CASE REPORT

Uncovering what lies beneath a *Salmonella enterica* empyema

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SUMMARY

A 67-year-old woman with myelodysplastic syndrome (MDS) and transfusional haemosiderosis developed *Salmonella* empyema caused by direct extension from splenic abscesses. She was successfully treated with antibiotics, pleural decortication and splenectomy. She had presented with fever after being treated for presumed pneumonia and parapneumonic effusion 2 months prior. CT scan showed splenic abscesses eroding through the diaphragm causing a left pleural empyema. Pleural fluid and spleen bacterial cultures grew *Salmonella enterica*. She was treated with 4 weeks of antibiotics and underwent surgical pleural decortication and splenectomy in the same sitting. She made a good postoperative recovery. Patients with severe iron overload are susceptible to various types of bacterial sepsis, including salmonellosis. It is unusual for enteric bacterial such as *Salmonella* to present with empyema, and should prompt a search for intra-abdominal infection. Pleural decortication and splenectomy can be performed during the same surgical sitting and can lead to good surgical outcomes.

BACKGROUND

Salmonella infections rarely cause empyema and splenic abscesses together. A literature review in 2005 found 38 reported cases of *Salmonella* empyema over the past century. Of these 38 cases, only four were postulated to be caused by direct extension from the spleen.¹ Owing to the rare occurrence of *Salmonella* empyema complicating a splenic abscess, there are no established treatment guidelines. Pleural decortication and splenectomy done during the same surgical sitting is rarely reported.¹ This has only been carried out in 2 of 39 cases in a review.¹ Our patient underwent both procedures during the same sitting and had good surgical outcome. Severe iron overload in this patient increased her susceptibility to salmonella infection. It is a reminder that severe iron overload not only leads to damage to the liver, heart and endocrine organs, but also predisposes the host to infections.

CASE PRESENTATION

We present a case of a 67-year-old woman with a background of transfusion-dependent myelodysplastic syndrome, requiring 2 units of packed red cells every 2 weeks, and transfusional haemosiderosis treated with the oral iron chelator, deferasirox. Baseline blood tests carried out 4 months prior to presentation showed white cell count $7.0 \times 10^9/L$, neutrophils $5.0 \times 10^9/L$, platelets $620 \times 10^9/L$,

haemoglobin 7 g/dL pretransfusion and serum ferritin 6400 µg/L.

The patient's first admission was for a 1 week history of dry cough and fever. She did not report any abdominal pain or discomfort. Chest X-ray showed a left lower lobe consolidation and small left pleural effusion. CT scan of the thorax and abdomen (figure 1) was performed, which showed bilateral small pleural effusions, larger on the left and an unexpected finding of thrombosis in the branches of the splenic vein, and an enlarged spleen measuring 14.9 cm, within which were multiple areas of hypoperfusion, suggestive of splenic infarcts. Blood cultures were negative, and the patient was treated with a 10-day course of amoxicillin-clavulanate, which resolved her initial symptoms. Stool cultures were sent, as she had developed self-limiting diarrhoea on the second day of admission, but these came back negative. Anticoagulation with enoxaparin followed by warfarin was also initiated for splenic vein thrombosis. Tests for thrombophilia, particularly of the type associated with myeloid malignancies, such as paroxysmal nocturnal haemoglobinuria, Janus kinase 2 (JAK2) mutation and antiphospholipid antibodies, were negative.

Two months later, the patient was again admitted with a 2-week history of intermittent fever, nausea and lethargy. Weight loss of 10% and anorexia were

Figure 1 Initial CT scan showing thrombosis in branches of the splenic vein and multiple areas of splenic hypoperfusion, suggestive of splenic infarcts.

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noted in the preceding 2 months. On examination, she appeared toxic and had a temperature of 38.2°C, blood pressure of 139/63 mm Hg, heart rate of 122/min and oxygen saturation of 98% on room air. The abdomen was soft to palpation, the tip of the spleen was palpable, but no tenderness was elicited. On auscultation, breath sounds were reduced over the base of the left lung. Total white cell count was $29.5 \times 10^9/\text{L}$, with absolute neutrophilia ($25.3 \times 10^9/\text{L}$). A clinical diagnosis of recurrent left lower lobe pneumonia with parapneumonic effusion was initially made, and the patient was started on piperacillin-tazobactam.

INVESTIGATIONS

Chest X-ray showed a persistent left pleural effusion but no lung consolidation. Thoracentesis was performed, which showed a pleural pH of 6.4, lactate dehydrogenase of 6452 U/L, protein of 48.8 g/L and 98.5% neutrophils. Pleural fluid bacterial Gram stain and culture showed no organisms on direct microscopy. After 18 h incubation at 37°C with 5% CO₂, there was growth of flat non-lactose fermenting colonies of a Gram-negative rod on blood, chocolate and MacConkey agar.

An identification of *Salmonella* species (score of 2.46) was obtained by MALDI-TOF Mass spectrometry (Bruker Daltonics), but serotyping was complicated by failure of O antigen typing despite repeated efforts. Hence the organism was reported as a monophasic variant of *Salmonella enterica* subspecies *enterica*. These findings were consistent with *Salmonella* empyema. Blood bacterial cultures obtained prior to antibiotics were repeatedly negative. A CT scan of the thorax and abdomen (figure 2) was obtained, which revealed multiple splenic

Figure 2 Multiple splenic abscesses ruptured through the left hemidiaphragm, resulting in large empyema with collapsed left lung. Arrow indicates area of diaphragmatic rupture.

abscesses extending beyond the splenic outline and eroding through the diaphragm into the left pleural space. The findings suggested that the *Salmonella* empyema originated from splenic abscesses that had eroded through the diaphragm.

DIFFERENTIAL DIAGNOSIS

Other pathogens that may cause splenic abscesses would include other enterobacteriaceae such as *Klebsiella pneumoniae*, and in an immunocompromised host, *Burkholderia pseudomallei* and *Mycobacterium tuberculosis*.^{2–3} Of note, *B. pseudomallei* that causes melioidosis is endemic in Singapore. Causes for empyema include *Streptococcus pneumoniae*, *Staphylococcus aureus*, coagulase-negative staphylococcus, *Pseudomonas*, *M. tuberculosis*, *K. pneumoniae* and, rarely, *B. pseudomallei*.^{4–6} Thus, other organisms that can cause both splenic abscess and empyema would include *K. pneumoniae*, *M. tuberculosis* and *B. pseudomallei*.

TREATMENT

The left empyema was initially treated with percutaneous chest tube drainage. Nevertheless, a repeat scan 4 days later revealed persistent retained large left empyema, and the patient eventually underwent left pleural decortication followed by splenectomy in the same setting.

The operation was performed under general anaesthesia with a double-lumen endotracheal tube inserted. The patient was placed in a right lateral decubitus position and the left lung was collapsed while the right lung was ventilated. Left pleural decortication was performed through a small 1.5 cm left uniportal VATS (Video-Assisted Thoracic Surgery) incision. All empyema fluid was drained and all empyema peel decorticated under direct thoracoscopic visualisation. Primary closure of the diaphragmatic defect was performed using non-absorbable sutures. The left lung was then completely re-expanded and ventilated.

Splenectomy was then performed via a left subcostal incision while both lungs were ventilated. The enlarged spleen, measuring 13 cm by 10 cm, was resected. It contained multiple large abscess cavities that were densely adherent to the adjacent diaphragm, kidney and stomach. *S. enterica* was cultured from samples obtained from spleen, abdominal cavity and empyema contents.

The patient's antibiotic treatment was continued with ceftriaxone, as the *Salmonella* was a susceptible strain. Deferasirox was temporarily withheld as a precautionary measure because of the association of another iron chelator, desferrioxamine, with enhanced growth of iron avid bacteria in vitro.⁷

OUTCOME AND FOLLOW-UP

Histology of the spleen revealed several abscesses, the largest of which had ruptured through the splenic capsule (figure 3). There was also extramedullary haematopoiesis as evidenced by presence of megakaryocytes, nucleated red cells and granulocyte precursors at varying stages of differentiation (figure 4), likely to be resulting from underlying myelodysplastic syndrome, and presence of haemorrhagic infarcts (figure 5) due to venous congestion from splenic vein thrombosis.

The patient recovered well after surgery. Chest tubes were removed on postoperative day 6, and abdominal drains were removed on postoperative day 10. She was discharged on postoperative day 14 with a course of ciprofloxacin for a total antibiotic duration of 4 weeks. She remained well 6 months after discharge, and post-treatment CT scan showed complete resolution of thoracic and abdominal infection. Deferasirox was since restarted and her ferritin has declined to 3000 µg/L. Anticoagulation was continued for a total of 9 months postsplenectomy.

Figure 3 Abscess cavity (H&E, ×20 magnification).

Figure 5 Haemorrhagic infarction (H&E, ×100 magnification).

DISCUSSION

Myelodysplastic syndrome is a clonal haematopoietic stem cell disorder, characterised by ineffective haematopoiesis, usually manifested as cytopenias and, often, dysfunction of neutrophils and platelets. Transfusion dependence invariably leads to iron overload. Iron overload is known to predispose to certain infections, such as *Vibrio*, *Yersinia*, *Listeria*, *Salmonella* and *M. tuberculosis*, because of the central requirement of iron for the growth and virulence of bacteria and pathogens.^{7–10} Iron overload and the resulting dysfunctional neutrophils are likely contributing factors to salmonella infection in the patient. Iron chelation may have the potential of lowering infection risk.¹¹

Splenic vein thrombosis in our patient's case most likely arose secondary to inflammation from splenic abscesses, rather than MDS. Intra-abdominal sepsis is a common cause of splanchnic vein thrombosis, induced by thrombophlebitis and damage of the intima of intra-abdominal vessels. MDS is not a common cause of splanchnic vein thrombosis unless associated with paroxysmal nocturnal haemoglobinuria, JAK2 mutation or Behçet's disease.¹² Other common causes of isolated splenic vein thrombosis absent in the patient are pancreatic pathology (acute and chronic pancreatitis, pancreatic tumours) and postsurgical manipulation,^{13 14} whereas common risk factors for splanchnic vein thromboses as a whole are classic myeloproliferative disease, inherited and acquired thrombophilia, antiphospholipid

syndrome and JAK2 mutation positivity.¹⁵ Postsplenectomy, Aleali *et al*¹⁶ reported massive thrombosis in a patient with sideroblastic anaemia, in association with marked postsplenectomy thrombocytosis. Therefore, our patient continued anticoagulation for a further 9 months until postsplenectomy thrombocytosis had resolved.

In cases of unexplained pleural effusion or isolation of enteric bacteria, such as *Salmonella* from pleural fluid, it is imperative to search for an intra-abdominal source of infection. As illustrated in this case, blood cultures may be negative even with large abscesses and there may be minimal abdominal symptoms.

Splenic abscesses from *Salmonella* have been treated either with splenectomy^{1 17 18} or percutaneous drainage.^{1 19} Percutaneous image-guided drainage for a single abscess and splenectomy for multiple abscesses are reported as safe and effective.²⁰ Percutaneous drainage may be considered, if preservation of the spleen is a priority, in patients unfit for surgery or as a bridge to surgery.²¹ *Salmonella* empyema may be treated by either percutaneous drainage or pleural decortication.¹ In this case, there was incomplete evacuation with persistent large retained empyema after percutaneous drainage. It was necessary to perform surgical drainage and decortication, together with diaphragmatic repair and splenectomy, to remove the massive spleen with large ruptured splenic abscesses. The good outcome of this high-risk patient supports pleural decortication and splenectomy as a viable treatment option together with antibiotics.

Figure 4 Extramedullary haematopoiesis with presence of megakaryocyte and nucleated red blood cells in the sinuses (H&E, ×600 magnification).

Learning points

- ▶ Empyema may be an extension of an intra-abdominal source of sepsis. Isolation of an enteric organism such as *Salmonella* in the pleural fluid suggests an intra-abdominal source.
- ▶ For a patient with *Salmonella* empyema from a splenic abscess, pleural decortication together with splenectomy followed by a 4-week course of antibiotics is an effective treatment option.
- ▶ Concomitant pleural decortication, diaphragmatic repair and splenectomy, in the same surgical setting, resulted in simultaneous decontamination of chest as well as abdominal cavities, reduced surgical morbidity and facilitated full resolution of this extensive salmonella infection.
- ▶ Iron overload can predispose patients to serious infections, which lends support to iron chelation in the management of transfusion-dependent anaemias.

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