

Shewanella: an important, emerging and lethal pathogen in a patient with recurrent presentations of cholangitis

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SUMMARY

We present a case of recurrent cholangitis caused by *Shewanella algae*, a lethal, emerging pathogen that clinicians should be made aware of. An 86-year-old man with a history of gastrectomy for peptic ulcer disease and a cerebrovascular accident with known choledocholithiasis presented with recurrent episodes of cholangitis that failed conservative antibiotic treatment regimens. *Shewanella* has been described to have increasing resistance to piperacillin and tazobactam. Both *S. algae* and multidrug-resistant *Escherichia coli* were co-isolated in this patient, which required broader spectrum antibiotics for successful treatment and management. A high index of suspicion is required if the history is suggestive of marine or aquatic exposure, which could expose the patient to this lethal pathogen. Re-thinking and re-taking the history are important cornerstones in refining the diagnosis when faced with recurrent presentations of the same problem.

BACKGROUND

This case highlights the significance of *Shewanella* as a causative pathogen for difficult to treat cholangitis.

Cholangitis is most commonly caused by colonic bacteria.¹ It can be caused by both gram-positive and gram-negative bacteria; however, *Escherichia coli* is the main gram-negative bacterium isolated, followed by *Klebsiella* and *Enterobacter*. *Enterococcus* is the most common gram-positive species.

The most common causes of biliary obstruction in patients with acute cholangitis without bile duct stents are biliary calculi (28%–70%), benign biliary stricture (5%–28%) and malignancy (10%–57%).² We describe a patient with choledocholithiasis.

CASE PRESENTATION

Our case is an 86-year-old man from a residential aged care facility with recurrent presentations of cholangitis with *Shewanella algae* isolated. His history included a partial gastrectomy for peptic ulcer disease, large left middle cerebral artery watershed infarct resulting in expressive aphasia, atrial fibrillation, benign prostatic hyperplasia, nephrolithiasis and hypercholesterolaemia.

He had previously presented with acute cholecystitis in October 2015 and was commenced on intravenous antibiotics (ceftriaxone and metronidazole). His liver function tests (LFTs) were all within normal range. As he was taking clopidogrel prior to presentation, a decision was made to treat him with

antibiotics and defer surgery unless he deteriorated. He improved clinically and was discharged with oral antibiotics and a planned elective laparoscopic cholecystectomy which he underwent in January 2016. His intraoperative cholangiogram showed a dilated common bile duct (CBD) but no filling defect (figure 1). He was discharged home on day 2 without complication. Histology showed chronic cholecystitis and cholelithiasis.

Two years later, he presented with cholangitis secondary to choledocholithiasis with an associated *E. coli* bacteraemia. His initial symptoms were dizziness and vomiting. He was febrile, tachycardic and hypotensive on arrival to the emergency department. LFTs showed a normal bilirubin of 8 $\mu\text{mol/L}$ (normal range: $<22 \mu\text{mol/L}$), an elevated alkaline phosphatase of 228 IU/L (normal range: 30–110 IU/L) and gamma-glutamyl transpeptidase of 323 IU/L (normal range: 10–71 IU/L). His white cell count (WCC) was $5.5 \times 10^9/\text{L}$ (normal range: $4 \times 10^9/\text{L}$ – $10 \times 10^9/\text{L}$) and C reactive protein (CRP) was 95 mg/L (normal range: $<5 \text{ mg/L}$). *E. coli* was isolated on blood cultures in both aerobic and anaerobic bottles. It was sensitive to amoxicillin/clavulanate, gentamicin and meropenem, and resistant to cefazolin, amoxicillin and ceftriaxone. Magnetic resonance cholangiopancreatography (MRCP) confirmed two large CBD stones (figure 2). He was treated with piperacillin and tazobactam (Tazocin) and gentamicin on advice from the infectious diseases (ID) team. He underwent an attempted endoscopic retrograde cholangiopancreatography (ERCP), initially starting with a gastroscop to confirm the post-gastrectomy anatomy. Clean bile was seen flowing through the biliary limb of the gastrojejunostomy using a paediatric gastroscop. Unfortunately, the biliary limb was unable to be entered with a duodenoscope despite multiple attempts so the procedure was abandoned with a plan for percutaneous transhepatic cholangiography (PTC) if he were to deteriorate. Fortunately, he improved daily following 10 days of Tazocin. His inflammatory markers and LFTs improved, and he was eventually discharged home on 5 days of oral amoxicillin and clavulanic acid.

Two months later, he re-presented with fever, nausea, vomiting, hypotension and collapse. Bloods showed a cholestatic picture with a bilirubin of 49 $\mu\text{mol/L}$ (normal range: $<22 \mu\text{mol/L}$), WCC of $16.8 \times 10^9/\text{L}$ ($4 \times 10^9/\text{L}$ – $10 \times 10^9/\text{L}$), CRP of 161 mg/L (normal range: $<5 \text{ mg/L}$) and international normalised ratio of 2.3. *E. coli* and *S. algae*



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Figure 1 Intraoperative cholangiogram from his laparoscopic cholecystectomy showing a dilated common bile duct (red arrow) with no filling defect.

were both isolated on blood cultures in both aerobic and anaerobic bottles. *E. coli* was only sensitive to gentamicin and meropenem, and resistant to cephazolin, ciprofloxacin, amoxicillin, amoxicillin/clavulanate and ceftriaxone. *S. algae* was sensitive to ciprofloxacin, gentamicin, ceftriaxone and meropenem, and resistant to cefazolin, amoxicillin and amoxicillin/clavulanate. Abdominal ultrasound scan (USS) showed biliary dilatation of 25 mm in the distal CBD with associated choledocholithiasis

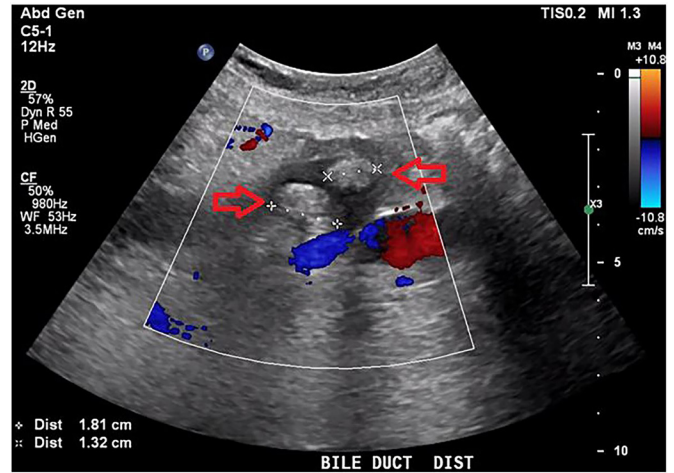


Figure 3 Abdominal ultrasound scan showing two gallstones in the distal common bile duct measuring 1.81 cm and 1.32 cm (red arrows).

(figure 3) and wall thickening of the CBD likely related to cholangitis (figure 4). PTC was discussed with the family and a decision was made not to proceed given he was improving clinically with current treatment. He was treated with 5 days of Tazocin and discharged home without any available effective oral antibiotic on advice of the ID team given the multidrug-resistant nature of *E. coli*.

Sadly, he was re-admitted 2 days later with recurrent symptomatic cholangitis. On this admission, he was commenced on meropenem, a broad-spectrum carbapenem antibiotic. Additionally, he underwent PTC with biliary drainage where the biliary stones in the CBD were able to be crushed and pushed into the duodenum (figure 5). Repeat cholangiogram showed no evidence of filling defects. After 17 days of meropenem, he improved significantly, the biliary drain was removed and he was discharged home.

DIFFERENTIAL DIAGNOSIS

Given he had previously undergone a laparoscopic cholecystectomy, acute cholecystitis could be ruled out. A biliary leak presenting 2 years after a laparoscopic cholecystectomy would be very rare and there was no evidence on CT imaging that this

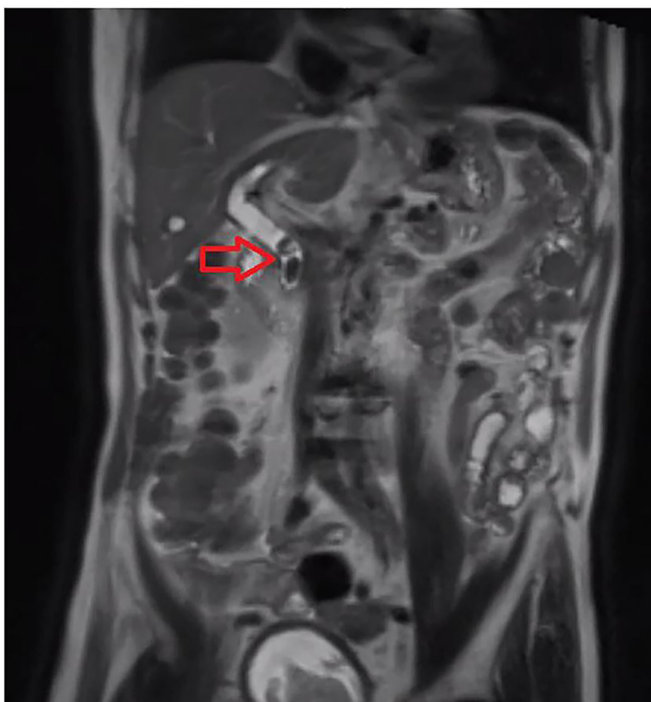


Figure 2 Magnetic resonance cholangiopancreatography showing two common bile duct gallstones (red arrow).

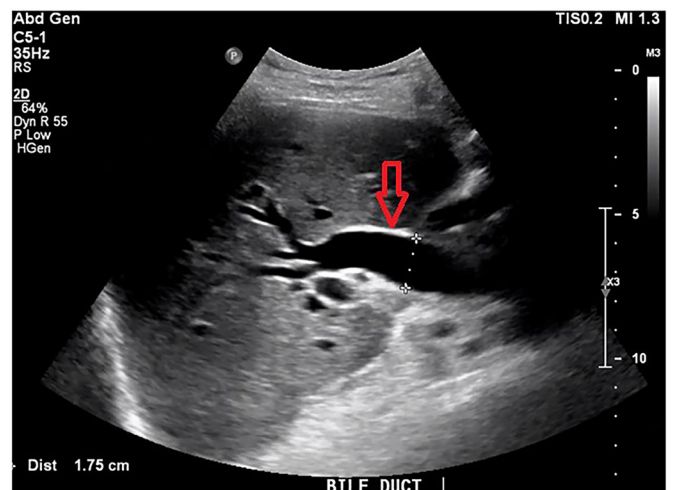


Figure 4 Abdominal ultrasound scan showing mild common bile duct wall thickening consistent with cholangitis (red arrow).

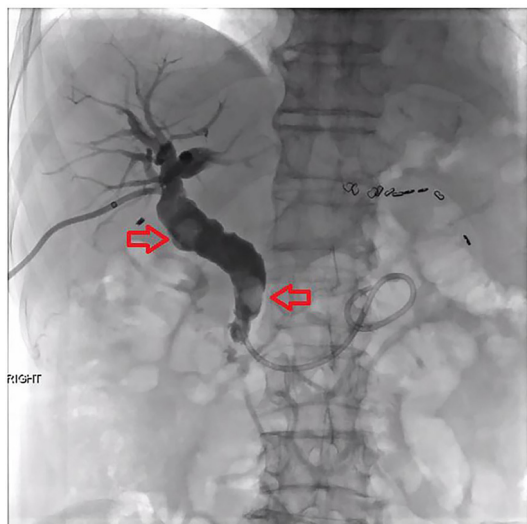


Figure 5 Percutaneous transhepatic cholangiogram. Two gallstones are seen in the common bile duct (red arrows) before they are crushed and pushed into the duodenum.

was the case. Lipase levels were never elevated with his recurrent presentations nor was there any radiographic evidence of focal or diffuse enlargement of the pancreas, thus excluding the possibility of acute pancreatitis. A liver abscess was certainly a possibility; however, there was no evidence on USS or CT imaging. Given his multiple presentations, as well as previous investigations (MRCP and USS) and a failed ERCP, this case was certainly concerning for untreated choledocholithiasis as a cause of acute cholangitis.

OUTCOME AND FOLLOW-UP

He has remained well since discharge and has not required admission to any health service for further management of cholangitis or any other medical problem.

DISCUSSION

Shewanella spp are commonly associated with marine and aquatic environments. They are saprophytic, motile, gram-negative bacilli that are widely distributed in nature.³ The genus *Shewanella* has been categorised into three species, namely, *S. putrefaciens*, *S. hanedai* and *S. benthica*. *S. putrefaciens* is organised into four groups genotypically (I-IV) and strains in group IV are recognised as *S. algae* by some authors.⁴ Our patient grew up near a lake and enjoyed eating all kinds of seafood such as fish and prawns. He never ate raw seafood and spent a short period of his childhood near water before moving to the city areas.

Khashe and Janda⁵ reported that *S. algae* is the predominant human clinical isolate (77%), whereas *S. putrefaciens* represents the majority of non-human isolates (89%). Both were initially considered to be colonisers thriving on previously damaged tissue⁴; however, reports of their clinical significance are emerging. *Shewanella* has been isolated from wounds, urine, faeces, cerebrospinal fluid, bile and various other clinical samples.⁴

Shewanella spp are susceptible to carbapenems, aminoglycosides, quinolones, extended-spectrum cephalosporins and β -lactamase inhibitor combinations.^{6,7} A study by Vignier *et al*⁸ reported that 50% of *Shewanella* infections were polymicrobial in origin. Co-isolates, as demonstrated in our case, of both *E. coli* and *S. algae* being identified are clinically significant in the development

of increased microbial resistance, resulting in limited treatment options and increased morbidity and mortality. There is recent epidemiological data showing increasing drug resistance especially to piperacillin–tazobactam and imipenem.^{9–12} This may explain the recurrent presentations of our patient.

Otsuka *et al*¹³ reported on a case of a 67-year-old Japanese man with primary sclerosing cholangitis who died from multi-organ failure from *Shewanella*. This was on a background of having had a distal gastrectomy for early gastric cancer 5 years prior. Several reports have demonstrated that *Shewanella* can cause lethal sepsis in patients with hepatobiliary disease.⁷ It would be interesting to research whether a distal gastrectomy and rearrangement of the gastrointestinal tract predisposes patients to developing *Shewanella* biliary infections as in our case and that reported by Otsuka *et al*¹³

Questions yet to be answered by the current body of research include whether *Shewanella* is contributing to more presentations of cholangitis. It would be also be interesting to investigate if *Shewanella* infections are contributing to increased morbidity and mortality, more intensive care admissions and increased hospital length of stay.

It is important to note that the presence of a foreign body such as a stone in the biliary tree can act as a nidus for bacterial colonisation. Bile taken from patients without biliary obstruction is sterile or almost sterile.¹⁴ Comparatively, approximately 70% of all patients with gallstones have evidence of bacteria in the bile.^{14,15} Our case highlights the development of biliary stones after a cholecystectomy, which were unable to be cleared by ERCP due to encountering difficult anatomy. It was not until the patient's third presentation of recurrent cholangitis where the stones were able to be successfully removed and appropriate targeted antibiotics used. Subsequently, the patient remained well and did not require any further hospital admissions.

History taking remains the cornerstone to an accurate diagnosis and a thorough list of differential diagnoses. Noting any exposure to marine or aquatic environments or the consumption of raw fish may be helpful clues for recognising *Shewanella* in cholangitis. In this case, he had some exposure to an aquatic environment growing up which may be a risk factor for being colonised with *Shewanella*. Importantly, the medical community must be made aware of this emerging pathogen as a rare cause for cholangitis, particularly if there is a high index of suspicion because of its worrying morbid features. This case aims to convey this awareness. Although *Shewanella* was not isolated until his second admission, it may have been in fact an underlying contributor to his original presentation, but may have just been difficult to isolate.

In this case, a multidisciplinary approach to this patient was required. It involved expertise from a surgical team, interventional radiologist and ID team.

Patient's perspective

His daughter, next of kin, had the following comments from her perspective: 'I am very appreciative of the medical care my father received over the course of multiple admissions. I am very grateful to the staff and their expertise. There were times when my father was very unwell and I am glad that the hospital and doctors were able to perform the necessary procedures to get him better and eventually discharge him back home'.

Contributors All authors have made an individual contribution to the writing of the article and not just been involved with the patient's care. JH and CS: conception

Learning points

- ▶ *Shewanella* and its spp are a rare but possibly emerging pathogen as a cause for cholangitis among other diseases. *Shewanella* is a potentially lethal organism, which can result in high morbidity and mortality. A high index of suspicion is required if the history is suggestive of exposure to marine or aquatic environments when seeing recurrent presentations of cholangitis.
- ▶ This case report is aimed to highlight the importance of re-thinking the diagnosis and thoroughly re-taking the patient's history to inform an accurate differential diagnosis in a patient with recurrent presentations of cholangitis. The identification of multidrug-resistant organisms can be a clue that a co-isolate, which may not be immediately identified, could be the cause of the recurrent presentations and an escalated treatment strategy may need to be employed earlier on.
- ▶ Treatment of cholangitis not uncommonly requires a multidisciplinary approach as outlined in our case. This patient required input from a surgical team, interventional radiologist and infectious diseases team, which resulted in a positive outcome for the patient.

and design. JH: acquisition of data or analysis and interpretation of data, and agreement to be accountable for the article and to ensure that all questions regarding the accuracy or integrity of the article are investigated and resolved. JH, CS, EW and BK: drafting the article or revising it critically for important intellectual content, and final approval of the version published.

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