



Peritonitis Due to Intestine Perforation and Appendicitis in Children with tyfoid Fever

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Abstract:

Introduction: Children account for more than 50% of all cases of intestinal perforation in typhoid fever, but acute appendicitis as a rare complication of *Salmonella Typhi* infection. **Case:** A 4 years-old boy was admitted to the hospital with the chief complaints of fever, diffused abdominal pain, and abdominal distension. IgM *Salmonella* showed positive 10. X-ray of the abdomen revealed pneumoperitoneum. When, emergency laparotomy surgery, discovered the appendix was swollen and red. **Conclusion** This case showed that there was a relationship of *Salmonella Typhi* infection with acute appendicitis and intestinal perforation causing peritonitis

Keywords -intestinal perforation, appendicitis, *Salmonella Typhi*, typhoid fever

I. INTRODUCTION

Typhoid perforation is still frequent in children in developing countries [1]. Intestinal perforation is a rare entity in the pediatric age group when compared to adults [2]. Even though, children account for more than 50% of all cases of intestinal perforation in typhoid fever [3].

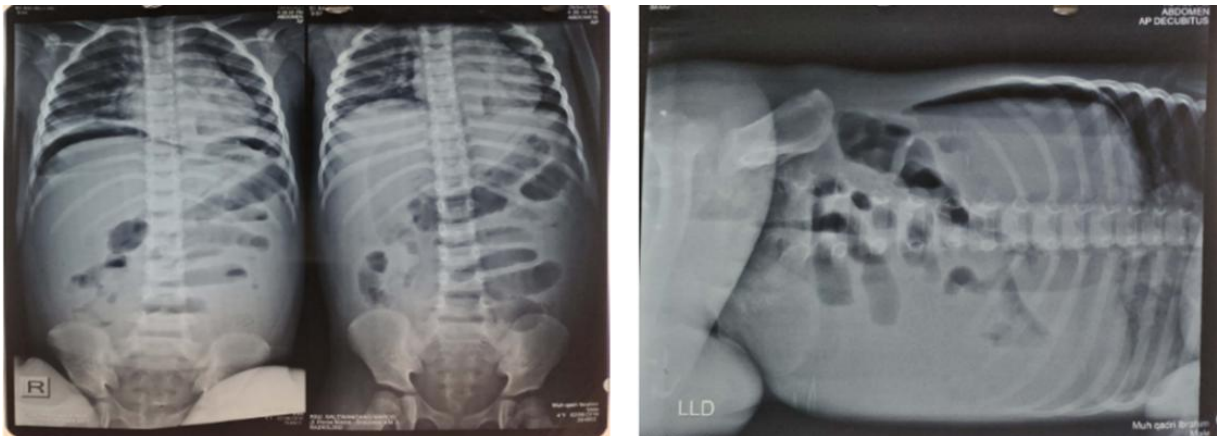
Typhoid Intestinal Perforation, which is the most common severe complication of typhoid fever, with a peak incidence aged 5-9 years. Intestinal perforation is a common cause of peritonitis requiring emergency surgical intervention. Intestinal perforation due to typhoid perforation is a serious complication [3]. Early recognition and prompt treatment are critical to prevent the morbidity and potential mortality of peritonitis and its systemic sequelae that result from the spillage of intestinal contents [4].

Infection with *Salmonella Typhi*, an enteric pathogen, is a rare cause of acute appendicitis. Typhoid fever may be associated with appendicitis as the primary presentation since the agent can lead to hyperplasia in the lymphoid tissue of the appendix or direct luminal invasion [5]. There are a few reports regarding appendicitis presentation in cases with typhoid fever [6,7]. Here, we report a child with typhoid fever presenting with peritonitis due to intestinal perforation with acute appendicitis.

II. CASE REPORT

A boy aged 4 years was admitted to our hospital with the chief complaint of pain all over the stomach, which he had experienced for 5 days before entering the hospital. Initially, the pain was felt in the periumbilical abdomen, with diarrhea, daily vomiting, and fluctuating fever for more than one week. There was no family with similar complaints. History of eating random snacks. History of being treated at Regional Hospital for 3 days receiving paracetamol and antibiotics ceftriaxone and gentamicin for 3 days, then referred to the Surgery Department of WahidinSudirohusodo Hospital with a diagnosis of generalized peritonitis and suspected intestinal perforation.

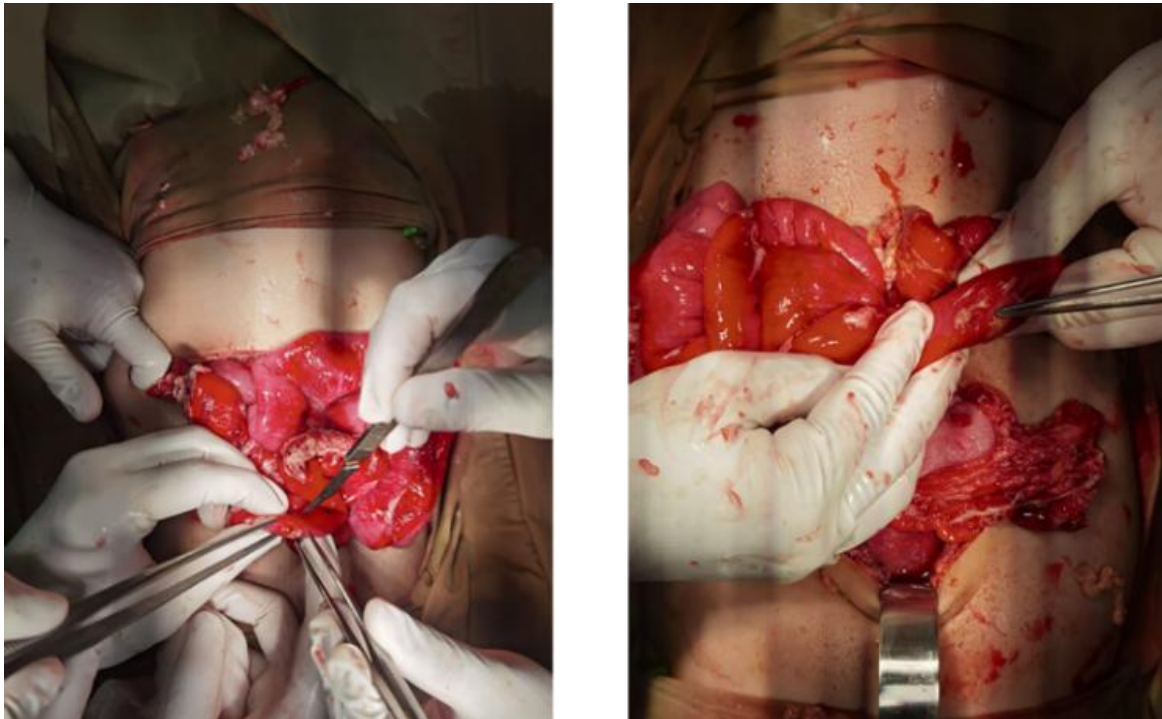
On presentation to the Emergency Department, the general condition was seriously ill, and vital signs revealed tachycardia, hyperthermia, and a pain scale of 4 FLACC (Face, Legs, Activity, Cry, and Consolability). Examination of the abdomen region revealed a decreased impression of peristalticity, muscular defansity, tenderness throughout the abdominal region, and hypertympanic liver (disappearance of liver deafness on percussion).



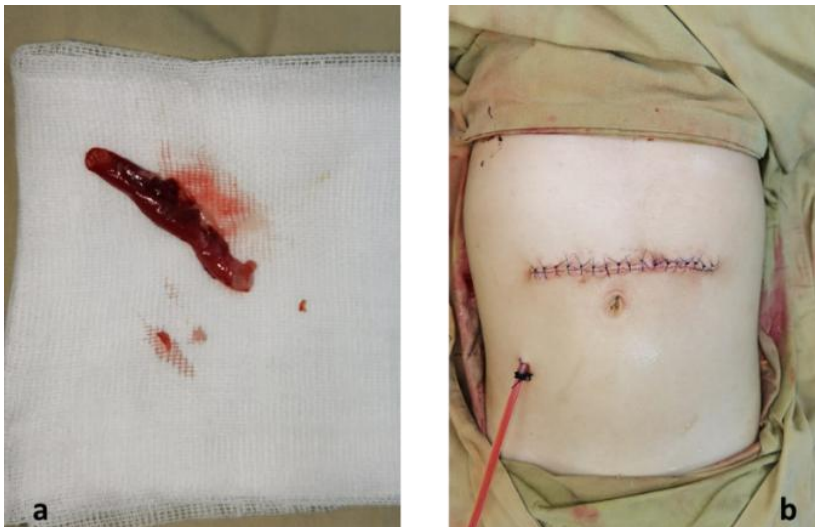
Picture 1. The presence of pneumoperitoneum is characterized by the presence of free air subdiaphragmatically

In the supporting examination, x-ray 3 positions of abdomen showed pneumoperitoneum(Picture 1) and the widal titers of *Salmonella thypi* O 1/320 and *Salmonella thypi* H 1/320 were also obtained, and the results of the *Salmonella* IgM examination (Tubex) were positive 10. The results of the supporting examination were also obtained hemoglobin 7.7 gr/dl and, albumin level 2.1 gr/dl.

The patient received a transfusion of packed red cells and albumin, administered antibiotics i.e.third generation of cephalosporin (ceftriaxone) and metronidazole. Then an emergency operation was immediately carried out.



Picture 2. A perforation with a diameter of ± 0.5 cm in the ileum



Picture 3. a) The appendix appeared hyperemic and swollen, so an appendectomy procedure was carried out.
b) The post-operative laparotomy wound

During the exploratory laparotomy surgery, fibrin was identified along the terminal ileum. Pus appeared in the pelvic cavity. A perforation with a diameter of ± 0.5 cm in the ileum which was 20 cm from the ileocaecal valve (picture 2) and appendix appeared swollen and hyperemic (picture 3a). Repair primary healing was carried out in the perforation area then the appendectomy procedure. Postoperative care was adequate antibiotic therapy, surgical wound care, and parenteral nutrition.

III. DISCUSSION

Typhoid fever is an acute and often life-threatening febrile illness that is transmitted via the fecal-oral route by the bacteria *Salmonella enterica* serotype Typhi [8]. Various risk factors for typhoid fever have been reported in many studies in Indonesia and can generally be divided into factors related to low level of education, contact

with typhoid patients, lack of access to clean water and sanitation, inadequate hand washing, poor practices and hygiene, and consumption of random food [9].

Intestinal perforation is the most common surgical complication, with a difficult challenge due to its high morbidity and mortality [10]. Children account for more than 50% of all cases of typhoid intestinal perforation (TIP), which is the most common severe complication of typhoid, with a peak age incidence of 5–9 years [11].

Typhoid fever has a wide range of manifestations in the pediatric age group. The clinical manifestations of typhoid fever in children are not typical and vary greatly, but usually there is a typhoid triad, namely fever for more than 5 days, gastrointestinal disorders and can be accompanied by or without impaired consciousness, and relative bradycardia. Gastrointestinal disorders are often seen in typhoid fever. Due to hypertrophy of Payer's patches, constipation may dominate diarrhea in some cases. Symptoms may be atypical in infants and toddlers. Approximately 10% of typhoid fevers may develop intestinal perforation under inadequate medical treatment, and symptoms may be masked in these patients [12].

On physical examination these patients usually appear very ill. Common findings include dehydration, pyrexia, pallor, due to anemia (about 50% of children with perforating typhus have a 30% decrease in hematocrit), and especially if the disease has lasted for several weeks [13].

Intestinal perforation in typhoid is often clinical, based on features of peritonitis, like in this case and investigations are performed to support the diagnosis. Plain radiographic examination of the abdomen, several patients with intestinal perforation were proven by the presence of air under the diaphragm (pneumoperitoneum), found in 55% of children with typhoid intestinal perforation. The absence of air under the diaphragm, however, does not exclude perforation [10].

The Widal test is a serological test for enteric fever, which detects antibodies against O (surface) and H (flagella) antigens. Antibody titers greater than 1:160 and greater than 1:80 for anti-H antigen and anti-O antigen respectively are considered cut-off levels for predicting recent typhoid fever infection in endemic areas. However, this cutoff depends on the geographic region. If the recovery titer is four times greater than the acute titer, the study is considered positive. Endemic areas will require higher titers to make a diagnosis and are still limited because they may represent previous infection. The Widal test is unreliable due to common false-negative and false-positive results, poor agreement with blood cultures, and poor performance. One of the main disadvantages of the Widal test is that cross-reactivity caused by other bacteria of the same genus often produces false positive results [14].

The Tubex typhoid fever serological test is a semiquantitative in vitro diagnostic examination to detect acute typhoid fever, through specific detection of the presence of serum IgM antibodies against the S.typhi O9 lipopolysaccharide antigen [15]. The advantage of Tubex over the Widal test and the gold standard blood culture is that it takes a short time to obtain results, and there is no need to set local cutoff values as with Widal. For screening and surveillance purposes, as well as in settings with limited financial and technical resources, the Widal tube agglutination test is a possible alternative that can provide the same performance as Tubex at a lower cost [16]. In this cases of positive tubex 10, it shows a strong indication of current typhoid fever infection

For Complete blood, count hemoglobin is done to identify anemia. Platelet counts were ascertained, especially in patients with evidence of coagulopathy. Although leukopenia is a more common finding in patients with uncomplicated typhoid fever, leukocytosis and neutrophilia are more common in those with intestinal perforation or cholecystitis [10]. The presence of hypoalbuminemia in this patient was associated with inflammation. Albumin decomposition increases in inflammatory conditions, and increased albumin leaving the capillaries can cause hypoalbuminemia [17].

This case report was a pediatric patient under 5 years of age, who experienced peritonitis due to intestinal perforation as a complication of typhoid fever. When an emergency laparotomy was carried out, it turned out that appendicitis was also found. This was a rare case of surgical emergency, especially in children.

It has been reported that *Salmonella typhi* may invade the intestinal mucosa at the ileocecal junction via M cells congregating in the follicle associated epithelium (FAE)[18], causing leukocytes to infiltrate into the lamina propria. Some bacteria even enter the intestinal lymphoid tissue and then flow to the mesenteric lymph nodes [19]. *Salmonella Typhi* can multiply in the submucosa, resulting in hyperplasia and hypertrophy of the mesenteric lymphoid and intestinal tissue as well as Peyer's spots. Hypertrophy followed by necrosis of

submucosal tissue may be responsible for abdominal pain followed by bleeding and/or perforation of the ileum [20, 21, 22].

Typhoid fever can present with mesenteric lymphadenopathy, ileocolitis, and even intestinal perforation, which mimics appendicitis [23, 24]. However, typhoid fever can also be associated with appendicitis. Most often, nonspecific obstruction of the lumen of the appendix causes appendicitis. Enlarged lymphoid follicles in the epithelial lining, undigested food, feces, other foreign bodies, and twisted or bent organs may cause appendicitis. Colic pain which then causes periumbilical abdominal pain is a typical symptom of early appendicitis which is caused by obstruction of the appendicitis lumen which also causes widening and thickness of the appendicitis wall. Less commonly, enteric pathogens can cause localized appendiceal lymphoid hyperplasia with obstruction or infect the appendix directly [25].

Some authors reported appendicitis in children with typhoid fever. However, no one has reported it occurring in children under 5 years. Kazlow et al presented a 13-year-old girl with abdominal pain at the right lower quadrant of the abdomen. The child underwent an appendectomy [26]. Kumar et al presented a 13-year-old boy with fever, abdominal pain, and vomiting. Based on clinical presentation and sonographic findings, acute appendicitis was diagnosed and appendectomy was done [27]. While, Likitukul in 2002 reported a 14-year-old female with symptoms similar to appendicitis but but apparently suffered from mesenteric adenitis due to *Salmonella Typhi* [28].

IV. CONCLUSION

This case showed that there was a relationship of *Salmonella Typhi* infection with acute appendicitis and Intestinal perforation causing peritonitis. This case rarely occurs, especially in children under 5 years, and this case was a surgical emergency that required immediate treatment.

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REFERENCES

- [1] Wabada S, Oyinloye AO, Usman B, Abubakar AM, Christopher RU. *Typhoid perforation in children below 5 years: a 10-year review of cases managed and outcome. PediatrSurg Int.*38(1), 2002, 143-148.
- [2] Gupta, et al. *Intestinal Perforation in Children - A Clinico-pathologic Evaluation of 67 Cases: 1451. American Journal of Gastroenterology* 106(10), 2011, 555.
- [3] Mehrabani S. 2020. *Acute Appendicitis Associated With Typhoid Fever: A Case Report and Review of Literature. Journal of Pediatrics Reviews.* 8(4), 2020, 255-260.
- [4] Hafner J, Tuma F, Hoilat GJ, et al. *Intestinal Perforation. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.* Available from: <https://www.ncbi.nlm.nih.gov/books/NBK538191/>
- [5] Zheng BH, Hao WM, Lin HC, Shang GG, Liu H, Ni XJ. *Samonellatyphi infection-related appendicitis: A case report. World J Clin Cases,*9(29), 2021, 8782-8788.
- [6] García-Corbeira P, Ramos JM, Aguado JM, Soriano F. *Six cases in which mesenteric lymphadenitis due to non-typhi Salmonella caused an appendicitis-like syndrome. Clinical Infectious Diseases,* 21(1), 1995, 231-232.
- [7] Sartori DJ, Sun K, Hopkins MA, Sloane MF. *Typhoid fever and acute appendicitis: A rare association not yet fully formed. Case Reports in Gastroenterology.* 11(2), 2017, 446-451.
- [8] Wong SY, Lee SKL, Er C, Kuthiah N. *Appendicitis in non-typhoidal salmonella bacteraemia. Oxford Medical Case Reports.*(11),2018, 082.
- [9] Alba S, Bakker MI, Hatta M, Scheelbeek PF, Dwiyanti R, Usman R, Sultan AR, Sabir M, Tandirogang N, Amir M, Yasir Y, Pastoor R, van Beers S, Smits HL. *Risk Factors of Typhoid Infection in the Indonesian Archipelago. PLoS One.* Jun 9;11(6),2016.
- [10] Ameh, Emmanuel & Abantanga, Francis. *Surgical complications of typhoid fever. Paediatric Surgery: A Comprehensive Text for Africa.*2010, 103-110.

- [11] Ameh EA. *Typhoid ileal perforation in children: a scourge in developing countries. Ann Trop Paediatr*, 19(2), 1999, 267–272.
- [12] Ahmed A, Ahmed B. *Jaundice in typhoid patients: differentiation from other common causes of fever and jaundice in the tropics. Ann Afr Med. Jul-Sep;9(3):*, 2010, 135-40
- [13] Ekenze SO, Okoro PE, Amah CC, Ezike HA, Ikefuna AN. *Typhoid ileal perforation: analysis of morbidity and mortality in 89 children. Niger J Clin Pract. 11(1)*, 2008, 58-62.
- [14] Mawazo, A., Bwire, G.M. & Matee, M.I.N. *Performance of Widal test and stool culture in the diagnosis of typhoid fever among suspected patients in Dar es Salaam, Tanzania. BMC*, 12, 2019, 316-322.
- [15] Marleni, Mimi et al. *Ketepatan Uji Tubex TF[®] dalam Mendiagnosis Demam Tifoid Anak pada Demam Hari ke-4. Jurnal Kedokteran dan Kesehatan : Publikasi Ilmiah Fakultas Kedokteran Universitas Sriwijaya*, 11, 2020, 1-7.
- [16] Ley B, Thriemer K, et al. *Assessment and comparative analysis of a rapid diagnostic test (Tubex[®]) for the diagnosis of typhoid fever among hospitalized children in rural Tanzania. BMC Infect Dis.* 24;11, 2011, 41-47.
- [17] Wiedermann CJ. *Hypoalbuminemia as Surrogate and Culprit of Infections. Int J Mol Sci.* 22(9), 2021, 4496.
- [18] Pier GB, Grout M, Zaidi T, Meluleni G, Mueschenborn SS, Banting G, Ratcliff R, Evans MJ, Colledge WH. *Salmonella typhi uses CFTR to enter intestinal epithelial cells. Nature.* 393, 1997, 79-82.
- [19] Bhan, M. K., R. Bahl, and S. Bhatnagar. *Typhoid and paratyphoid fever. Lancet* 366, 2005, 749-762.
- [20] Toapanta FR, Bernal PJ, Fresnay S, Darton TC, Jones C, Waddington CS, Blohmke CJ, Dougan G, Angus B, Levine MM, Pollard AJ, Sztein MB. *Oral Wild-Type Salmonella Typhi Challenge Induces Activation of Circulating Monocytes and Dendritic Cells in Individuals Who Develop Typhoid Disease. PLoS Negl Trop Dis.* 9(6):e0003837, 2015, 1-18.
- [21] Hoffman SL, Punjabi NH, Kumala S, Moechtar MA, Pulungsih SP, Rivai AR, dkk. *Pengurangan angka kematian pada demam tifoid berat yang diobati dengan kloramfenikol dengan deksametason dosis tinggi. Jurnal Kedokteran New England.* 310(2), 1984, 82-88.
- [22] Ochoa TJ, Santisteban-ponce J. *Salmonella. Masuk: Cherry JD, Demmler-Harrison GJ, Kaplan SL, Steinbach WJ, Hotez PJ. Buku Teks Penyakit Menular Anak Feigindan Cherry. London: Elsevier; 2019, 1066-1081.*
- [23] García-Corbeira P, Ramos JM, Aguado JM, Soriano F. *Enamkasus di mana limfadenitis mesenterika akibat Salmonella non-typhi menyebabkan sindrom mirip radang usus buntu. Penyakit Menular Klinis.* 21(1):, 1995, 231-232.
- [24] Parry CM, Hien TT, Dougan G, White NJ, Farrar JJ. *Demam tifoid. Jurnal Kedokteran New England.* 347(22), 2022:1770-82.
- [25] Bundy DG, Byerley JS, Liles EA, Perrin EM, Katznelson J, Rice HE. *Does this child have appendicitis?. JAMA*, 298(4), 2007, 438-451
- [26] Kazlow PG, Freed J, Rosh JR, Reiner M, Dische R, Benkov K, LeLeiko NS. *Salmonella typhimurium appendicitis. J Pediatr Gastroenterol Nutr.* 13 (1), 1991, 101-103.
- [27] Kumar, K. J., Chavan, A., Deb, P., Manoli, P. *Acute abdomen caused by typhoid fever mimicking acute appendicitis. MJPCH* 21(4), 2015, 1–3.
- [28] Likitnukul S, Wongsawat J, Nunthapisud P. *Appendicitis-like syndrome owing to mesenteric adenitis caused by Salmonella typhi. Ann Trop Paediatr.* 22 (1), 2002, 97-99.