# SHORT COMMUNICATION

# Salmonella enteritidis abdominal aorta mycotic aneurysm presented with acute cholestatic jaundice: A case report and literature review

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### **ABSTRACT**

Mycotic aneurysm is one of the extra-intestinal manifestations of *Salmonella* Enteritidis infection. The diagnosis of this condition is challenging owed to its variation in clinical presentations. We presented a case of a 54-year-old man with underlying diabetes mellitus and chronic smokers presented with acute right flank pain and fever associated with mild jaundice. The initial laboratory investigations suggested features of obstructive jaundice and urinary tract infection. The contrast enhancing computed tomography of the abdomen revealed the presence of saccular mycotic aneurysm located at the infrarenal abdominal aorta. The blood culture grew *Salmonella* Enteritidis which was susceptible to ceftriaxone, trimethoprim-sulfamethoxazole, ciprofloxacin, ampicillin, and amoxicillin-clavulanic acid. Intravenous ceftriaxone was initiated, and he underwent open surgery and artery repair at day 8 of admission. He responded well to the treatment given and subsequently discharged home after completed three weeks of intravenous ceftriaxone.

Keywords: Infrarenal; mycotic aneurysm; Salmonella Enteritidis.

### **INTRODUCTION**

Salmonella species are gram-negative bacilli and facultative anaerobe. There are two species of salmonella exist which are Salmonella enterica and Salmonella bongori. Majority of the medically important Salmonellae belongs to Salmonella enterica. Non-typhoidal salmonella serotypes have broad vertebrate host range, and they cause wide spectrum of clinical presentation but most of the time it is associated with diarrheal diseases (Feasey et al., 2012). Predominantly, patients with non-typhoidal salmonella infection have underlying medical conditions or they are immunocompromised (Lee et al., 2005). Although most of the time the infection is limited to gastrointestinal tract, extra-intestinal involvement does occur. The extra-intestinal infections can manifest as meningitis, osteomyelitis or arthritis and urinary tract infection. Endovascular infection that includes mycotic aneurysm is one of the extra-intestinal manifestations by this bacteria.

Mycotic aneurysm can be defined as the localized abnormal dilatation of the arterial wall secondary to an infective process that leads to the destruction of the vessel wall. The prevalence of the infected aneurysm was stated to be around 0.7 to 1% of the population and any artery can be involved in this process (Lee et al., 2008). Staphylococcus and Streptococcus spp. are the most commonly isolated bacteria, but in East Asia Salmonella spp. are the most important causative agent (Lee et al., 2008). Prompt diagnosis and treatment are required in the case of mycotic aneurysm to prevent morbidity and mortality in the patient.

#### **CASE REPORT**

A 54-year-old man with long standing diabetes mellitus and heavy smoker presented with three days history of acute right flank abdominal pain and fever. This was associated with urinating teacolored urine, pale stool, and nausea. Apart from that there was no other gastrointestinal complaint such as vomiting, diarrhea and constipation. He denied any other symptoms. Physical examination noted he was hypertensive with blood pressure of 164/93 mmHg, tachycardia with pulse rate of 138 beats per minute and mildly tachypnea with respiratory rate of 22 breaths per minute. He was mildly jaundice and febrile with body temperature of 39.2°C. The abdominal examination revealed tenderness mainly at the right hypochondriac and right lumbar regions but no abdominal mass palpable.

The blood investigations showed that his diabetic control was poor with HbA1c level of 11% (normal range: 4.4%-6.4%) and fasting blood glucose of 18.19 mmol/L (normal range: 3.89-5.83 mmol/L). Leucocytosis with total white cell count (WCC) of  $14.9\times10^9/L$  predominantly neutrophilia with neutrophil count of  $12.4\times10^9/L$ , elevated C-reactive protein (CRP) level at 22.88 mg/dL, deranged liver enzymes with markedly increased alkaline phosphate (ALP) at 506 U/L and mildly increased in alanine transaminase (ALT) at 62 U/L were also noted. The bilirubin concentration was raised at 115.2  $\mu$ mol/L. Urine leukocyte was positive for 3+. Thus, the initial working diagnosis was obstructive jaundice to rule out ascending cholangitis and urinary tract infection. He was given stat

dose of 2-gram ceftriaxone intravenously. The blood and urine for culture was taken before antibiotic commencement and was sent to microbiology laboratory. He was admitted to the ward for further management.

The ultrasound abdomen was performed on the day of admission noted presence of gallbladder polyp but was unable to rule out ascending cholangitis. Subsequently, contrast-enhanced computer tomography (CECT) of the abdomen was performed and revealed the presence of saccular infrarenal aortic aneurysm measuring 1.8 cm  $\times$  1.3 cm  $\times$  1.7 cm with periaortic hematoma measuring 1.8 cm  $\times$  1.3 cm noted. There was also small splenic abscess. The blood for culture was positive after one day of incubation revealed the presence of gram-negative bacilli bacteria. After overnight incubation, the gram-negative bacteria were noted to be non-lactose fermenter, motile, oxidase negative and producing hydrogen sulfide in the triple sugar iron medium. The isolate was identified as Salmonella spp. by the VITEK-2 GN (bioMirieux, France). The isolate was sensitive to ceftriaxone, trimethoprim-sulfamethoxazole, ciprofloxacin, ampicillin, and amoxicillin-clavulanic acid. Urine culture was negative. The diagnosis

of mycotic aneurysm secondary to *Salmonella* spp. was made. The intravenous ceftriaxone was continued with dosage of 2-gram 12-hourly. The repeated blood culture after one week of treatment was negative. However, increasing trend of total white cell to 23.3  $\times$  10 $^9/L$  predominantly neutrophils was noted but the CRP level was maintained at 20.73  $\mu$ mol/L as shown in Table 1. The repeat CECT abdomen revealed an increasing size of the aneurysm to 5.6 cm  $\times$  3.9 cm  $\times$  5.5 cm with also increasing periaortic hematoma.

Subsequently, the patient was scheduled for open aneurysm repair. The surgery was performed uneventfully. The aortic and periaortic tissue was sent for histopathology reporting and microbiology culture. There was inflamed and partly necrotic fibromuscular vascular wall with denuded endothelium of the excised aorta visualized histologically while the viable part of the aorta showed dystrophic calcification, fibrin depositions and cholesterol clefts within intima as shown in Figure 1. The microbiological culture of the aorta and periaortic tissues also grew Salmonella spp. with similar antibiogram pattern as the one previously isolated from blood sample. The Salmonella spp. was as Salmonella Enteritidis by serotyping. Intravenous antibiotic

Table 1. Blood parameters of this patient taken at different points during admission

Parameters	On Day of Admission	Day 7	Day 2 post operation	Day 7 post operation	One day before discharge	Normal range
Total white cell count	14.9	23.3	15.6	11.2	12.4	4-10 × 10 <sup>9</sup> /L
Neutrophil	12.4	19.5	13.7	7.4	8.5	$2-7 \times 10^9/L$
CRP	23.88	20.83	14.48	5.99	1.51	< 0.5 mg/dL
Bilirubin	115.2	70.8	39.3	19.1	_	3.4-20.5 μmol/L
ALP	506	373	287	180	-	40-150 U/L
ALT	62	60	50	29	_	0-55 U/L
Sodium	128	124	126	130	-	136-145 mmol/L
Potassium	4.2	4.5	4.5	4.4	_	3.5-5.1 mmol/L
Urea	8.5	5.3	4.8	3.1	-	3.2-7.4 mmol/L
Creatinine	78.3	54.1	55.7	45.5	_	63.6-110.5 μmol/L

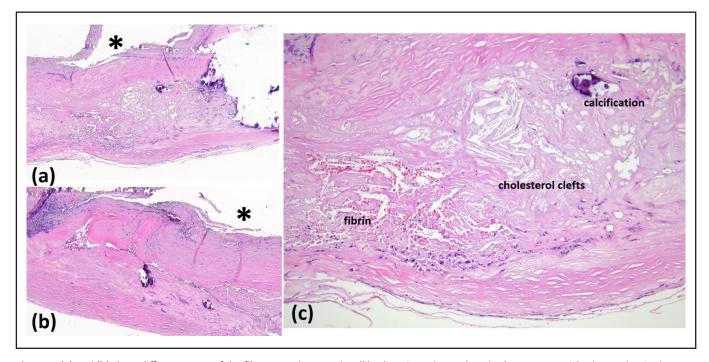


Figure 1. (a) and (b) show different areas of the fibromuscular vessel wall harbouring atherosclerotic changes. Asterisks denote luminal aspect (H&E, 40×). (c) Higher magnification show dystrophic calcification, cholesterol clefts and fibrin deposition (H&E, 100×).

was continued for three weeks, and he was discharged with oral amoxicillin-clavulanic acid for another two weeks. The ALP level was on reducing trend while the ALT and bilirubin levels were normalized before discharged. His follow-up one month later noted that he was well. He was also started on subcutaneous insulin which consisted of actrapid 8 units three times daily and insulatard 10 units on night for his diabetes management.

#### **DISCUSSION**

The incidence of endovascular infection by nontyphoidal Salmonella was estimated around 4.4 per 1,000,000 person year among adults age above 50 years (Nielsen et al., 2006). In another report, the frequency of nontyphoidal Salmonella endovascular infection among those with bacteraemia was 10% (Benenson et al., 2001). Infected aneurysm or mycotic aneurysm is one of the most common manifestations of the endovascular infection caused by this bacteria. The condition is predominantly diagnosed among adult above 50 years of age. Previous studies described adult age above than 50 years as the population at risk of acquiring mycotic aneurysm following nontyphoidal Salmonella infection (Cohen et al., 1978; Nielsen et al., 2006; Sorelius & di Summa, 2018). Majority of these patients already had underlying diseases such as hypertension and diabetes mellitus that contributed to atherosclerotic changes in the artery wall (Cohen et al., 1978; Fernandez Guerrero et al., 2004; Hsu & Lin, 2005). However, the underlying diseases were absent in as many as 31% of the cases (Wang et al., 1996). Age above 50 years with underlying diabetes mellitus and chronic smoker were the most likely risk factors for developing mycotic aneurysm in our patient. Similarly, the recent cases of abdominal aorta endovascular infection by the Salmonella Enteritidis as shown in Table 2 demonstrated that all patients were above 50 years and all except in one had underlying diseases. Diabetes mellitus can cause decrease in gastric acidity and autonomic neuropathy of small bowel resulted in reduce motility and prolonged transit time. This increases the susceptibility of gastrointestinal pathogen such as nontyphoidal Salmonella to infiltrate the circulatory system resulting in bacteraemia (Telzak et al., 1991). Together with the pre-existing intimal defect due to atherosclerotic changes in the artery wall, the bacteria can seed and subsequently resulted in aneurysm formation (Lee et al., 2008).

The clinical presentations of nontyphoidal Salmonella mycotic aneurysm are diverse and this can make the diagnosis challenging. However, only minority of the patients are asymptomatic (Lee et al., 2008). Fever is the most common clinical feature, and it occurs in the majority of patients. Pain is another important clinical feature, and it is usually related to the location of aneurysm. Pulsatile and tender lump was found in 37.5% of the patients with abdominal aneurysm (Fernández Guerrero et al., 2004). Patients with renal artery aneurysm can present with hypertension and hematuria (Lee et al., 2008). Because of these wide clinical manifestations, the diagnosis can be delayed. This was shown in previous reported case where the patient was initially diagnosed with pyelonephritis before the diagnosis of mycotic aneurysm was made after the patient was readmitted due to recurring symptoms (Sabak et al., 2020). Similarly, our patient presented with clinical features suggestive of cholestatic jaundice but fortunately the diagnosis of mycotic aneurysm was not delayed due to the imaging investigation performed. The deranged liver enzymes in our patient was most likely due to underlying bacteraemia as demonstrated in previous studies (Tung et al., 2005; Kanai et al., 2008). Interestingly, between 40 to 63.6% of the patients did experienced episode of gastroenteritis before the onset of mycotic aneurysm (Fernández Guerrero et al., 2004). However, this was not noticed in our patient.

Salmonella Enteritidis was isolated from the blood, aortic and periaortic tissues from our patient. Blood specimen must be sent for bacterial culture in endovascular infection although it can be negative in 18 to 50% of the cases (Lee et al., 2008). In a retrospective review, it was shown that nearly all patients had a positive blood culture at least once (Guo et al., 2018). Thus, the important of sending blood sample for culture needs to be emphasized. Salmonella Cholerasuis and Salmonella Enteritidis were the two nontyphoidal Salmonella species most commonly isolated in the previous reported series of mycotic aneurysm (Wang et al., 1996; Huang et al., 2014; Guo et al., 2018). Leukocytosis was also frequently detected in this infection in more than 50% of the cases. The inflammatory marker such as C-reactive protein was elevated in all the cases as demonstrated in Table 2. The diagnosis of aneurysm is frequently helped by the used of radiological imaging. Imaging modalities are not only important for diagnosis but also for treatment planning, surveillance of treatment and detection of the development of new infected aneurysm (Lee et al., 2008). Computed tomography angiography is considered as the imaging modality of choice but in some case magnetic resonance imaging has also been used. The lesion can appear as focal, contrast-enhancing dilatation that is usually saccular which was also demonstrated in our patient. When there is active extravasation of intravascular contrast material or hematoma formation adjacent to the aneurysm, this indicates the rupture of the aneurysm (Lee et al., 2008). Between 47 to 61% of the patients had concealed or impending rupture at presentation (Lee et al., 2008). As shown in Table 2, most of the cases of S. Enteritidis abdominal mycotic aneurysm were located at infrarenal. It was suggested that patients who are above 50 years of age who had positive blood culture for nontyphoidal Salmonella with fever, back pain or abdominal pain should have extensively work up for underlying aortitis (Nielsen et al., 2006).

Combination of antimicrobial therapy and surgical intervention are important to ensure a successful management of the patient. The use of antibiotic alone without treating the infected artery is associated with poor outcome (Cohen et al., 1978). Antibiotic treatment is based on the susceptibility testing. There is no standard guideline for the duration of antibiotic therapy in the case of mycotic aneurysm due to S. Enteritidis but as practiced in previous reported cases in Table 2, the antibiotic course is prolonged for about one month. In our patient, the antibiotic treatment given was intravenous ceftriaxone for about 3 weeks followed by oral amoxicillin-clavulanic acid for two weeks. There are various methods of vascular repair that can be performed which include open repair with graft or minimally invasive surgery such as endovascular aneurysm repair with the insertion of stent graft. The most feared complication in the case of mycotic aneurysm is the rupture of the aorta. The mycotic aneurysm is not static rather keep expanding and subsequently will lead to its rupture (Lee et al., 2008). It was reported that the overall mortality rate from mycotic aneurysm was 43.2% in which 18.2% was aneurysmal-related, 13.6% was surgicalrelated and 22.7% was in-hospital mortality (Huang et al., 2014).

In conclusion, this case highlighted that early detection of abdominal mycotic aneurysm allowed appropriate management for the condition to ensure better prognosis of the patient. This case emphasized the need of thorough radiological investigation to look for underlying mycotic aneurysm in a patient above 50 years of age with *Salmonella* spp. bacteremia.

Table 2. The reported cases of the abdominal aorta mycotic aneurysm/aortitis caused by Salmonella Enteritidis in the last 10 years (2012-2021)

Case	Age	Gender	Underlying diseases	Clinical feature	Blood test	Imaging	Culture positive	Management/Outcome
Kordzadeh <i>et al.,</i> 2013	99	Male	Coronary artery bypass Polymyalgia rheumatica on steroid	Fever Right flank to groin pain	1WCC 1CRP	CT-thoracoabdominal: Infrarenal aneurysm	Blood Excised aorta Lymph Node	Antibiotic: IV ciprofloxacin 1 week followed by oral ciprofloxacin 4 weeks Surgical: laparotomy, graft, end to end anastomosis Follow up: at 6 weeks and 6 months, patient well
Gerada <i>et al.,</i> 2013	65	Female	Orthotopic liver transplant on therapy Hypertension Hyperlipidaemia Chronic renal impairment Multinodular goitre	Fever Abdominal pain Diarrhoea	1CRP 1ALP	CT-abdomen: infrarenal	Blood Urine	Antibiotic: Oral ciprofloxacin for 3 months Surgery: Excision of aneurysm and allograft
Tomek <i>et al.,</i> 2013	71	Male	Chronic lymphocytic Ieukaemia	Constitutional symptom and low back pain for 6 weeks Had bout of gastroenteritis	<b>1</b> CRP	CT-thorax/abdomen: Distal thoracic aorta to renal arteries MRI spine: T11 to L2 osteomyelitis and discitis	Blood Aneurysm wall	Antibiotic: IV ceftriaxone and azithromycin for 6 weeks Surgery: Open aneurysm repair and graft Follow up: at 6 months, patient was well
Chao, 2014	61	Male	IVDU Major depression	Fever Mild diarrhoea	Not stated	CT-thorax/abdomen: Abdominal aortic aneurysm + pleural effusion	Blood Pleural fluid	Antibiotic: Ciprofloxacin for 6 weeks Surgery: Endovascular aneurysm repair Follow up: at 6 months, well
Reijnen <i>et al.,</i> 2014	78	Male	Diabetes Dyslipidaemia Laparotomy for bowel perforation	Fever Abdominal pain Progressive back pain	↑WCC ↑CRP	CT-abdomen: Saccular aneurysm at superior mesenteric artery	Blood	Antibiotic: IV ceftriaxone and amoxicillin, discharged with oral ciprofloxacin. Surgery: Stenting Follow up: at 2 and 18 months, well, patent stent
Pasveer et al., 2017	28	Male	BPH Atrial fibrillation Percutaneous coronary intervention	Abdominal pain Altered bowel habit Weight loss	↑WCC ↑CRP ↑ESR	CT-abdomen: Saccular aneurysm of abdominal and left iliac artery	Aneurysm wall Faeces	Antibiotic: Intravenous amoxicillin- clavulanic acid Surgery: open repair with aorto-bi-iliac biological prosthesis

Sabaka <i>et al.,</i> 2020	09	Male	Hypertension	Fever Left flank pain	†WCC †CRP	CT-abdomen: fusiform aneurysm from offset of ranal arteries to	Blood Urine	Initially treated as pyelonephritis but readmit and aneurysm diagnosed.
				16 days prior has gastroenteritis		bifurcation at left internal iliac artery		Antibiotic: Intravenous ceftriaxone for 30 days Surgery: Recanalization of infrarenal aorta, left internal liac artery ligation and partial extirpation of the aneurysm
Zeng <i>et al.,</i> 2020	288	Male	Diabetes Smoker	Fever Low back pain	1CRP ↑ESR	CT- abdomen: Infrarenal saccular aneurysm Left psoas muscle abscess at day 40	Abscess	Antibiotic: IV ciprofloxacin the IV panipenem/Betamipron for 2 weeks Surgery: Endovascular aortic repair and drainage of left psoas muscle abscess Follow up: at 2 year, well
Strahm <i>et al.,</i> 2012	67	Male	Colorectal cancer Coronary bypass	Fever Back and abdominal pain Mild gastroenteritis prior to this	1wcc ↑cRP	CT-abdomen: Infrarenal mural hematoma with paraaortic fat stranding (no gross aneurysm)	Blood	Antibiotic: IV ceftriaxone/ciprofloxacin for 26 days and oral ciprofloxacin for 12 months Surgery: endovascular aortic repair
Ng et al., 2021	80	Male	Hypertension BPH Cholecystectomy	Back pain radiating to right flank	†CRP	CT abdomen: Infrarenal saccular aneurysm with perianeurysmal hematoma Repeated CT at 40 days after surgical: Left psoas abscess MRI: L3/L4 spondylodiscitis	Blood	Antibiotic: IV ceftriaxone for 6 weeks Surgery: Percutaneous endovascular aneurysm repair

BPH: Benign prostatic hyperplasia, ESR: erythrocyte sedimentation rate, IVDU: intravenous drug user.

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#### **Conflict of interest**

The authors declare they have no conflict of interest.

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