

CASE REPORTS

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Portomesenteric venous thrombosis as a rare complication of acute appendicitis in pediatric patient: a case presentation and literature review

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Abstract

Background: Appendicitis is one of the most common paediatric surgical emergencies, however complication with acute portomesenteric venous thrombosis is rare. Our aim is to report a case in our locality and review the clinical features and management of such rare complication.

Case presentation: A 12-year-old boy presented with a 5-day history of fever, periumbilical and right lower quadrant abdominal pain, blood-stained diarrhea and vomiting. Physical examination showed tenderness and guarding over right upper quadrant. Laboratory tests showed elevated inflammatory markers and deranged liver function. Contrast computed tomography scan showed acute appendicitis and superior mesenteric vein thrombosis. Our patient was treated with laparoscopic appendicectomy, antibiotics, and anticoagulant, with gradual improvement of thrombus observed.

Conclusion: Our patient and seventeen pediatric case reports regarding the condition since 1990 were included. Atypical presenting symptoms were noted, including RUQ pain ($n = 10$, 56%), diarrhea ($n = 8$, 44%), fever ($n = 16$, 89%), deranged liver function ($n = 13$, 72%). Patient presenting with RLQ pain were only seen in 22% ($n = 4$). Diagnosis was made by USG ($n = 1$, 5%) and computer tomography ($n = 15$, 83%). Surgical intervention includes early ($n = 9$, 50%) or interval ($n = 4$, 22%) laparoscopic or open appendicectomy, laparotomy etc. The most common causative organisms were *Escherichia coli* and *Bacteroides fragilis*. Anticoagulant use and its duration remained controversial. Anticoagulant was used in 14 patients with a mean treatment duration of 7 months, while 4 cases reporting resolution of thrombus without anticoagulant use. A high index of suspicion is needed to diagnose patient with acute appendicitis complicated by portomesenteric thrombosis.

Background

Acute appendicitis is one of the most common acute pediatric surgical condition and is commonly seen in 10–19-years-old teenage patients [1]. Septic thrombophlebitis, which is more commonly seen in adults, is an uncommon but severe complication of intra-abdominal

infection such as appendicitis, diverticulitis, and pancreatitis. In view of the potential complication of mesenteric or liver infarction and its high mortality, early identification of portomesenteric venous thrombosis is crucial. The exact pathophysiology of septic thrombophlebitis and thrombosis remained unknown, but it is proposed to be related to sepsis-induced endothelial injury, which was one of the risk factors of thrombosis according to Virchow's triad [2].

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In the case report, we will present a case of acute appendicitis complicated with portomesenteric venous thrombosis and discuss on its diagnosis and management.

Case presentation

A 12-year-old boy with insignificant past health presented with a 5-day history of fever, periumbilical and right lower quadrant (RLQ) abdominal pain, blood-stained loose stool, and vomiting. There was no family history of hematological diseases.

At the time of presentation, he had fever 39.2 °C with otherwise stable vital signs. Examination showed diffuse abdominal tenderness, which was most severe over right upper quadrant (RUQ) with guarding but negative Murphy's sign. Laboratory tests showed elevated white cell count (WCC) of $15.7 \times 10^9/L$ with absolute neutrophil counts (ANC) of $12.7 \times 10^9/L$ and C-reactive protein (CRP) of 272.0 mg/L. There was also deranged liver function at presentation, with normal total bilirubin 20 $\mu\text{mol/L}$, alkaline phosphatase (ALP) up to 552 U/L and alanine aminotransferase (ALT) 141 U/L, and deranged clotting profile with prolonged prothrombin time (PT) 13.9 s and activated partial thromboplastin time (APTT) 39.5 s. Platelet count was normal $201 \times 10^9/L$. X-rays were unremarkable.

Top differential diagnosis upon clinical assessment included ruptured appendicitis, ruptured hollow viscus, gastroenteritis, and hepatitis. Therefore, contrast computed tomography (CT) scan was arranged in view of the atypical presentation, showing a ruptured dilated 1.2 cm acute necrotic appendicitis and filling defect in superior mesenteric vein before joining the portal vein (Fig. 1a). Patchy hypoenhancement was also detected over right hepatic lobe (Fig. 1b), suspicious of suboptimal blood supply to the liver.

Emergency laparoscopic appendectomy was performed on day 1 of hospitalization with operative findings of ruptured appendicitis with no evidence of bowel or liver ischemic changes seen laparoscopically. Preoperative intravenous antibiotics with Meropenem 40mg/kg was given. No anticoagulation was started before operation. Aerobic and anaerobic cultures were performed, with the blood culture yielding *Escherichia coli* and peritoneal fluid culture yielding multiple organisms from the genera of *Bacteroides*, *Slackia*, *Gemella*, and *Parvimonas*.

The early post-operative course was eventful with systemic inflammatory response syndrome with tachycardia, fever, bilateral pleural effusion requiring respiratory support and elevated WCC, requiring admission to pediatric intensive care unit. He was kept nil by mouth to promote bowel rest and prevent bowel ischemia. He was also started on intravenous antibiotics (initially Amikacin 15 mg/kg/dose Q24H, Meropenem 40mg/kg/dose Q8H,

Vancomycin 10 mg/kg/dose Q8H and Flagyl 7.5/kg/dose Q8H, later to Cefotaxime 40 mg/kg/dose Q8H and Flagyl 10 mg/kg/dose Q8H according to culture results, respiratory support by high flow oxygen and started on fish-oil based total parenteral nutrition with aggressive fluid replacement regimen. However, there was progressive derangement of liver function with ALP 791 U/L, ALT85U/L, aspartate transaminase (AST) 356 U/L, gamma-glutamyl transferase (GGT) 356 U/L, bilirubin 22 $\mu\text{mol/L}$ and elevation of platelet up to $1112 \times 10^9/L$. A follow-up contrast CT scan was arranged on day 7 showing interval progression of portomesenteric thrombosis involving superior mesenteric vein (SMV), main portal vein, proximal right portal vein and left portal vein and its branches. In view of the progression of thrombosis, low molecular weight heparin (LMWH) at a dosage of 0.8 mg/kg Q12H was started (Fig. 2).

Patient showed gradual improvement clinically with resolution of tachycardia, fever, and weaned off respiratory support. Inflammatory markers and liver function were normalized at post-operative 4 weeks. LMWH dose was further titrated against regular blood anti-Xa monitoring for LMWH was done with a target range of 0.5–1.0units/ml. He was discharged at post-operative 5 weeks with oral levofloxacin, flagyl, and intramuscular enoxaparin. All hematological workup so far showed that patient has no underlying clotting disorder.

Gradual improvement of thrombus was observed on the 4 weeks post-operative CT scan and partial recanalization of hepatic and portal veins. Multidisciplinary approach was adopted with expert opinions from Radiologist and Paediatric Hematologist obtained. Since the infective source was removed, LMWH was stopped at post-operative 6 months as thrombosis likely secondary to the infective episode. Also, long term follow-up for portal hypertension with ultrasound was planned.

Discussion

Septic thrombophlebitis is a rare but potentially fatal complication of intra-abdominal infection. Therefore, early detection and proper management is paramount. A literature review of all reported case in English language using PubMed, MEDLINE, and ScienceDirect since 1990 was reviewed. The clinical presentation, laboratory results, diagnostic modalities, extent of thrombosis, culture results and final treatment were summarized and presented. Our patient and the 17 pediatric case reports regarding the condition since 1990 were included (Table 1).

Presentation of acute appendicitis with septic thrombosis can vary from days to weeks of abdominal pain, diarrhea, vomiting or fever [3, 4, 6–12, 14–17] to persistent pain or vomiting and diarrhea post-appendectomy



Fig. 1 Computed tomography scan on day of admission. **a** Computed tomography scan on day of admission showing filling defect in superior mesenteric vein (arrow). **b** Computed tomography scan on day of admission showing patent left and right portal vein and filling defect in superior mesenteric vein. **c** Computed tomography scan on day of admission showing patent main portal vein. **d** Computed tomography scan showing patchy hypoenhancement over right hepatic lobe (arrow)

[5, 13, 16]. The most common presenting symptom were fever ($n = 16/18$, 89%), deranged liver function ($n = 13$, 72%), RUQ pain ($n = 10$, 56%) and diarrhea ($n = 8$, 44%). Patient presenting with RLQ pain were only seen in ($n = 4$, 22%). Only one patient out of the whole case series was found to have an underlying Protein S/C, anti-thrombin III deficiency. The most common causative organisms were *Escherichiae coli* and *Bacteroides fragilis*.

In regard of the diagnostic imaging modality, even though ultrasound remains the first-line imaging modality for suspected acute appendicitis in pediatrics to minimize childhood radiation [18], computed tomography (CT) scan was helpful in case of acute appendicitis with septic thrombosis. Diagnosis was made by computer

tomography ($n = 15$, 83%), ultrasound (USG) ($n = 1$, 5%), magnetic resonance imaging (MRI) ($n = 1$, 5%) and laparotomy ($n = 1$, 5%). CT scan also allowed detection of other complications including liver abscess and bowel ischemia. Five cases developed liver abscess following the portal branches of septic thrombophlebitis [3, 9–11, 14] However, there was no reported case developing bowel ischemia following portomesenteric thrombosis-complicating appendicitis in pediatrics. Regarding the follow-up imaging for thrombosis, there was no consensus over the modality of imaging used. Doppler ultrasound, CT scan, or even magnetic resonance imaging were used in the case reports. Comparing to doppler ultrasound, CT scan might bear the advantage of detailed and

Table 1 Summary of 17 pediatric cases of acute appendicitis with portomesenteric thrombosis since 1990

Case report (year)	Age/sex	Presentation	Epigastric/RUQ pain	Deranged liver function	Underlying hematological condition	Modality of diagnosis	Extent of portomesenteric thrombosis	Causative organisms	Treatment	Use of anticoagulants (type/duration)	Outcome of thrombosis
Scully [3] (1991)	15/M	40-day RUQ pain, fever	Yes	Yes	No	CT scan	Splenic and portal (with cavernous transformation and liver abscess)	Not identified	Antibiotics, right hemicolectomy	No	Resolution of thrombosis by follow-up USG scan at 5 weeks
Sprounson [4] (1996)	11/M	26 days of diarrhea, vomiting, headache; later spiking fever and RLQ pain, also epigastric pain with RUQ tenderness on palpation	Yes	N/A	No	USG followed by doppler study followed by CT	Superior mesenteric, intrahepatic, and extrahepatic vessels of the portal vein	Yersinia enterocolitica (serology)	Antibiotics, interval appendectomy (4 months later)	No	No stated
Eire [5] (1998)	12/F	Vomiting and diarrhea 2 days after appendectomy	No	N/A	Protein S/C, anti-thrombin III deficiency	CT scan (no occlusion of portal vein/SMV), followed by laparotomy	Small thrombi in the venous branches of the peripheral mesenteric arcades and vasa rectae	N/A	Second look laparotomy, anticoagulants	Yes (IV heparin then warfarin/1 year)	Asymptomatic. Not mentioned on follow-up imaging
Kader [6] (1998)	15/M	2.5 weeks of periumbilical then right-side abdominal pain, poor appetite, fatigue, fevers, vomiting and watery diarrhea	No	Yes	No	USG followed by ultrasound doppler then CT scan	Superior mesenteric, portal, splenic	Bacteroides fragilis (in blood culture), Clostridium difficile toxin in stool	Antibiotics, anticoagulants, interval appendectomy (10 days later)	Yes (IV heparin then warfarin/6 months)	Resolution of thrombosis by follow-up USG scan at 3 months
Schmutz [7] (1998)	18/M	RLQ pain fever 2 weeks after appendectomy	No	N/A	No	CT scan	SMV	Not identified	No additional treatment	No	Resolution of thrombosis by follow-up CT scan at 6 months

Table 1 (continued)

Case report (year)	Age/sex	Presentation	Epigastric/RUQ pain	Deranged liver function	Underlying hematological condition	Modality of diagnosis	Extent of porto-mesenteric thrombosis	Causative organisms	Treatment	Use of anticoagulants (type/duration)	Outcome of thrombosis
Vanamo [8] (2001)	7/M	2-week recurrent fever, epigastric and RUQ pain, vomiting and diarrhea	Yes	Yes	No	CT scan	SMV, portal	Microaerophilic streptococci, Bacteroides fragilis (blood culture)	Antibiotics, anticoagulants, appendectomy	Yes (warfarin/1 year)	Resolution of thrombosis by follow-up MRI at 6 months
Chang [9] (2001)	8/M	6-week RUQ and back pain, vomiting, diarrhea, chills and fever	Yes	Yes	No	CT scan	SMV, splenic, portal (with liver abscess)	Escherichiae coli, anaerobic GI flora, and Streptococcus viridans (abdominal fluid culture), CD toxin (stool)	Antibiotics, anticoagulants, ileocolic resection	Yes (LMWH then warfarin/3 months)	Asymptomatic. Not mentioned on follow-up imaging
Pitcher [10] (2003)	17/M	3-week epigastric and RUQ pain, constipation, weight loss, fever	Yes	N/A	No	Ultrasound	Portal (with liver abscess)	N/A	Antibiotics, anticoagulants, appendectomy	Yes (not mentioned/not mentioned)	Resolution of thrombosis by follow-up USG at 4 months
Nishimori [11] (2004)	16/M	7-day fever, nausea and diffuse abdominal pain	No	Yes	No	Ultrasound followed by CT scan	SMV, portal (with liver abscess)	Bacteroides fragilis (blood culture)	Antibiotics, anticoagulants, appendectomy, thrombectomy	Yes (IV heparin then warfarin/not mentioned)	Resolution of thrombosis by follow-up CT scan at 3 weeks
Stitzenbeg [12] (2006)	5/F	7-day fever, vomiting, anorexia and 1-day diffuse abdominal pain	No	Yes	No	CT scan	SMV, left, portal	N/A	Antibiotics, anticoagulants, interval appendectomy (4 months)	Yes (LMWH then warfarin/3 months)	No further thrombotic events. Not stated if any follow-up imagings

Table 1 (continued)

Case report (year)	Age/sex	Presentation	Epigastric/RUQ pain	Deranged liver function	Underlying hematological condition	Modality of diagnosis	Extent of portomesenteric thrombosis	Causative organisms	Treatment	Use of anticoagulants (type/duration)	Outcome of thrombosis
Levin [13] (2008)	13/M	High fever, jaundice, mild RUQ discomfort	Yes	Yes	No	Ultrasound followed by CT scan	SMV, portal, ileocolic, other SMV tributaries		Antibiotics, anticoagulants, appendectomy	Yes (LMWH then warfarin/6 months)	Resolution of thrombosis by follow-up doppler ultrasound at 3 weeks
Patel [14] (2009)	14/M	2-day fever and night sweats, 3-day RUQ and upper back pain	Yes	Yes	No	CT scan followed by MRI scan	Anterior branch of the right portal (with liver abscess)	Not identified	Antibiotics, laparoscopic appendectomy	No	Resolution of thrombosis by follow-up MRI scan at 2 weeks
Gatibelza [15] (2009)	12/F	10-day epigastric pain and fever	Yes	No	No	CT scan	SMV	Bacteroides distans (blood culture)	Antibiotics, anticoagulants and open appendectomy	Yes (LMWH then Fluidione/6 months)	Resolution of thrombosis by follow-up ultrasound at 6 months
Gatibelza [15] (2009)	13/M	7-day persistent fever, vomiting and diffuse abdominal pain	No	Yes	No	CT scan	SMV, portal trunk, intrahepatic veins of segment V, VI, VIII	Escherichiae coli (blood culture)	Antibiotics, anticoagulants and appendectomy	Yes (Fluidione/1.5 year)	Resolution of thrombosis by follow-up ultrasound at 1.5 year
Granero-Castro [16] (2010)	17/M	8-day diffuse abdominal pain, fever and diarrhea	No	Yes	No	Ultrasound followed by CT scan	SMV and its branches, progression at 1 week to intrahepatic branches of portal vein at segments II, III	Escherichiae coli, Bacteroides fragilis (blood culture)	Antibiotics, anticoagulants, appendectomy	Yes (LMWH/4 months)	Progression of thrombus at 1 week, collateral through colic vein at 2 months
Harris [2] (2016)	13/M	Abdominal pain (RUQ and suprapubic), diarrhea, vomiting and hallucination	Yes	Yes	No	Ultrasound followed by CT scan	SMV, portal, ileocolic, other SMV tributaries	Not identified	Antibiotics, anticoagulants, interval appendectomy (3 months)	Yes (LMWH/not mentioned)	Resolution of thrombosis by follow-up CT scan at 1 month
Yoon [17] (2019)	15/M	2-day RLQ pain with 1-day fever	No	Yes	No	CT scan	SMV	Not identified	Antibiotics, anticoagulants, appendectomy	Yes (IV heparin then apixaban/3 months)	Resolution of thrombosis by follow-up ultrasound at 1 month

RLQ right upper quadrant, RLQ right lower quadrant, CT computed tomography, SMV superior mesenteric vein, IV intravenous, LMWH low molecular weight heparin

non-operator-dependent scanning, but also bear risks of radiation if repeated follow-up scans are needed. In our case, patient was initially followed up by CT scan for progress of progression and later by ultrasound for any portal hypertension as a long-term follow-up.

For the management of acute appendicitis complicated with portomesenteric thrombophlebitis, adequate sepsis

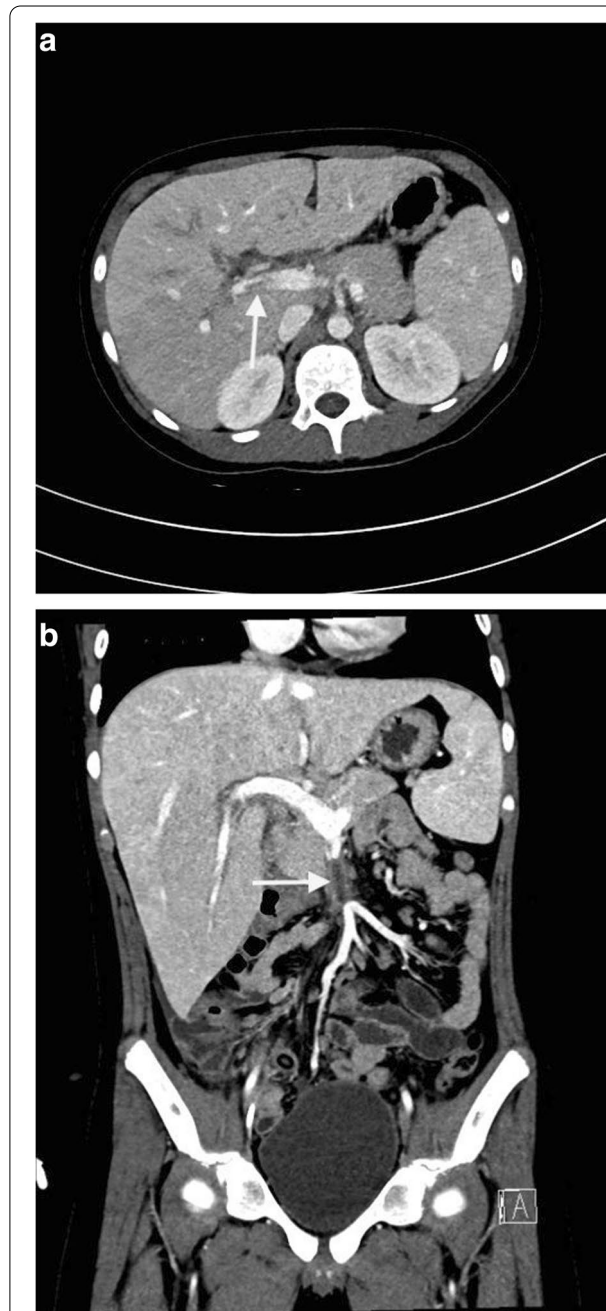


Fig. 2 Computed tomography scan on post-operative day 7. **a** Axial view CT scan showing interval progression of portomesenteric thrombosis involving main portal vein (arrow). **b** Coronal view CT scan showing interval progression of portomesenteric thrombosis involving superior mesenteric vein (arrow)

control including broad-spectrum antibiotics and appendectomy were well adopted in the reported cases [2–17]. Surgical intervention includes early operative intervention ($n = 13$, 50%) including laparoscopic or open appendectomy ($n = 12$, 66.7%), ileocolic resection ($n = 1$, 5.6%), and right hemicolectomy ($n = 1$, 5.6%). Concomitant thrombectomy was seen in 1 patient. Four patients ($n = 4$, 22.2%) had interval appendectomy with a median time of 3.5 months after presentation (range 0.5 to 4 months).

Anticoagulant was used in 14 patients with a mean treatment duration of 7 months (ranged from 3 months to 1.5 years) [2, 5, 6, 8–13, 15–17]. However, anticoagulant use and its duration remained controversial with 4 cases reporting resolution of thrombus without anticoagulant use. The American Society of Hematology 2018 Guidelines for management of venous thromboembolism suggested that for provoked venous thromboembolism events, duration of anticoagulation should be less than or equal to 3 months in pediatrics if provoking factor resolves [19]. Antithrombotic Therapy in Neonates and Children Guideline suggested thromboembolism to be managed with pediatric hematologists with a monitoring of anti-Xa blood level if low molecular weight heparin (LMWH) is prescribed [20]. In our case, we had consulted pediatric hematologists for their expert opinions before starting on LMWH with regular anti-Xa monitoring. Sepsis was well controlled with appendectomy and board-spectrum antibiotics with follow-up CT scans showed interval reduction of portomesenteric thrombus at post-operative 1 month and partial recanalization at post-operative 6 months. Therefore, anticoagulant was offered at post-operative 6 months.

Conclusion

Portomesenteric thrombosis as a rare but severe complication of acute appendicitis. A high index of suspicion is needed to diagnose patient with acute appendicitis complicated by portomesenteric thrombosis. It should be considered in patient with atypical presentation especially with fever and RUQ pain. Management might include appendectomy, antibiotics and anticoagulants. In view of the controversial use of anticoagulants, multidisciplinary management with pediatric hematologist consultation for individualized management might provide additional benefit.

Abbreviations

ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; APTT: activated partial thromboplastin time; AST: Aspartate transaminase; ANC: Absolute neutrophil count; CRP: C-reactive protein; CT: Computed tomography; GGT: Gamma-glutamyl transferase; IV: Intravenous; LMWH: Low molecular weight heparin; MRI: Magnetic resonance imaging; PT: Prothrombin time; RLQ: Right lower quadrant; RUQ: Right upper quadrant; SMV: Superior mesenteric vein; USG: Ultrasound; WCC: White cell count.

Acknowledgements

Not applicable.

Authors' contributions

Lai collected the data, reviewed the literatures, and drafted the manuscript. Hung and Leung supervised and advised in preparation of the manuscript. All authors have read and approved the final manuscript.

Funding

Not applicable.

Availability of data and materials

Available upon request.

Declarations**Ethics approval and consent to participate**

Not applicable.

Consent for publication

Written informed consent had been obtained from parents as patient is a minor.

Competing interests

Not applicable

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Received: 18 March 2022 Accepted: 8 October 2022

Published online: 31 October 2022

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