Computed Tomography Features in Enteric Fever

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Abstract

Introduction: Enteric fever is a common infection in endemic areas; however, there are few reports describing the computed tomography (CT) manifestations of enteric fever. We aim to describe and illustrate CT findings in enteric fever in this study. Materials and Methods: A retrospective search of medical records in our institute for patients with positive blood cultures for Salmonella typhi, and Salmonella paratyphi organisms yielded 39 cases. Among these patients, 12 had undergone a CT study of the abdomen. The CT images, laboratory and clinical findings of these 12 patients were reviewed. Results: The most common clinical presentation was fever (100%). Typical features of gastroenteritis were present in only over half of the patients. Liver function tests were abnormal in all patients. The most common abdominal manifestations on CT were the presence of mesenteric lymphadenopathy and splenomegaly (75%). Other features were circumferential small bowel wall thickening (58.3%) and free intraperitoneal fluid (50%). Three patients were found to have complications; one with bleeding from terminal ileal ulceration, another with an ileal perforation and the third with renal abscess formation. Conclusion: CT is useful in evaluating enteric fever in patients with severe forms of presentation, a longer clinical course or less specific symptoms. Although the imaging features overlap with other abdominal infections, when combined with clinical features, travel history to endemic areas and presence of transaminitis, the diagnosis of enteric fever should be considered. CT in particular, is useful for the detection of complications such as perforation, bleeding and abscess formation.

Key words: Salmonella infections, Imaging, Typhoid, Paratyphoid

Introduction

Enteric fever is a potentially fatal multi-systemic febrile disease caused by Salmonella.¹ Salmonella are gram-negative, rod-shaped facultative intracellular anaerobic bacteria with more than 2500 serotypes that cause a broad spectrum of clinical manifestations.²,³ Clinically, Salmonella can be divided into 2 distinct categories. The first group being the non-typhoidal species that cause a majority of salmonella infections (non-typhoidal salmonellosis) with S. enteritidis and S. typhimurium being the most frequently isolated serotypes.⁴ The second group is the typhoidal species including S. Typhi and S. Paratyphi serotypes A, B and C responsible for enteric fever (also known as typhoid fever). In contrast to the non-typhoidal species, the typhoidal species are restricted only to human hosts.⁵ Worldwide, there are an estimated 22 million cases of enteric fever with the highest incidence in Asia.⁶ A high incidence of enteric fever correlates with poor sanitation and lack of access to clean drinking water. However, increasing global travel and movement of population has increased the risk of Salmonella infections, in addition to food contamination.

Clinically, the onset of enteric fever is slow with fever and constipation predominating as opposed to vomiting and diarrhoea, which are traditionally encountered in gastroenteritis.⁶ The clinical presentation and severity of symptoms are varied and the most frequently encountered symptoms include fever, headache, anorexia, nausea and
myalgia. The incubation period averages 10 to 14 days but ranges from 3 to 21 days. This wide range is likely reflective of the inoculum size and host immune status. The disease begins to resolve by the third week but complications including gastrointestinal haemorrhage, gastrointestinal perforation, neurologic effects, disseminated intravascular coagulation, pneumonia, hepatic or splenic abscess, hemophagocytic syndrome, pericarditis, endocarditis, haemolytic uremic syndrome and pancreatitis can arise. Enteric fever has a mortality rate of 10% to 20% in untreated cases; however, this decreases to less than 1% following treatment with appropriate antibiotics.

In majority of the cases, Salmonella infections produce mild and self-limiting clinical manifestations. If patients do present, they are usually treated empirically with supportive therapy and broad-spectrum antibiotics. Therefore, radiological work-up is rarely performed. There are reports describing radiological manifestations of non-typhoidal Salmonella. However, to the best of our knowledge, there are few reports written in English on the computed tomography (CT) manifestations of enteric fever and are mostly case reports.

The purpose of this study is to describe the CT manifestations of enteric fever. CT can aid in diagnosis, but more importantly, is useful in cases of severe or prolonged disease where a complication is suspected.

Materials and Methods

Institutional review board approval was obtained for this retrospective study. Written informed consent was not required for retrospective analysis. Data collection over a 7.5-year time frame, from January 2004 to July 2011 was performed. Thirty-nine patients were found to have Salmonella-positive blood cultures that grew one of the following: Salmonella typhi, Paratyphi A or Paratyphi B serotypes.

Of the 39 patients, there were 25 males and 14 females with a mean age of 24.9 years (range, 3 to 65). The blood cultures grew Salmonella typhi in 27 (69.2%), Paratyphi A in 11 (29.2%) and Paratyphi B in 1 (2.6%). Twelve of the 39 patients (30.7%) underwent CT of the abdomen and pelvis for various clinical indications. The final study population comprised these 12 patients.

The indications for CT included severe abdominal pain, sepsis, gastrointestinal bleeding and an altered mental state. CT scans were performed primarily to look for complications such as perforation, bleeding or abscess formation. The mean interval between onset of symptoms and CT scan was 13.7 days (range, 6 to 39).

Results

In the study population, the most consistent symptom encountered was the occurrence of fever which was seen in all patients. Gastrointestinal manifestations including vomiting and/or diarrhoea were only seen in 6 patients (50%). Abdominal pain was present in 9 out of 12 patients (75%). Six (50%) of the patients exhibited neurological symptoms, either in the form of confusion, drowsiness, behavioral changes or headache. All but one patient had a history of recent travel to a developing country.

Laboratory tests revealed varying degrees of abnormal liver function tests with elevation of serum transaminases.
(Normal, alanine amino transferase >70 U/L; aspartate amino transferase >50 U/L) occurring in 11 of the patients (91.7%). Eight patients (75%) demonstrated raised bilirubin levels (>30 umol/L). Anaemia (Hb <11.3 g/dL) was encountered in 9 of the 12 patients (75%). Leukopenia (Total white count <3.26 x 10^9/L) was found in 4 patients (33.3%).

The most common abdominal manifestations on CT scan were the presence of mesenteric lymphadenopathy (Figs. 1 and 2) and splenomegaly (Figs. 1 and 3), which were both seen in 8 of the 12 patients (75%). Free intra-peritoneal fluid seen in 6 patients (Figs. 1 to 3) (50%) and hepatomegaly was presented in 3 patients (25%) (Fig. 3).

Circumferential small bowel wall thickening was encountered in 7 patients (58.3%); 6 involving the terminal ileum (Fig.1) and one with diffuse jejunal wall thickening (Fig. 2). In addition, 3 of the 6 patients with small bowel thickening also showed evidence of right colon wall thickening. There was no evidence of left colon involvement. Gall bladder wall thickening was seen in one patient (8.3%) (Fig. 3). The clinical, laboratory and radiological findings are summarised in Table 1.

There were 3 patients wherein complications were demonstrated on CT; one with bleeding from terminal ileal ulceration, another with an ileal perforation (Fig. 4) and the third with renal abscess formation (Fig. 5). The former 2 underwent urgent laparotomy with subsequent small bowel resections and the latter was treated conservatively with

<table>
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<th>(%)</th>
<th>Laboratory</th>
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<th>Radiological</th>
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<td>Raised serum transaminases</td>
<td>92</td>
<td>Mesenteric lymphadenopathy</td>
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<td>92</td>
<td>Raised serum bilirubin</td>
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<td>Splenomegaly</td>
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<td>Abdominal pain</td>
<td>75</td>
<td>Anaemia</td>
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<td>Gallbladder wall thickening</td>
<td>8</td>
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*The numbers are in percentages.
intravenous antibiotics.

Discussion

Patients in our study group presented with fever and one or more gastrointestinal symptoms. More than half of our subjects also had neurological symptoms, which is reported to be variable (5% to 35%) in enteric fever, depending on geographic region and drug resistance.15 Headache can occur in up to 90% and stupor and delirium can be present in up to 40% to 70%.16

Abnormal liver functions tests and/or anaemia and leucopenia were seen in nearly all patients. Deranged liver biochemical tests are frequently seen in enteric fever with transaminases increasing up to 2 to 3 times of the normal range.17,18 The elevation of the liver enzymes is due to asymptomatic hepatitis that occurs in most patients and more than one-third may manifest clinical jaundice.19

All patients in our study population had a positive blood culture for one of the typhoidal species as it was an inclusion criteria for the study. Positive blood cultures for typhoidal organisms are seen in 60% to 80% of enteric fever cases.20 Blood culture positivity decreases after the first week and becomes negative in the fourth week. The organism can usually be cultured during the initial 2 weeks of illness. Urine and stool cultures are less frequently positive.16 It is therefore possible that we have potentially not included some of the enteric fever cases which were blood culture negative. Other tests like bone marrow aspirate which is 90% sensitive can also be performed; however, since it is an extremely painful technique, this may outweigh its benefit.21 Several serological tests, including the classic Widal test for “febrile agglutinins” are available, however, none are as sensitive or specific as culture-based methods.5 Nested polymerase chain reaction (PCR) which involves 2 rounds of PCR offers the best sensitivity and specificity. Combining assays of blood and urine, this technique has achieved a sensitivity of 83% and specificity of up to 100%.22

The literature on imaging findings are few and CT findings in enteric fever is limited, especially on the abdominal manifestations. This is due to the self-limiting nature of the disease in most of the cases with few indications for cross-sectional imaging during the course of illness. In our study, the indications were that of an acute abdomen and CT was performed to rule out intra-abdominal complications.

Mesenteric lymphadenopathy and splenomegaly were the most common CT findings in our study. Bowel wall thickening especially of the terminal ileal was seen in more than half of the patients in our study. Bowel wall thickening occurs secondary to inflammation and development of typhoidal lesions in the terminal ileum, which is the favoured site for Salmonella species. Typhoid lesions essentially consist of altered macrophages which phagocytose the typhoid bacteria as well as erythrocytes and degenerating lymphocytes.23 Well-formed granulomas as such are rare within typhoid lesions,24 but they have been described in the liver, spleen and bone marrow.25 Presumably, accumulation of typhoid lesions and the associated inflammation contribute to bowel wall thickening, mesenteric lymphadenopathy and organomegaly encountered in enteric fever.

Imaging findings of terminal ileal wall thickening and enlargement of regional lymph nodes in enteric fever was first reported in 1989 by Puylaert et al26 who used ultrasonography for evaluation. They found that although these findings were not specific for typhoid fever, the history of recent travel, neurological symptoms and leucopenia had to be considered for a diagnosis of typhoid. In 25% of our cases, right-sided colon thickening was found. In one case, we found diffuse jejunal loop thickening, and this finding has not been reported previously on CT. However in a recent review article by the authors,27 we also noted diffuse bowel wall thickening including the ileum loops, terminal ileum.

Figs. 5. (A, B). Salmonella typhi renal abscess in a 30-year-old female. Axial sections of CT (A) show a right renal abscess (arrow) at presentation that demonstrated improvement in the follow-up CT (B) after 15 days of antibiotic therapy.
and right-sided colon caused by non-typhoidal *Salmonella* enteritis and skip lesions with involvement of the right-sided colon. Findings of a thickened terminal ileum associated with mesenteric lymphadenopathy appear to be specific for bacterial enteritis of the ileocaecal region but not limited to *Salmonella*.28

Splenomegaly is a very common clinical finding in enteric fever and not surprisingly, a common finding on CT. The occurrence of anaemia and leucopenia may be explained by splenic sequestration due to an enlarged spleen, bone marrow granulomatous inflammation and haemophagocytosis.29 In our series, splenomegaly was diffuse and showed uniform attenuation in all cases except one which showed a hypodensity. This was thought to represent an abscess as it resolved with antibiotic treatment. Presence of areas of hypodensity should be looked for carefully as splenic infarction and abscesses can develop in an enlarged spleen in typhoid fever.13,14,30 Rarely, the enlarged spleen can rupture anytime during the course of illness and splenectomy is the treatment of choice with excellent outcome.31

Liver involvement is common in enteric fever as evidenced by transaminitis seen in most of the patients. In our series, 25% of patients had hepatomegaly which was mild to moderate compared to the splenomegaly. Increase in activity of the reticuloendothelial system in the liver and spleen may be responsible for the observed organomegaly. Dilation and congestion of the sinusoids along with hyperplasia of the Kupffer cells may also play a role.23 Hepatitis seen in enteric fever is generally a non-specific reactive hepatitis and the formation of hepatic granulomas is a rare complication.25

Rarely, hepatic abscesses may form in the liver and imaging with ultrasound or CT helps in detection and in guidance of drainage of the abscesses.30,32 A very rare complication of fulminant hepatitis secondary to *Salmonella typhi* has also been reported.33

In our series, gall bladder wall thickening was seen in only one patient. The thickening was general and non-specific and appeared uniformly hypodense on the contrast enhanced images. Gall bladder wall thickening is a common finding and seen in up to 62% of subjects with ultrasound.28 The low incidence of gall bladder wall thickening in our series may be due to low sensitivity of CT which was performed after 2 weeks of onset of fever as compared to within 3 days of onset of fever in the study by Mateen MA et al.28 Although the exact reason for the thickening is not known, it is most likely related to the hepatitis secondary to *Salmonella*. Rarely, acute acalculous cholecystitis can complicate the clinical course which usually responds to conservative management.4,5,35 Pancreatitis is also known to occur in enteric fever. Usually this is self-limiting and responds to conservative management.36

The development of complications depends on strain virulence, inoculum and host factors including immunosuppression and antacid therapy. Complications occur at a rate of approximately 10% to 15%.37 The incidence of intestinal hemorrhage in typhoid fever varies from 1% to 13.8%.38 Gastrointestinal bleeding and perforation result from ulceration and necrosis of the ileocaecal Peyer’s patches at the initial site of bacterial infiltration.39 This also corresponds to the most common location of ulcers due to enteric fever. It has been found that the terminal ileum was involved in 100%, the ileocaecal valve in 57%, ascending colon in 43% and transverse colon in 29% of cases; involvement of the left side of the colon was unusual.40 Therefore, in a case of known enteric fever presenting with acute abdomen, careful search should be done in these locations for presence of perforation or bleeding on CT or any other cross-section imaging techniques. Intestinal perforation can lead to generalised peritonitis, septicemia and fluid and electrolyte derangement, this is potentially life threatening and requires immediate surgical intervention.41

A rather uncommon complication of enteric fever may occur in the form of multi-organ involvement with disseminated intravascular coagulation, which can present with lower gastrointestinal tract bleeding and is potentially fatal.42

**Conclusion**

In conclusion, CT is useful in evaluating patients with severe forms of presentation, a prolonged clinical course or less specific manifestations of enteric fever. CT findings in enteric fever include splenomegaly, mesenteric lymphadenopathy, terminal ileal thickening and free fluid. The imaging features are largely non-specific but when combined with clinical history, travel to endemic areas and the presence of transaminitis, the diagnosis should be considered and is particularly useful in culture negative cases of suspected enteric fever. CT is also useful for the detection of complications such as perforation, bleeding and abscess formation.

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**REFERENCES**