

## Typhoid Perforation Associated With Rectal Bleeding in HIV- Infected Patient

Elroy Patrick Weledji<sup>[a],\*</sup>; Sophie Makajio Lemoupa<sup>[b]</sup>; Anne Njunda<sup>[c]</sup>; Dickson Nsagha<sup>[d]</sup>

<sup>[a]</sup>Department of Surgery, Faculty of Health Sciences, University of Buea, Cameroon.

<sup>[b]</sup>Muea Sub-Divisional Medical Centre, Buea, Cameroon.

<sup>[c]</sup>Department of Biomedical Sciences, Faculty of Health Sciences, University of Buea, Cameroon.

<sup>[d]</sup>Department of Public Health, Faculty of Health Sciences, University of Buea, Cameroon.

\*Corresponding author.

Received April 14, 2014; accepted July 6, 2014

Publish online August 31, 2014

### Abstract

Typhoid (enteric) fever is a common worldwide water-borne disease generally transmitted via the faecal-oral route, the causative organism being the bacterium *salmonella typhi*. Intestinal perforation is a serious complication but the preoperative diagnosis of typhoid ulcer perforation can be difficult. Both complications were concurrently treated by an emergency ileo-caecal resection alongside antibiotic treatment of typhoid. The high incidence of perforation has been attributed to late diagnosis and the emergence of multi-drug resistant and virulent strains of *salmonella typhi*. The prognosis may be poor in patients with ongoing HIV enteropathy and not on anti-retroviral treatment.

**Key words:** Typhoid fever; HIV; Perforation; Haemorrhage

.....  
Weledji, E. P., Lemoupa, S. M., Njunda, A., & Nsagha, D. (2014). Typhoid Perforation Associated With Rectal Bleeding in HIV- Infected Patient. *Gastroenterology and Hepatology*, 1(1), 11-15. Available from: <http://www.cscanada.net/index.php/css/article/view/5257> DOI: <http://dx.doi.org/10.3968/5257>  
.....

### INTRODUCTION

Typhoid fever is caused by the human specific gram negative bacillus *salmonella typhi* (Figure 1). It is

estimated that more than 33 million cases of typhoid fever occur annually causing more than 500,000 deaths<sup>[1]</sup>. If untreated or undiagnosed about 1-3% of patients may experience the most serious complications- intestinal perforations in the third week of illness<sup>[2]</sup>. The terminal ileum, colon and associated mesenteric lymph nodes are mostly affected. More than 50% of typhoid ileal perforations occur in children with a peak age of 5-9 years<sup>[3]</sup>. The prognosis is hopeless if the patient is moribund 36 to 48 hours after a perforation, with a distended or board-like abdomen, a thready pulse, and hypotension. 10% of typhoid patients may present with gastrointestinal bleed from the congested lymphoid follicles (Peyer's patches) in the submucosa of the antemesenteric border of the distal ileum, of which 2% may be severe. It is postulated that ileal lesions are due to enterotoxin produced from parasitized macrophages that caused hyperplasia, necrosis and ulceration whereas colonic involvement is due to direct bacteria invasion. The process involves both bacterial factors and the host inflammatory response<sup>[4]</sup>. Typhoid fever is one of the commonest causes of an acute abdomen with 90% of patients, many of them children perforating outside hospital<sup>[5-6]</sup>. Perforations which occur in hospital are easily missed if not suspected as it may

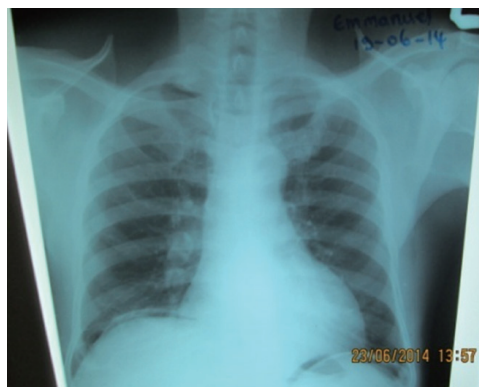


**Figure 1**  
Scanning-Electron Micrograph of *Salmonella Typhi* (With Permission<sup>2</sup>)

occur during convalescence. Most typhoid perforations present insidiously because loops of diseased gut stick together, so that leaking gut contents do not spread widely and sometimes the leak is small<sup>[7]</sup>. The surgical complications of typhoid fever are a cause of significant morbidity and mortality particularly in the resource-limited areas of sub-saharan Africa where the mortality rate from typhoid perforation have been reported to range from 9%-22%<sup>[4-5, 8]</sup>

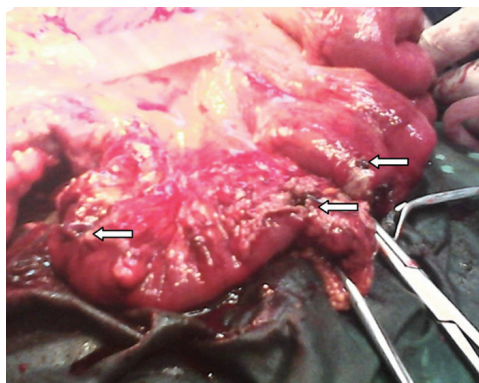
## CASE PRESENTATION

A 42-year old farmer was admitted as an emergency following a 1 week history of progressive non-specific (diffuse) and constant abdominal pain following a febrile illness of about 3 days. The pain was exacerbated by movement and standing which prevented him from farming. There was associated vomiting but no diarrhoea. He has a past history of intermittent fever but had never been tested for typhoid. He is a known HIV patient on highly-active anti-retroviral treatment (HAART) for the past nine years, and, has been clinically well since. On examination he was in great distress and although ill-looking his general condition was good. His vital signs revealed a normal blood pressure (BP 115/78 mmHg), tachycardia (104/min) and a pyrexia of 38°C. There was guarding but no board-like rigidity. The abdomen was soft but generally tender on deep palpation. Hernia orifices were normal and bowel sounds were present. The haemoglobin level was 13g/dl and a white cell count was 6.600 cells/mm<sup>3</sup>. The CD4 count was not available. Blood film was positive for malaria (820 trophozoites/ml). Serum agglutinin titres (Widal test) to the 'O' and 'H' antigens of *Salm typhi* were positive ('BO' 1/320, 'TH' 1/320 respectively). Stool microscopy showed scanty entamoeba histolytica and a few leucocytes. He was managed conservatively on the medical ward for 3 days with analgesia, intravenous fluids, broad spectrum antibiotics(i/v ceftriaxone (1 gm bd)and metronidazole (500 mg bd)) and systemic antimalaria treatment. His abdominal pain, however, progressed, and on the 4<sup>th</sup> day he complained of fresh rectal bleeding. The temperature was 38.5°C, BP 111/85 mmHg and pulse 105/min. The abdomen became more distended centrally with generalized rebound tenderness but no board-like rigidity. An erect chest x-ray revealed pneumoperitoneum (Figure 2). An ultrasound scan demonstrated an enlarged homogeneous liver with a smooth, regular outline and a hyperechoic, thickened gall-bladder wall of 6 mmd. The differential diagnosis included, a perforated typhoid ulcer, perforated peptic ulcer, a perforation from other cause e.g. diverticular or appendicular abscess, intestinal lymphoma or tuberculosis, gall-bladder empyema, strangulated gut as with volvulus, and necrotizing amoebic colitis. Following further resuscitation with i/v fluids to obtain a satisfactory urine output of at least 30 ml/ hr a



**Figure 2**  
**Erect Chest X-Ray of the Patient Showing Pneumoperitoneum From Typhoid Perforation**

laparotomy was performed. This revealed purulent free fluid in the peritoneal cavity emanating from a right lower quadrant mass consisting of omentum stuck to loops of terminal ileum including the caecum. Mobilization of the omentum off the mass revealed multiple perforations extending from the ileo-caecal junction to about 40 cm of terminal ileum seeping copious amount of dark blood (Figures 3, 4). The gall-bladder appeared normal. An ileocaecal resection including about 60 cm of terminal ileum was performed. Further copious amount of dark blood was aspirated from the ascending colon stump. An end-to-end anastomosis was fashioned with 2.0 vicryl. No abdominal drain was inserted and the abdomen was closed en-masse with 1.0 nylon. Post operatively the patient was treated with a 2- week course of oral ciprofloxacin 750 mg orally twice daily against typhoid septicaemia and a 1 week course of i/v ceftriaxone and metronidazole against intra-abdominal sepsis, the causative organisms being Gram negative bacilli and anaerobes. He had a stormy post operative recovery as he continued to have rectal bleeding for a few days post operation. His post operative haemoglobin level was 8 g/dl for which he received iron supplements. He developed a suppurating wound infection on the 5<sup>th</sup> post operative day associated



**Figure 3**  
**Terminal Ileum Showing Multiple Perforations Intraoperatively**



**Figure 4**  
**Resected Ileo-Caecal Specimen Demonstrating the Unhealthy Terminal Ileum**

with an elevated white blood cell count of 20,000/ul. This was managed with daily dressing for 10 days and the wound allowed to heal by second intention. The patient recommenced his HAART treatment 5 days post surgery when he tolerated liquid diet. He was discharged on the 20<sup>th</sup> day post surgery for typhoid perforation and rectal bleeding.

## DISCUSSION

The diagnosis of typhoid perforation is often clinical, based on the history and features of peritonitis. A precise pre-operative diagnosis can be difficult as the differential diagnosis is wide. Following resuscitation, investigations may confirm or refute the diagnosis but should not delay intervention for peritonitis<sup>[10-13]</sup>. Fever preceding the pain is a hallmark of typhoid. The patient usually complains of abdominal pain 2 or 3 weeks following the febrile illness and then suddenly has an acute exacerbation which suggests a probable perforation. Sometimes a history of peptic ulceration may suggest a perforated peptic ulcer corroborated by the resonant percussion note over the lower ribs if there is gas between them and the liver (pneumoperitoneum)<sup>[10-11]</sup>. An erect chest X-ray or a lateral decubitus film if the patient is too weak to sit up will reveal gas under the diaphragm in 50% of patients with perforation (Figure 1). There may also be loops of dilated small bowel with gas but usually with no fluid levels<sup>[11]</sup>. Rectal bleeding may further confuse the picture. A history of diarrhoea (especially with the passage of blood and mucus), followed by acute pain in the right lower quadrant, with guarding and a silent abdomen may also suggest necrotizing amoebic colitis but trophozoites would be found in the stool. Blood cultures in the first week and urine or faecal culture in the second week are diagnostic. Bone marrow culture is the most reliable test and may be positive even after prior antibiotic treatment. Culture of intraperitoneal fluid/pus may be useful. Serology (Widal test) is of no value in the

acute illness. Previous typhoid (TAB) immunization, in endemic typhoid areas where raised antibody titres are often found which does not represent current typhoid fever, antigenic cross- reactions during other infections and non-specifically in other illnesses, such as liver disease when 'amnestic reactions' may occur would have positive serology. It is only of occasional use in patients with negative blood /stool cultures.<sup>[2, 10]</sup>

Complications of typhoid may occur between 2 and 5 weeks after the onset of the illness, including intestinal perforation, intestinal haemorrhage, myocarditis, endocarditis, osteomyelitis, pancreatitis, cholecystitis and meningitis<sup>[12]</sup>. Death occurs in about 10% of patients not receiving antibiotics suggesting the importance of early goal-directed therapy<sup>[11,14]</sup>. Antibiotics are promptly required, particularly in infants, and geriatrics, debilitated, immunosuppressed patients and patients with the acquired immune deficiency syndrome(AIDS)<sup>[14-17]</sup>. Many salmonella strains are multiple antibiotic resistant due to the possession of R factors and their protecting intracellular persistence in macrophages against the humoral antibody defence mechanisms and against some antibiotic<sup>[18]</sup>. The quinolone, ciprofloxacin 200 mg intravenously or 750 mg orally twice daily is now indicated for treating multiple antibiotic resistant strains of *salmonella typhi*, although multiresistance may also arise early with the development of quinolone resistance<sup>[2, 4, 10]</sup>. For children, alternatives are trimethoprim or amoxicillin. However, the incidence of perforation and relapse is not affected by antibiotic therapy<sup>[10, 19-20]</sup>. Resuscitation is critical for typhoid complications of perforation or bleeding. Careful resuscitation in order to avoid the congestive heart failure from toxic myocarditis and prompt surgical intervention has reduced the mortality rate from typhoid perforation from 50% to 20%. A patient's prognosis will depend on the interval between the onset of his illness, and his perforation; and between this, and its closure<sup>[12]</sup>. This highlights the importance of source control<sup>[13, 15]</sup>. Surgical management is aimed at doing just as much as is necessary as these patients are compromised with septicaemia, generalized peritonitis (from enteric Gram-negative bacilli and anaerobes), dehydration and electrolyte imbalance<sup>[19-21]</sup>. Operatively the small bowel is thin and difficult to suture. A sutured small leak easily becomes larger. Thus, classically, the perforated ulcer is excised by wedge excision, a single area of diseased bowel with multiple perforations may be resected or, in the very ill patient, exteriorization of the small bowel may be the best procedure<sup>[10]</sup>. Caronna et al reported that further interventions from a second-look laparotomy (via laparostomy) after 48-72 hrs, for treatment of any new perforation, anastomotic or primary repair dehiscence improved surgical outcome<sup>[22]</sup>. This may suggest that the conventional primary repair of typhoid perforation should be preferred to intestinal resection with the risk of

anastomotic leakage and increased mortality. Some authors suggest simple peritoneal drainage under local anaesthesia in moribund patients<sup>[12]</sup>. Non-operative management may be considered for a perforation which presents insidiously, and appears to be localized, the patient is in good general condition and not deteriorating<sup>[4, 11, 16]</sup>. Intestinal haemorrhage is a less serious complication than intestinal perforation as it may stop spontaneously or a blood transfusion if required (haemoglobin level <8 g/dl) may suffice. Only if it is persistent and copious that a limited resection at the suspected level of intestinal bleeding or a right hemicolectomy including up to 60 cm of terminal ileum may be required. This is because the bleeding ulcers may be difficult to find despite an enterostomy<sup>[4,8,12]</sup>. In our case an ileo-caecal resection was performed for expedition and as colonic involvement from direct bacteria invasion is not common<sup>[17]</sup>. Post-operatively, the administration of an appropriate therapeutic antibiotic regimen for the on-going typhoid septicaemia, and intravenous broad spectrum antibiotics for the peritonitis are mandatory. Post-operative complications relating to surgical management of typhoid perforation or bleeding include wound sepsis, a burst abdomen, intestinal obstruction, intra-abdominal abscesses, fistulae, respiratory complications (e.g. pneumonia), anaemia and many weeks of inadequate nutrition and hospitalization<sup>[23]</sup>. These are the sequelae from a delayed operation, severe peritoneal contamination, a compromised nutritional status from a prolonged illness (> 2 weeks) and a high (ASA) class (II-V)<sup>[3, 23-25]</sup>. There is no significant correlation between the number of perforations and prognosis or mortality<sup>[22, 24]</sup>. Late complications may include an incisional hernia from surgical site infection<sup>[23, 25]</sup>.

## CONCLUSION

Typhoid intestinal perforation is still endemic in the developing world because of poor preventive measures such as safe drinking water, appropriate sewage disposal, and typhoid vaccination. It carries a high morbidity and mortality mostly due to delayed presentation or delay in presentation, co-morbidities and limited peri-operative care. The prognosis may be poor in HIV patients who are not on anti- retroviral treatment. A high level of suspicion is necessary as early delivery of broad-spectrum antibiotics with low resistance and appropriate surgical intervention may abort the septic process.

*Consent:* Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.”

*List of Abbreviations used:* HIV (Human immunodeficiency virus), HAART (Highly active antiretroviral therapy), TAB (Typhoid antigen bacilli immunization

*Conflict of interest:* The author(s) declares that they have no competing interests’.

*Author contributions:* EPW is the surgeon, main author, SL referred the patient and contributed to the early management of the patient, AN gave scientific advice and carried out some literature search, DN gave an epidemiological input.

*Acknowledgments:* We acknowledge Mbelley Yvan Arnaud (medical student) for promptly photographing the operative specimen

## REFERENCES

- [1] Crump, A., Luby, S. P., & Mintz, E. D. (2003). The global burden of typhoid fever. *World Health Organ Bull*, 82, 346-53.
- [2] Pegues, D. A., & Miller, S. I. (2009). Salmonella species, including salmonella typhi. In G. L. Mandell, J. E. Bennet, & R. Dolin (7<sup>th</sup> ed), *Douglas, and bennett's principles and practice of infectious diseases* (pp.2287-2903). Philadelphia: Elsevier Churchill Livingstone.
- [3] Hosoglu, S., Aldemir, M., Akalin, S., Geyik, M. F., Tacyildiz, I. H., & Loeb, M. (2004). Risk factors for enteric perforation in patients with typhoid Fever. *Am J Epidemiol*, 160, 46-50.
- [4] Chalya, P. L., Mabula, J. B., Koy, M., & Kataraihya, J. B., et al. (2012). Typhoid intestinal perforations at a university teaching hospital in Northwestern Tanzania: A surgical experience of 104 cases in a resource-limited setting. *World Journal of Emergency Surgery*, 7, 4.
- [5] Uba, A. F., Chirdan, L. B., Ituen, A. M., & Mohammed, A. M. (2007). Typhoid intestinal perforation in children: A continuing scourge in a developing country. *Pediatr Surg Int*, 23, 33-9.
- [6] Hadley, G. P. (2014). Intra-abdominal sepsis, epidemiology, aetiology and management. *Seminars in Pediatric Surgery*. *Sempedsurg*, (06), 008 (In press).
- [7] Ukwenya, A.Y., Ahmed, A., Garba, E.S. (2011). Progress in management of typhoid perforation. *Ann Afr Med*, 10, 259-65.
- [8] Sumer, A., Kemik, O., Dulger, A. C., Olme, A., Hasirci, I., Kışli, E., VedatBayrak, ... Kotan, C. (2010). Outcome of surgical treatment of intestinal perforation in typhoid fever. *World J Gastroenterol*, 16, 4164-4168.
- [9] Jayasarhya, A., Robertson, C., & Allan, P. S. (2007). Twenty five years of HIV management. *J. R. Soc Med*, 100, 363-6.
- [10] Bhutta, Z. A. (2006). Current concepts in the diagnosis and management of typhoid fever. *Br Med J*, 333, 78-82. .
- [11] Saxe, J. M., & Crospey, R. (2005). Is operative management effective in the treatment of perforated typhoid? *Am J Surg*, 189, 342-4.
- [12] Crum, N. F., (2003). Current trends in typhoid fever. *Current Gastroenterol Rep*, 5(4), 279-86.
- [13] Weledji, E. P., & Ngowe, N. M. (2013). The challenge of intra-abdominal sepsis. *Int J Surgery*, 11(4), 290-5.

- [14] River, S. E., Nguyen, B., & Haystd, S., et al. (2001). Early goal directed therapy in the treatment of severe sepsis and septic shock. *N Eng J Med, 345*, 1368-77.
- [15] Marshall, J.C., Maier, R.V., & Jimer, M., et al. (2004). Source control in the management of severe sepsis and septic shock: an evidence-based review. *Crit Care Med, 38*, 5513-26.
- [16] Nuhu, A., Dahwa, S., & Hamza, A. (2010). Operative management of typhoid ileal perforation in children. *Afr J PaediatrSurg, 7*, 9-13.
- [17] Chang, Y. T., & Lin, J. Y. (2006). Typhoid colonic perforation in childhood: a ten year experience. *World J Surg, 30*, 242-7.
- [18] Rowe, B., Ward, L. R., & Threlfall, E. J. (1997). Multidrug-resistant *Salmonella typhia* worldwide epidemic. *Clin Infect Dis, 24*, S106-S109.
- [19] Edino, S. T., Yakubu, A. A., Mohammed, A. Z., & Abubakar, I. S. (2007). Prognostic factors in typhoid ileal perforation: A prospective study of 53 cases. *JAMA, 99*, 1043-1045.
- [20] Kella, N., Radhi, P. K., Shaikh, A. R., & Leghari, F. (2010). Qureshi MA: Factors affecting the surgical outcome in typhoid intestinal perforation in children. *PaedSurg, 16(4)*, 567-570.
- [21] Wolters, U., Wolf, T., Stutzer, H., & Schroder, T. (1996). ASA classification and perioperative variables as predictors of postoperative outcome. *British Journal of Anaesthesia, 77*, 217-222.
- [22] Roberto, C., Alassan, K., Dieudonné, B., Thierry, Z., Rènè, H., Gayito, C., Ahononga, C., & Adeniran, S. (2013). Comparative analysis of primary repair vs resection and anastomosis, with laparostomy, in management of typhoid intestinal perforation: results of a rural hospital in northwestern Benin. *BMC Gastroenterology, 13*, 102.
- [23] Oheneh-Yeboah, M. (2007). Postoperative complications after surgery for typhoid ileal perforation in adults in Kumasi. *West Afr J Med, 26*, 32-6.
- [24] Atamanalp, S. S., Aydinli, B., Ozturk, G., Oren, D., Basoglu, M., & Yildiran, M. I. (2007). Typhoid intestinal perforations: twenty-six year experience. *World J Surg, 31*, 1883-1888.
- [25] Mawalla, B., Mshana, S. E., Chalya, P. L., Imirzalioglu, C., & Mahalu, W. (2011). Predictors of surgical site infections among patients undergoing major surgery at Bugando Medical Centre in Northwestern Tanzania. *BMC Surgery, 11*, 21.

## APPENDIX

**Table 1**  
**Centre for Disease Control- 1993 Revised Classification System for HIV Infection**

	Asymptomatic primary infection or PGL	Symtomatic (not A or C) conditions	AIDS, indicator conditions present
1. >500 CD4 cells/ul	A1	B1	C1
2. 200-499 CD4 cells/ul	A2	B2	C2
3. <200 CD4 cells/ul	A3	B3	C3

Note. PGL- Persistent Generalised Lymphadenopathy.