICU again due to fever and persistent tachycardia. Urgent CT revealed mural thickening at multiple gut segments, which included the terminal ileum, distal ileum, descending colon, and sigmoid colon. Pathology of the appendix showed granulomatous inflammation, but endoscopy was required to obtain histological specimens for diagnosis and commencement of immunosuppressive therapy. He continued to have bloody diarrhea which resulted in anemia warranting transfusion and transamine infusion. Early esophagogastroduodenoscopy and colonoscopy were done, confirming ileocolic Crohn's disease. Anti-

tumor Necrosis Factor (anti-TNF) therapy *i.e*., infliximab, was started accordingly.

3.5. Case 5

A 12-year-old boy presented with a 5-day history of on-and-off fever and progressive abdominal pain over periumbilical and right lower abdominal region. He vomited once and had blood-tinged diarrhea 3 to 4 times over preceding 2 days. Upon hospital admission, the child was febrile with gram negative bacilli septicemia. Past health was unremarkable except that he had an attention deficit hyperactivity disorder, which was treated with Ritalin IR 15 mg twice a day. USG and CT abdomen showed ruptured appendicitis and peritonitis. In view of multi-systemic involvement as evidenced by deranged liver function, common hepatic artery stenosis, and superior mesenteric vein thrombosis, he was transferred to PICU after appendectomy and treated with meropenem and amikacin. Peritoneal fluid culture showed gram positive cocci and vancomycin was added. A maculopapular rash appeared on the lower trunk and bilateral upper thighs with worsened peripheral perfusion shortly after vancomycin infusion was started - likely red man syndrome. His sepsis was further complicated by pleural effusion and acute respiratory distress syndrome. On day 6, the patient was stabilized and transferred back to the surgical ward.

3.6. Case 6

A 16-year-old boy with mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes syndrome (MELAS) had an episode of acute appendicitis which was managed conservatively in hospital with antibiotics for 4 months. However, the patient developed abdominal distention and appendicectomy was performed. He was monitored at the PICU. The appendectomy was complicated by adhesive intestinal obstruction, which required a laparotomy two days later to relieve the mechanical obstruction. On post-operative day 6, he developed pancreatitis as evidenced by increased serum amylase (plateaued at 418 IU/L), serum lipase (plateaued at >4000 U/L), and hyperglycaemia requiring insulin injections. However, CT and ultrasound scan of the abdominal did not show definite features of acute pancreatitis. His pancreatitis was managed conservatively, and enteral feed was resumed with total parenteral nutrition support. The ascitic fluid grew extended spectrum *beta-lactamase Escherichia coli* and *Pseudomonas aeruginosa*. He was treated with meropenem and amikacin for 10 days. He was discharged home 25 days after his initial operation of appendectomy, with insulin injections for impaired pancreatic function.

3.7. Case 7

An 8-year-old girl had sudden-onset of right-sided abdominal pain whilst returning from school. The pain became generalized but more severe at the periumbilical region. The pain was aggravated by movement and relieved by rest. The patient had a fever of 37.8°C. She had nausea but no vomiting. The girl was referred by her physician to the emergency department with a clinical diagnosis of appendicitis. Her blood pressure was 91/50 mm Hg, pulse 127/min with capillary refill of less than 2 seconds. Hemoglobulin was 9.7 g/dL, white cell counts 23.9 x 10^9/L, and platelet count 550 x 10^9/L. Chest and abdomen roentgenography were unremarkable. However, CT scan with contrast showed a heterogeneous vascular mass over left lobe of the liver and a hematoma, diagnosis consistent as a ruptured hepatic tumor and not appendicitis. She promptly underwent pre-emptive embolization and received chemotherapy as hepatoblastoma.

4. DISCUSSION

The diagnosis of appendicitis is largely clinical [1]. Medical imaging, and laboratory tests can be helpful in cases where the diagnosis is unclear [2, 3]. Imaging is recommended in most guidelines for management of suspected acute appendicitis [4-6]. The two most common imaging tests used are USG and CT. CT is more accurate than USG for the diagnosis of appendicitis in adults and adolescents [7]. CT has a sensitivity of 94% and a specificity of 95% [7]. On the other hand, USG had an overall sensitivity of 86% and a specificity of 81% [8]. However, USG may be preferred as the first imaging test in children and pregnant women because of the risks of radiation exposure associated with CT. In children with an acute abdomen, the clinical examination is important to determine the need for immediate surgical consultation and diagnostic imaging [9]. Because of the health risks of exposing children to radiation, USG is the preferred first choice with CT being a legitimate follow-up if the USG is inconclusive [10, 11]. In the PICU setting at the Hong Kong Children's Hospital, all our patients had imaging studies to confirm the diagnosis. Further, pseudo-appendicitis was diagnosed in one patient. Hence, imaging is important and useful in confirming and refuting the diagnosis of appendicitis.

Differential diagnoses of appendicitis in children include gastroenteritis, mesenteric adenitis, Meckel's diverticulitis, intussusception, Henoch-Schönlein purpura, lobar pneumonia, urinary tract infection (abdominal pain in the absence of other symptoms can occur in children with urinary tract infection), new-onset Crohn's disease (as in our 5th case) or ulcerative colitis, pancreatitis (6th case), abdominal trauma, distal intestinal obstruction syndrome in children with cystic fibrosis, and typhlitis in children with leukemia [3, 12-14]. We also managed a case of hepatocellular tumor misdiagnosed as appendicitis. To our knowledge, this is the first description of a ruptured hepatic tumor mistaken for appendicitis (*i.e*., pseudo-appendicitis). A rare paediatric case of gastrointestinal basidiobolomycosis mimicking appendicitis (*i.e*., pseudo-appendicitis) has also been reported [15]. Pseudoappendicitis refers to any condition mimicking appendicitis [16]. Acute right lower quadrant abdominal pain with anorexia and point tenderness (McBurney's sign) are characteristic symptoms of appendicitis [6, 16].

PICU care might be needed in approximately 1% of children with appendicitis. Predictors of more severe appendicitis have been evaluated in paediatrics emergency and ICU settings [17-19]. While children with appendicitis usually have good clinical outcomes, some develop life-threatening

complications including sepsis and organ dysfunction requiring PICU support.

Biomarker patterns derived from metabolomics and inflammatory protein mediator profiling are capable of distinguishing children with severe appendicitis from those with less severe disease which may provide an important step towards developing non-invasive diagnostic tools for clinicians in early identification of children who are at a high risk of developing severe appendicitis [17-19]. However, these markers are expensive and not time sensitive. They probably can assist but not replace scrupulous clinical skills.

Interestingly all patients with appendicitis in this PICU series were male. Two of our patients had premorbid acute myeloid leukemia treated with chemotherapy and one with MELAS [20]. Crohn's disease was an unusual but known aetiology associated with often complicated appendicitis as is illustrated in one of our patients. Complications such as gangrene of bowel, perforation of the appendix, and peritonitis occur in about 30% of children, and were present in three patients in our PICU series [20, 21].

CONCLUSION

In conclusion, significant premorbid conditions, inflammatory bowel disease and complications are present in patients with appendicitis needing intensive care.

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

LIST OF ABBREVIATIONS

ADHD	=	Attention Deficit Hyperactive Disorder
AML	=	Acute Myeloid Leukaemia
Anti-TNF	=	Anti-tumor Nerosis Factor
ARDS	=	Acute Respiratory Distress Syndrome
CT	=	Computerized Tomography
ESR	=	Erythrocyte Sedimentation Rate
MELAS	=	Mitochondrial Encephalopathy Lactic Acidosis Syndrome
PICU	=	Paediatric Intensive Care Unit
USG	=	Ultrasound

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This audit of cases is approved by the Hong Kong Children's Hospital Ethics Committee (HKCH REC 2019 009).

HUMAN AND ANIMAL RIGHTS

Helsinki Declaration has been followed for this audit of cases involving human subjects in the study.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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CONFLICT OF INTEREST

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