

Case Report

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Fluoroquinolone-resistant *Salmonella typhi* causing mirizzi syndrome and cholangitis: A case report

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ABSTRACT

Rationale: The emergence of fluoroquinolone-resistant *Salmonella enterica* serovar *Typhi* has become increasingly prevalent across South Asia, Southeast Asia, and sub-Saharan Africa, with resistance rates exceeding 90% in some regions. Hepatobiliary complications, particularly cholangitis and Mirizzi syndrome, are rare manifestations.

Patient concerns: A 13-year-old male developed high-grade fever, progressive jaundice, upper abdominal pain, and multiple episodes of non-bilious vomiting for 8 days.

Diagnosis: Fluoroquinolone-resistant *Salmonella typhi* complicated with acute gangrenous cholecystitis, Mirizzi syndrome and cholangitis.

Treatment: Emergency cholecystectomy and subsequent endoscopic retrograde cholangiography with biliary drainage were performed. Blood and bile cultures isolated a fluoroquinolone-resistant *Salmonella enterica* subspecies *enterica* serovar *Typhi*. The patient responded to intravenous ceftriaxone.

Outcomes: The patient was discharged after 9 days of admission, and the common bile duct stent was removed after 8 weeks following discharge.

Lessons: This case emphasizes the critical importance of culture-based diagnosis over serological testing in endemic areas and a multidisciplinary approach in complicated invasive salmonellosis.

KEYWORDS: *Salmonella typhi*; Fluoroquinolone resistance; Mirizzi syndrome; Cholangitis

1. Introduction

Typhoid fever is endemic in countries with inadequate sanitation, contaminated water supplies and overcrowding. Hepatobiliary involvement occurs in 1%-26% of cases, of which cholangitis occurs in fewer than 0.5% of cases[1]. Acute cholangitis secondary to typhoid fever is an uncommon manifestation, with most cases occurring in the setting of underlying biliary pathology. Multi-drug resistant (MDR) *Salmonella enterica* serovar *Typhi* (*S. typhi*) has been endemic in India since 1989[1]. These strains exhibit resistance to chloramphenicol, amoxycillin, and co-trimoxazole. Fluoroquinolones (FQ), introduced in the 1990s as the treatment of choice for MDR typhoid, have experienced rapidly increasing resistance rates across the Indian subcontinent. In South Asia, particularly India, Pakistan, and Bangladesh, FQ resistance rates have risen to up to 95% of isolates, with a concerning upward trend[2].

Southeast Asian countries have also witnessed rising FQ-resistance. Vietnam reported an increase from 5% in 1993-1996 to over 80% by 2013-2014. Indonesia and Cambodia have reported similar trends, with FQ-resistance detected in up to 40%-70% of isolates in recent years[2].

Recently, the emergence of third-generation cephalosporin resistance in typhoid fever now poses an escalating threat in South Asia with sporadic reports of treatment failure documented in India and Pakistan, culminating in an extensively drug-resistant (XDR) typhoid outbreak in densely populated regions of Pakistan[2].

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We present a case of Mirizzi syndrome complicated by suppurative cholangitis due to FQ-resistant *Salmonella typhi* in a 13-year-old male following empirical fluoroquinolone treatment failure, highlighting the clinical challenges posed by emerging antimicrobial resistance in endemic regions.

2. Case history

A 13-year-old male was referred for evaluation of an 8-day history of high-grade fever, progressive jaundice, upper abdominal pain, and multiple episodes of non-bilious vomiting. Loss of appetite and dark-coloured urine were also reported. Notably, the patient had experienced similar symptoms one month earlier, for which he received treatment with ciprofloxacin and cefpodoxime for 7 days based on a positive Widal test (titre 1:160) and normal abdominal ultrasonography. The initial antimicrobial therapy with ciprofloxacin and cefpodoxime was empirical, based on the clinical suspicion of enteric fever supported by a positive Widal test, and was not guided by culture and susceptibility testing. Despite initial symptomatic improvement, he developed recurrent symptoms within two weeks of completing antimicrobial therapy. The patient had no significant past medical history, no recent travel, and no family history of hepatobiliary disease or hemoglobinopathies.

On examination, the patient appeared acutely ill and icteric. Abdominal tenderness with guarding was noted. Initial laboratory investigations (complete blood count, biochemistry, inflammatory markers) revealed conjugated hyperbilirubinemia (3.4 mg/dL), elevated alkaline phosphatase (305 U/L), gamma-glutamyl transferase (313 U/L), mild anemia (hemoglobin 10 g/dL), and grossly elevated C-reactive protein (104 mg/L) (Table 1). Blood culture was obtained prior to antibiotic administration. Contrast-enhanced computed tomography of the abdomen demonstrated features of acute calculous cholecystitis with calculi in the distal cystic duct and mild intrahepatic biliary dilatation (Figure 1A). Magnetic resonance cholangiopancreatography revealed a 6-mm calculus in the distal cystic duct causing extrinsic compression and indentation of the common hepatic duct. Proximal intrahepatic biliary dilatation was confirmed. The distal cystic duct drained into the posterior aspect of the mid-third of the common bile duct. Based on these findings, emergency cholecystectomy was performed. Histopathological examination of the resected gallbladder specimen demonstrated acute inflammation with focal gangrenous necrosis. Gram stain of the resected specimen revealed occasional gram-negative bacilli.

On postoperative day two, the patient remained febrile with persistent hyperbilirubinemia and elevated inflammatory markers (Table 1). With a suspicion of biliary sepsis, endoscopic retrograde cholangiography was performed. Purulent bile was seen draining spontaneously from the ampulla of Vater, consistent with suppurative cholangitis (Figure 1B). Bile aspiration yielded frank pus which was sent for Gram stain and culture and sensitivity (Figure 1B). A 5-mm pigmented stone was extracted from the distal common bile duct (Figure 1B). A double plastic biliary stent was placed for adequate biliary decompression.

Table 1. Serial laboratory parameters during hospitalisation.

Parameters	Admission	Day 3	Day 9	Reference range
Total bilirubin, mg/dL	4.90	5.49	1.96	0.3-1.2
Direct bilirubin, mg/dL	3.40	3.99	0.86	0-0.3
ALT, U/L	54	88	73	13-32
AST, U/L	131	128	101	9-22
ALP, U/L	305	316	379	44-154
GGT, U/L	313	242	304	2-42
CRP, mg/L	104	112	14	<5

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transferase; CRP, C-reactive protein.

Gram stain of the bile aspirate demonstrated sparse Gram-negative bacilli (Figure 1C). Bile cultures grew *S. enterica* subspecies *enterica* serovar *Typhi*. The organism was identified using an automated identification system (Vitek 2 automated identification system with a GN (Gram-negative) identification card). Similar growth was also observed in blood cultures. Antibiotic susceptibility testing, performed by Kirby-Bauer disc diffusion and automated minimum inhibitory concentration (MIC) determination methods interpreted in accordance with Clinical and Laboratory Standards Institute (CLSI) M100, 35th edition guidelines revealed fluoroquinolone resistance. The isolate was resistant to ciprofloxacin (MIC=1 μg/mL) and sensitive to ceftriaxone (MIC≤0.25 μg/mL) and trimethoprim/sulfamethoxazole (MIC≤20 μg/mL). The patient was initially started on empirical piperacillin-tazobactam, which was de-escalated to intravenous ceftriaxone following culture and sensitivity results. Clinical improvement was noted within 72 hours and normalisation of laboratory parameters (Table 1). He was discharged on day nine of hospitalisation and the biliary stent was removed successfully at 8-weeks post-procedure. This case report was exempt from ethics committee review in accordance with the policy of SIMS Hospital Institutional Ethics Committee, under which single-case reports do not require formal approval. Written informed consent for publication of this report was obtained from the patient.

3. Discussion

In tropical endemic areas, several region-specific factors such as dense population, inadequate water and sanitation infrastructure have favoured the emergence of resistance. The H58 haplotype has

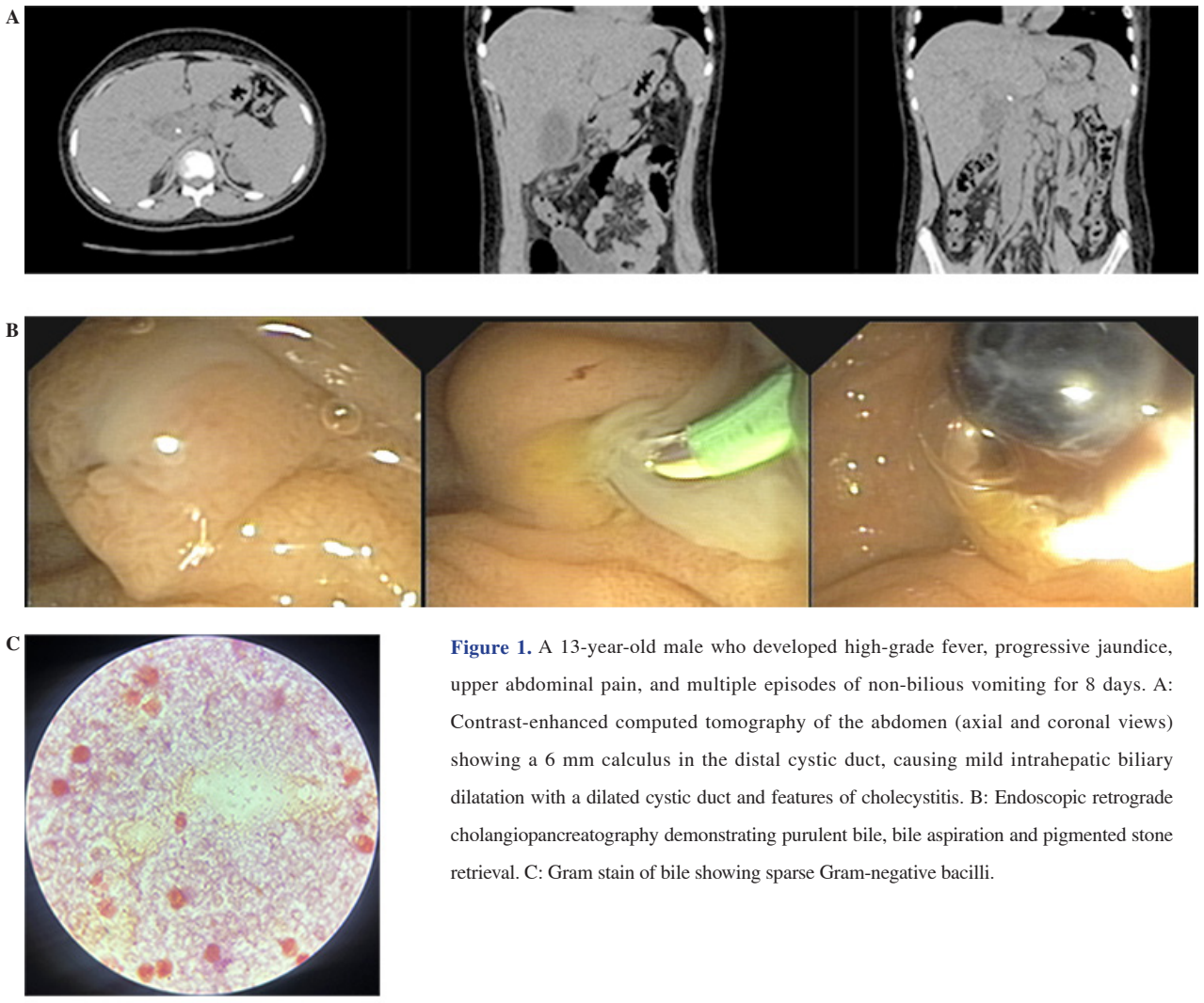


Figure 1. A 13-year-old male who developed high-grade fever, progressive jaundice, upper abdominal pain, and multiple episodes of non-bilious vomiting for 8 days. A: Contrast-enhanced computed tomography of the abdomen (axial and coronal views) showing a 6 mm calculus in the distal cystic duct, causing mild intrahepatic biliary dilatation with a dilated cystic duct and features of cholecystitis. B: Endoscopic retrograde cholangiopancreatography demonstrating purulent bile, bile aspiration and pigmented stone retrieval. C: Gram stain of bile showing sparse Gram-negative bacilli.

emerged as the dominant globally disseminated clone and is strongly associated with both MDR and FQ resistance[2]. FQ-resistance is associated with higher rates of complications, higher economic burden and more severe disease. Mortality rates, while still relatively low, are doubled in FQ-resistant strains, particularly among children and those with delayed diagnosis[3]. Vaishnavi *et al.* showed that in patients requiring biliary drainage for acute suppurative cholangitis, only 5.8% of 445 patients grew *S. typhi*[4].

Despite initial treatment with oral cephalosporins to which the organism was susceptible, our patient failed to respond. This treatment failure was likely attributable to gallstone-associated biofilm formation, which can shield bacteria from antimicrobial effects[5]. The etiology of the cholelithiasis remained undetermined, as hemolysis screening was negative and stone composition analysis was not performed.

Empirical fluoroquinolone therapy for suspected enteric fever should be avoided in regions with documented high resistance rates like India[6]. Novel genotypes resistant to cephalosporins have also been recently detected in many parts of the world, including India[2].

In endemic regions with high antimicrobial resistance, empirical treatment should be based on local resistance patterns, with adjustment according to culture and sensitivity results when available[7]. Current guidelines recommend ceftriaxone or azithromycin as first-line agents for invasive salmonellosis in regions with high fluoroquinolone resistance[8]. Cases of extensively resistant *S. typhi* have been reported to respond to carbapenems and azithromycin[2]. For complicated biliary infection, source control through cholecystectomy and/or biliary drainage is essential in addition to appropriate antimicrobial therapy.

Hepatobiliary complications of typhoid fever, while rare, have been increasingly reported in the literature. Rajan *et al.* reported a case of typhoidal acute acalculous cholecystitis with ciprofloxacin-resistant *S. typhi* requiring cholecystectomy and subsequent meropenem therapy[9]. However, the combination of Mirizzi syndrome with suppurative cholangitis caused by fluoroquinolone-resistant *S. typhi* in a pediatric patient, as in our case, has not been previously

reported.

Broader integration of typhoid vaccination into national immunization programs in endemic countries represents a strategic approach to reducing overall disease incidence and morbidity. This case highlights the alarming global emergence of fluoroquinolone resistance in salmonellosis within tropical endemic regions. It emphasizes the importance of antimicrobial stewardship, culture-based diagnosis over serological testing, and multidisciplinary management in complicated invasive salmonellosis.

Conflict of interest statement

The authors declare that they have no conflict of interest.

Ethical approval and consent for publication

Ethics approval was exempt for single-case reports as per SIMS Hospital Institutional Ethics Committee. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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Authors' contributions

RS conceived the study, designed the manuscript framework, defined the intellectual content, performed literature retrieval, collected clinical data, drafted the original manuscript and revised the manuscript. BR conducted manuscript review. ABR and SSG participated in data acquisition. All authors read and approved the final version of the manuscript.

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