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An Unusual Case of Deep Vein Thrombosis and Mycotic Aneurysms Secondary to *Salmonella* Bacteraemia

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Abstract

Salmonella, a food-borne pathogen, can cause mild self-limiting gastroenteritis. However, immunocompromised hosts and older adults with complex medical conditions may develop a complicated form of bacteraemia, with a high mortality rate involving extra-intestinal foci of infection and mycotic aneurysms. We report the case of a 61-year-old man with poorly controlled diabetes mellitus, hypertension, dyslipidaemia, and congestive heart failure, who presented with unilateral left lower limb swelling, extensive deep vein thrombosis, and concomitant *Salmonella* bacteraemia. An oral anticoagulant and intravenous antibiotic therapy were initiated. Although the patient remained haemodynamically stable, he complained of constant left lower limb weakness and lower back pain. A computed tomography angiography scan of the thorax and abdomen revealed saccular aneurysms with contained hematoma of the left common iliac artery. The oral anticoagulant was discontinued, and an inferior vena cava filter was inserted as part of the venous thrombosis management. The patient was offered aorto-uni-iliac endovascular aneurysm repair and received intravenous antibiotic therapy, postoperatively, for six weeks. The postoperative blood cultures remained negative, and he was discharged with a course of ciprofloxacin administered orally. However, three months after the surgery, the patient died of recurrent septicaemia. This case illustrates the importance of remaining vigilant for potential endovascular complications of *Salmonella* bacteraemia, such as mycotic aneurysms and deep vein thrombosis, among high-risk patients. Further, this case highlights the challenges of eliminating *Salmonella* bacteraemia and its related complications, albeit treating it with both a prolonged course of medical therapy and surgical intervention.

Keywords

Deep Vein Thrombosis, Endovascular Aneurysm Repair, Infective Endarteritis, Mycotic Aneurysm, *Salmonella*

1. Introduction

Gastroenteritis is a common clinical feature of *Salmonella* infections and is often self-limiting, without complications. However, approximately 5% of affected patients develop *Salmonella* bacteraemia [1]. Disseminated infections are more likely to occur in immunocompromised hosts and older adults with complex medical conditions [2] [3] [4] [5]. These patients may develop complications involving endovascular infection and deep bone and visceral abscesses, which are challenging to treat and have a high mortality rate [6]. A recent study reported that *Salmonella* bacteraemia is the second most common cause of mycotic aneurysms and that its incidence is higher in Asian countries than in the West [7] [8]. In addition, *Salmonella* bacteraemia can present with atypical features, such as deep vein thrombosis [9] [10] [11]. Awareness of the rare and unusual clinical presentations of invasive *Salmonella* infection is essential for accurate diagnosis and prompt management.

Therefore, clinicians caring for high-risk patients with complex medical conditions need to remain vigilant and perform comprehensive evaluations to assess potential complications of *Salmonella* bacteraemia, such as mycotic aneurysms and deep vein thrombosis. Mycotic aneurysms involving multiple anatomical sites are challenging to treat, even when using a combination of medical and surgical interventions. Negative blood cultures, after a specific duration of antibiotic therapy and in the postoperative period, do not necessarily indicate complete bacterial elimination.

Here, we present the case of a 61-year-old man who presented with extensive deep vein thrombosis of the left lower limb with concomitant *Salmonella* bacteraemia and subsequently developed mycotic aneurysms.

2. Case Presentation

A 61-year-old man, with poorly controlled diabetes mellitus (Haemoglobin A1c: 12.5%), hypertension, dyslipidaemia, and congestive heart failure, presented with a gradual onset of unilateral left lower limb swelling for two weeks, which rendered him unable to walk. He had not been previously investigated for ischaemic causes of heart failure and had defaulted follow-up. He reported a subjective feeling of shortness of breath and had symptoms equivalent to the New York Heart Association Class III that were limiting his daily activities. He also reported significant tobacco use (smoking history of 40 pack-years).

On admission, his vitals were stable, with a low-grade fever of 37.6˚C; blood pressure of 128/78 mmHg; pulse rate of 96 beats/min; respiratory rate of 18

breaths/min and oxygen saturation of 100% breathing ambient air. Examination of the left lower limb revealed asymmetric calf swelling of more than 3 cm compared to the contralateral leg, without any pus discharge or skin excoriation. The active range of movement of the left hip, knee, and ankle was limited, owing to pain. Blood investigations revealed a white blood cell count of $9.46 \times 10^3/\mu L$ with a neutrophil predominance of 77% and an erythrocyte sedimentation rate of 79 mm/h (Table 1). Based on the elevated inflammatory markers and low-grade fever, a presumptive diagnosis of left lower limb cellulitis was made, and the patient was started on intravenous ceftriaxone. A chest radiography scan revealed cardiomegaly. Based on elevated D-dimer levels of 2251 ng/ml and a Wells score of 3, an urgent lower-extremity venous ultrasound examination revealed extensive thrombi in the left common femoral, superficial femoral, and popliteal veins (Table 1). There were no focal loculated fluid collections indicative of septic arthritis in the hip, knee, or ankle joints. He denied any long-distance travel, recent surgery, or a malignancy history. To prevent further clotting and an embolism, he was started on subcutaneous enoxaparin and bridged with dabigatran.

Table 1. Progress of patient's relevant blood investigations throughout hospital admission.

	Normal Values	Day 1	Day 7	Day 14	Day 28	Day 42
WCC (10^3/uL)	3.60 - 10.20	9.46	13.71	7.14	7.90	9.9
Neutrophil percentage	43% - 73%	77%	80.6%	74%	70%	72%
Haemoglobin (g/dL)	12.5 - 16.0	11.2	10.5	9.2	7.8	7.7
MCV (fL)	80 - 100	79.3	75	75	81.6	90
MCH (pg)	27 - 33	27	27	26	27	26
Platelet (10^3/uL)	152 - 347	188	335	292	311	279
ESR (mm/h)	≤15 mm/h	79	49	100	104	64
D-Dimer(ng/ml)	0 - 253.5	2251				
PT (sec)	11 - 16	16.1	17	20	14.7	15.9
PTT (sec)	30 - 40	54.3	52	74	49.7	61.9
INR		1.3	1.3	1.4	1.2	1.3
Urea (mmol/L)	1.7 - 8.3	8.2	7.8	3.7	2.9	4.0
Creatinine (umol/L)	80 - 115	83	97	67	75	78
Sodium (mmol/L)	133 - 145	126	131	128	128	134
Potassium (mmol/L)	3.3 - 5.1	4.7	4.1	3.8	4.3	3.7
Albumin (g/L)	38 - 51	24	24	21	29	29
AST (U/L)	5 - 41	116	93	73	60	63
ALT (U/L)	5 - 37	93	45	31	30	25
Hepatitis B & C		NR				
HIV		NR				
Syphilis		NR				

Continued

Stool Culture		Neg	Neg	
Blood Culture and Susceptibility		*Salmonella enteritidis* Susceptible to: - Ceftriaxone - Ampicillin - Co-trimoxazole	Neg	Neg
PSA (ng/mL)	1 - 1.5	0.9		
CEA (ng/mL)	0 - 2.5	0.21		
AFP (ng/mL)	10 - 20	4		
CA 19-9 (U/mL)	0 - 37	2.1		
ANA		Neg		
Anti-ds DNA		Neg		
RF		Neg		
Direct & Indirect Coomb's		Neg		
Haemoglobin A1C	<6.0%	12.5%		
Total Cholesterol (mmol/L)	0.1 - 5.2	5.4		
HDL (mmol/L)	0.91 - 3.12	1.25		
LDL (mmol/L)	0.9 - 3.9	4.2		
Triglycerides (mmol/L)	0.1 - 2.27	1.1		

Abbreviations: AFP, alpha-fetoprotein; ALT, alanine aminotransferase; ANA, anti-nuclear antibodies; Anti dsDNA, anti-double-stranded DNA antibody; AST, aspartate aminotransferase; CA 19-9, cancer antigen 19-9; CEA, carcinoembryonic antigen; ESR, erythrocyte sedimentation rate; HIV, human immunodeficiency virus; INR, international normalized ratio; MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; Neg, negative; NR, non-reactive; PTT, partial thromboplastin time; PT, prothrombin time; PSA, prostate specific antigen; RF, rheumatoid factor; WCC, white cell count.

A preliminary report showed a gram-negative organism in the blood culture. Intravenous ceftriaxone was continued, and the patient remained haemodynamically stable and afebrile. The inflammatory markers improved, whereby the erythrocyte sedimentation rate decreased from 79 mm/h to 49 mm/h (Table 1). However, the patient continued to report a subjective feeling of fatigue and constant lower back pain, with a pain score of 4/10, which did not improve even after receiving intravenous antibiotics for a few days. Later, it became apparent that he was harbouring *Salmonella enteritidis*, which was susceptible to ampicillin, ceftriaxone, and co-trimoxazole (Table 1). The patient was co-managed by an infectious disease team, and the antibiotic was changed to intravenous ampicillin.

Collaborative history from the patient and his family members did not reveal prior gastroenteritis symptoms and significant risk factors for infection, such as travel, consumption of fast foods, poultry, raw eggs, or contact with pets were absent. The patient denied having constitutional symptoms, weight loss, or a prior history of thrombosis, and his family history was unremarkable. The stool culture and susceptibility tests were negative (Table 1). Infective screening for

hepatitis B and C, human immunodeficiency virus, and syphilis were negative (Table 1). Extensive investigations, including tumour markers and computed tomography (CT) scans of the thorax and abdomen, did not reveal any evidence of a solid organ tumour (Table 1). A peripheral blood smear revealed microcytic hypochromic anaemia but otherwise unremarkable for haematological malignancies. The result of comprehensive panel of rheumatological markers also tested negative (Table 1).

During the second week post admission, the patient reported worsening of lower back pain that hindered his walking abilities. The neurological examination was unremarkable, with localised pain over the left gluteal area and a severely restricted range of movement of the left hip owing to pain. The patient continued to remain haemodynamically stable and afebrile. Blood investigations revealed worsening inflammatory markers with a white blood cell count of 7.14 $\times 10^3/\mu L$ with a neutrophil predominance of 74% and an elevated erythrocyte sedimentation rate of 100 mm/h. The patient's haemoglobin levels decreased from 11.2 g/dL to 9.2 g/dL. An urgent esophago-gastro-duodenoscopy and colonoscopy did not reveal active gastrointestinal bleeding. Subsequently, an urgent multi-slice spiral CT combined with computed tomography angiography (CTA) of the thorax, abdomen, and pelvis was performed to identify potential invasive complications of *Salmonella* bacteraemia such as discitis, psoas abscess, and mycotic aneurysms. The CTA scan of the thorax, abdomen and pelvis revealed the presence of a 1.0 cm anteroposterior (AP) × 0.8 cm width (WT) saccular aneurysm at superolateral wall and 5.7 cm (AP) × 7.7 cm (WT)× 6.4 cm craniocaudal (CC) lobulated saccular aneurysm at the inferomedial wall of the left common iliac artery with contained hematoma (Figure 1 and Figure 2). Large saccular aneurysm does laterally displace the psoas muscle and compress the left distal ureter, which results in mild proximal hydroureter and hydronephrosis. The CTA abdomen also revealed infrarenal dissecting abdominal aortic aneurysm (AAA) measures 3.2 cm in its widest diameter (Figure 1). The true and false lumens measure 1.6 cm in diameter respectively. An echocardiogram revealed an ejection fraction of 20%, with hypokinesia in the apical and septal regions, with no evidence of valvular vegetation.

With these observations, the oral anticoagulant was discontinued due to the risk of aneurysmal rupture. As an alternative, the patient received an inferior vena cava filter to prevent embolic events from the extensive left lower-limb deep vein thrombosis. Further discussions occurred with the vascular team about the surgical interventions. After six weeks of intravenous antibiotic therapy and negative blood cultures, the patient was transferred to their facility. Considering the patient's poor cardiac reserve and multiple comorbidities, which carry an enhanced perioperative risk, the patient was offered aorto-uni-iliac endovascular aneurysm repair (EVAR) of the left common iliac artery. Postoperatively, the patient remained haemodynamically stable, received six weeks of intravenous ceftazidime, and had negative blood cultures with no evidence of leakage. However, endovascular cultures were not evaluated. At six-weeks post EVAR and

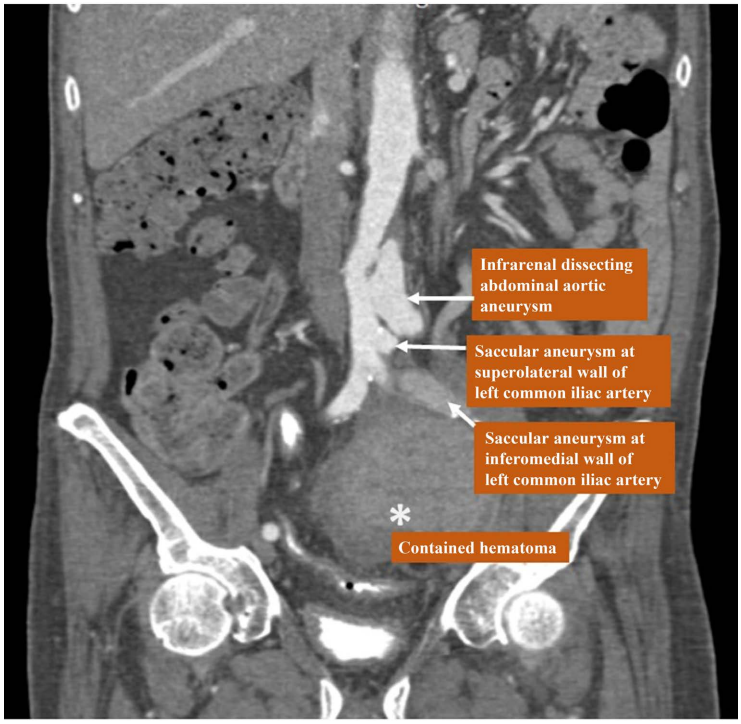

Figure 1. Computed tomography angiography (CTA) of abdomen, coronal view shows presence of two contrast filled lobulated saccular anurysms seen at left common iliac artery. The smaller aneurysm at superolateral wall of left common iliac artery measures 1.0 cm × 0.8 cm (AP × WT) with the defect opening measures 0.8 cm in diameter. Another larger aneurysm arising from inferomedial wall of left common iliac artery measures 5.7 cm × 7.7 cm × 6.4 cm (AP × WT × CC) with the defect opening measures 1.2 cm in diameter. The area marked with * shows contained hematoma from the aneurysms. CTA abdomen also shows infrarenal dissecting abdominal aortic aneurysm (AAA) measures 3.2 cm in its widest diameter. The true and false lumens measure 1.6 cm in diameter respectively.

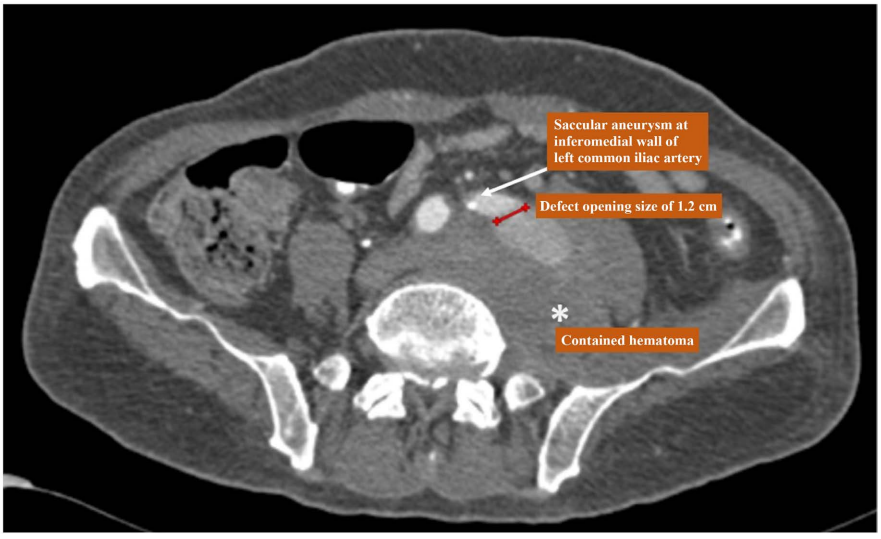

Figure 2. Computed tomography angiography (CTA) of abdomen, axial view shows presence of saccular aneurysm arising from inferomedial wall of left common iliac artery measures 5.7 cm × 7.7 cm × 6.4 cm (AP × WT × CC) with the defect opening measures 1.2 cm in diameter. The area marked with * shows contained hematoma from the aneurysm.

based on a susceptibility test, he was discharged with an extended course of oral ciprofloxacin. However, during the third postoperative month, the patient presented with extensive left lower limb gangrene and severe septicaemia. The patient later died despite extensive medical and surgical intervention.

3. Discussion

Invasive *Salmonella* infections can present with a variety of clinical features and varying degrees of complications, particularly in high-risk patients. These patients are notably immunocompromised and warrant a comprehensive evaluation. Clinicians caring for these patients need to increase their awareness, improve their clinical acumen, and should anticipate and manage any potential complications during the course of the disease (Table 2).

This case report is unique and relevant. The patient presented with severe *Salmonella* bacteraemia and extensive deep vein thrombosis and later developed multiple saccular mycotic aneurysms of the left common iliac artery. A thorough evaluation did not reveal other potential causes for the extensive deep vein thrombosis, except the severe *Salmonella* bacteraemia. Severe infection inducing a hypercoagulable state and thrombosis may explain the development of extensive deep vein thrombosis [12]. Atypical manifestations of invasive *Salmonella* infection with deep vein thrombosis have been previously reported but are notably rare [9] [10] [11]. Another possible explanation could be the compression of the ipsilateral iliac vein by a mycotic aneurysm arising from the left common iliac artery; however, this was not evident on a CTA scan of the abdomen. It would have been interesting if thrombophilia panels had been used to investigate the possibility of inherited or autoimmune causes of venous thrombosis. Thrombophilia panels were not done for this patient as inherited or autoimmune prothrombotic conditions seemed unlikely based on his negative family and personal history

Table 2. Patients with enhanced risk factors to develop invasive *Salmonella* bacteraemia.

Category	Risk Factor
Non-modifiable	Extreme age group (Age > 65 years old and neonates)
Cardiovascular	Chronic smoking Hypertension Poorly controlled diabetes mellitus Previous history of stroke Hyperlipidaemia Congestive heart failure
Immunocompromised State	Long term steroid usage Rheumatological disease Liver cirrhosis End stage renal failure Acquired Immunodeficiency Syndrome Active Malignancy Recent Chemotherapy

of thromboses. The extensive venous thrombosis was strongly suggestive of severe invasive *Salmonella* bacteraemia, a sepsis-induced hypercoagulable state and possible external compression of the ipsilateral iliac vein from the large mycotic aneurysm, causing venous stasis and thrombosis. Although the adjunctive clinical history and inflammatory markers were strongly suggestive of the extensive venous thrombosis because of severe salmonellosis and external compression, without additional thrombophilia screening, it was difficult to arrive at a definite conclusion that this was indeed the case.

It is possible that the patient had developed a mycotic aneurysm earlier, but this was missed during the initial admission and assessment, as the focus remained largely on the extensive left lower limb deep vein thrombosis. Later, the development of enlargement of the mycotic aneurysms with contained hematoma led to severe and persistent lower back pain along with a concomitant decrease in haemoglobin level. This led to further evaluation and a final diagnosis of multiple saccular mycotic aneurysms of the left common iliac artery. It is very difficult and challenging to determine whether deep vein thrombosis or mycotic aneurysms was the first potential complication of the invasive *Salmonella* bacteraemia. This case highlights the importance of closely monitoring a patient's progress and re-evaluating the initial diagnosis whenever there is a clinical doubt, especially when more information becomes available or if there is a change in the patient's condition. This case report is unique because mycotic aneurysms of the iliac artery are rarely reported in the literature, with previous reported cases of mycotic aneurysms predominantly occurring in the abdominal aorta [13] [14].

Salmonella has a strong affinity to adhere to damaged vessel walls, which causes inflammation, destruction, and localised abnormal dilatation, ultimately leading to mycotic aneurysm formation [2]. The process of infective endarteritis is postulated to be enhanced in patients with increased risk for developing atherosclerosis [2] [13]. Therefore, in such patients, imaging examinations should be performed to identify endovascular complications. Although mycotic aneurysms are a rare occurrence, once they develop, they can be severe and expand rapidly, leading to rupture, contained hematoma, and abscess formation. This patient did report poorly controlled diabetes, hypertension, dyslipidaemia, and possibly undiagnosed coronary artery disease, which increased his risk of atherosclerosis. The adjunctive clinical and biochemical markers, such as persistent lower back pain, increased inflammatory markers, and decreasing haemoglobin levels, prompted further investigation and evaluation of the mycotic aneurysms using CTA of the abdomen. Extensive venous thrombosis is life-threatening, and it becomes even more challenging when venous thrombosis and mycotic aneurysms coexist. This patient had aneurysms at multiple anatomical sites with contained hematoma that made the management of the venous thrombosis difficult. An inferior vena cava filter was inserted to prevent further embolization.

Currently, medical treatment for mycotic aneurysms alone has no lasting curative effect. Owing to aneurysmal rupture, formation of septic emboli, recurrent bacteraemia, abscess formation, and multi-organ failure, mortality may reach

100%. Therefore, treatment should involve a combination of intensive targeted antibiotic therapy and surgical interventions, such as open vascular surgery or EVAR, to prevent aneurysmal rupture and remove the infected vessel foci. As the patient was unfit for open vascular surgery, he was offered EVAR. The EVAR is beneficial in preventing lethal aneurysmal rupture in the acute phase but provides less protection from recurrent sepsis complications [15] [16]. Despite achieving negative cultures from the peripheral blood before and after EVAR and continued intensive antibiotic therapy, the patient experienced septic complications and succumbed to these complications. Endovascular cultures may have provided more accurate results than peripheral blood cultures. Clinicians must remember that peripheral blood cultures have poor sensitivity and specificity for mycotic aneurysms, particularly when the patient has received long-term antibiotic therapy. In such patients, negative cultures do not guarantee elimination of the foci of infection. However, this patient was already at an increased risk for mortality given his older age, poorly controlled comorbidities, and the delay in seeking care at a facility during the initial illness.

4. Conclusion

The main observations from this case report are first, clinicians should be vigilant and consider potential endovascular complications arising from *Salmonella* bacteraemia in patients with multiple comorbidities. Second, *Salmonella* bacteraemia can present with rare, atypical manifestations such as deep vein thrombosis, either in isolation or with infective endarteritis. Clinicians need to be aware of this association, and such cases need to be reported to the scientific community. With more reported cases, identification of the temporal relationship between *Salmonella* bacteremia, infective endarteritis and deep vein thrombosis will be eased in the future. Third, among high-risk patients, *Salmonella*-induced mycotic aneurysms are associated with exaggerated morbidity and mortality. These patients may have severe medical conditions that reduce the benefits of open vascular surgery. Currently, treatment options available for such patients are limited and prolonged medical therapy alone or in combination with EVAR is yet to achieve satisfactory results. Further, more in-depth research on effective treatment of severe endovascular infection among high-risk patients, where open vascular surgery is considered unsuitable, is urgently needed.

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Data Availability

The patient data used to support the findings of this case report are available

from the corresponding author upon request.

Informed Consent

Written informed consent was obtained from the patient's daughter for the publication of this article (including a case history and radiographic imaging).

Author's Contribution

MS was directly involved in the treatment of the patient, literature search, and scientific writing. APR participated in providing expert opinion on patient care and review of the manuscript.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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