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Case Report

Microbiology Section

# Rare Presentation of Pleural Empyema due to Non Typhoidal Salmonella- A Case Report

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## ABSTRACT

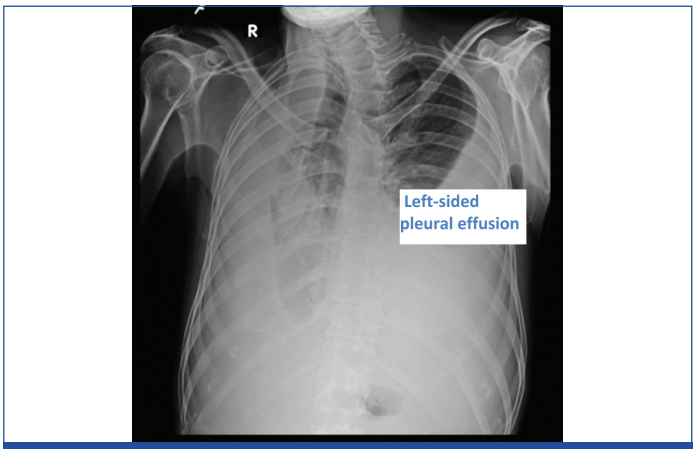
Non typhoidal *Salmonella* usually causes bacteraemia, enterocolitis, and endovascular infection, but pleuro-pulmonary illness is uncommon, mainly observed in patients with a background of malignancy, underlying pulmonary diseases. Localisation of the infection has been witnessed at various sites following a bacteraemia, but case reports on pulmonary focus are minimal. Here, we report a case of a 36 year old male patient who presented to Emergency Department with an underlying Non-Hodgkin's Lymphoma along with a left sided pleural effusion. Pleural fluid tapping was done and the sample was sent for microbiological analysis. The pleural fluid culture along with serotyping confirmed the organism as *Salmonella enterica* serovar Typhimurium. The patient was discharged after parenteral Ceftriaxone therapy and symptom resolution. The present case adds to the growing body of evidence of rare presentation of non typhoidal *Salmonella*, as a probable aetiological agent of infection in exudative pleural effusions.

**Keywords:** Gram-negative bacteria, Immunocompromised, Lymphoma, Pleural effusion, Pulmonary illness, Serotyping, Underlying diseases

## CASE REPORT

A 36-year-old male patient, presented to the Emergency Department with complains of breathing difficulty. He was a known case of low-grade B-cell Non-Hodgkin's Lymphoma Follicular (NHLF) type with Follicular Lymphoma International Prognostic Index (FLIPI) score of 3 (based on the clinico-biological features) indicating the patient falls under high-risk category. The patient was due for chemotherapy for his underlying condition but deferred due to the presenting complaints. Following initial evaluation, he was admitted and therapeutic thoraco-centesis was done and around 1.5 L chylous effusion was removed and sent for culture and sensitivity. The analysis showed a transudative picture with no bacterial growth on culture following which intrapleural streptokinase was initiated. The patient showed marked clinical improvement and was discharged. Following two months of this episode, he presented to Emergency Department, again with complaints of left-side chest pain, worsening dyspnoea and orthopnoea for two days.

Physical examination revealed afebrile state with an oxygen saturation ($SpO_2$) of 88% initially, respiratory rate of 20 breaths/min and tachycardia (irregular) with normal blood pressure (120/70 mmHg). Following this, patient was started on supplemental oxygen and was found to be comfortable. Cardiovascular examination was normal. Respiratory system examination revealed dullness to percussion in the left middle to lower zones, with reduced breath sounds noted in the same area. Initial pathology revealed white blood cell count of 12×109 per litre with 74% neutrophils and 14.6% lymphocytes (20-40% lymphocytes). C-Reactive Protein (CRP) was elevated at 130 mg/L. Chest X-ray revealed left-sided pleural effusion [Table/Fig-1].




**[Table/Fig-1]:** Postero-anterior chest X-ray view.

The patient was transferred to the ward and left Inter-Costal Drainage (ICD) was done. And around 1500 mL of chylous fluid was drained. The Triglyceride (TGL) level was observed to be 524 mg/dL. The Triglyceride (TGL) level was observed to be 524 mg/dL. Pleural fluid was also sent for GeneXpert to rule out tuberculosis and conventional microbiological analysis. The pleural fluid was cultured on blood agar and MacConkey agar. Non haemolytic grey moist colonies and non lactose fermenting colonies were observed in blood and MacConkey agar, respectively after 24 hours of incubation at 37°C. Following this, the manual biochemical tests were done, which included indole (negative), Triple Sugar Iron (TSI) slant (alkali/acid), Mannitol motility (motile), citrate (positive), urease (negative). The identification was confirmed by Vitek 2 GN ID card (21341). Bacterial serotyping was done using antisera (Denka Seiken, Japan) which confirmed the strain as Typhimurium (H-i). The serotyping was further verified by sending the isolate to Central Research Institute (CRI), Kasauli whose result was in concordance with the laboratory result (*Salmonella typhimurium*).

The isolate was finally confirmed as *Salmonella enterica* serovar Typhimurium. Thus, the patient was diagnosed as a case of pleural empyema caused by *Salmonella enterica* serovar Typhimurium (*Salmonella typhimurium*). The isolate was sensitive to ceftriaxone and azithromycin but resistant to quinolones by manual disc diffusion performed in accordance to Clinical and Laboratory Standards Institute (CLSI) 2022. (Perfloxacin was reported resistant) [1]. The patient was started on i.v. ceftriaxone therapy for one week. Simultaneously, he was reviewed for chemotherapy, and was deferred due to the ongoing infection. The patient showed a marked clinical response to i.v. therapy, which was followed with two week course of oral cefixime. There was a marked improvement in inflammatory markers. The Inter-Costal Drainage (ICD) was removed when fluid was less than 100 mL. Additionally analgesics, antiemetics and vitamin supplements were given. He was discharged with stable condition and advised follow-up in four weeks. In the review, the

patient was stable and referred to medical oncology for initiation of chemotherapy for his underlying condition.

## DISCUSSION

The most common symptom of *Salmonella* infection is acute enterocolitis. Any *Salmonella* serotype can produce *Salmonella* bacteraemia following a primary focus. In England and Wales, Threlfall EJ et al., found that infections with *Salmonella enteritidis* and *Salmonella typhimurium* resulted in most of the bacteraemias, but infections with *S.choleraesuis, S.dublin*, and *S.virchow* resulted in the highest rate of septicaemia [2]. Salmonella infections, on the other hand, can cause extraintestinal symptoms, as well as, localised infections such as septic arthritis, osteomyelitis, vascular infection, endocarditis, urinary tract infection, and splenic abscess. With non typhoidal gastroenteritis, bacteraemia can develop in upto 8% of patients, and localised infection can happen primarily in newborns, the elderly and immunocompromised patients. In less than 1% of patients, *Salmonella* may be observed as a chronic carrier. There are very few cases of pleural empyema caused by *Salmonella enteritidis* [3]. A review of case reports of Salmonella associated with pulmonary infections, has been listed in the [Table/Fig-2] [4-14].

Those with co-morbid conditions such as diabetes mellitus, sickle cell anaemia, malignancies such as lung cancer, leukaemia, and lymphoma, as well as, patients undergoing corticosteroid therapy, are most commonly affected by Salmonella empyema. The present case discussed here, on the contrary was young, but a known case of B-cell Non-Hodgkin's lymphoma. Salmonella syndrome is common in people with cellular immunodeficiency, such as Acquired Immunodeficiency Syndrome (AIDS), because *Salmonella* is an intracellular pathogen. The treatment of these patients is typically challenging, and they frequently become victims of repeated infections [3,15]. Interesting feature accounting in the present case is that, the patient had a similar admission nearly seven weeks back and the thoraco-centesis revealed a transudative picture, with negative bacterial culture analysis of pleural fluid. Leukocytosis is a common symptom of non typhoidal empyema [16]. Immunosuppression in the background of malignancy and chemotherapy could be related to absence of leukocytosis. The raised CRP would have been a better way to track the immune response [17,18]. In individuals with positive blood cultures for *Salmonella*, the possibility of localised infections like empyema should be considered with non typhoidal strains despite its rare occurrence [3].

*Salmonella* species is thought to lie dormant in the Reticuloendothelial System (RES), where it could be reactivated and spread haematogenously. Due to the low bacterial burden in *Salmonella* bacteraemia, blood cultures are frequently negative. With the progression of the illness, the sensitivity of blood culture detection also decreases [17,19]. Patients with Hodgkin's disease have consistent cellular immune abnormalities that they endure during active presentation or in remission. Patients' depressed cell-mediated immunity has an impact on humoral immunity also. These elements together make the patient more vulnerable to opportunistic infections and make them susceptible to infections due to intracellular organisms as *Salmonella* [20].

*Salmonella* bacteraemia or localised infection can be treated with a variety of antimicrobial agents as per sensitivity report. Ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, and third-generation cephalosporins have demonstrated to have an acceptable action. Infection of the pleuro-pulmonary area with Salmonella associated with a high death rate. This, however, could be due to other contributing features [15]. Fortunately, patient in the present study, was prescribed parenteral Ceftriaxone, based on the antibiotic sensitivity report, and he showed a marked clinical response. In the follow-up, the symptoms fully resolved that, he was referred for further chemotherapy, to treat his underlying disease.

| Authors and year of publication of study | Age of the patient (s) | Sex | Immune status | Medical and social status | Organism detected | Type of pulmonary involvement | Treatment | Outcome |
|---|---|---|---|---|---|---|---|---|
| Ramanathan RM et al., 2000 [4] | 51 years | Female | Compromised | Diabetes and adenocarcinoma of gall bladder | *S. Senftenberg* | Left pleural empyema | Pig-tail catheter drainage+treatment with i.v. imipenem and amikacin, and oral doxycyclin | Initial resistance to antibiotics then improved |
| Samonis G et al., 2003 [5] | 72 years | Male | Compromised | Lung cancer | *Salmonella enterica* serotype Enteritidis | Pneumonia | Antibiotic treatment | Died |
| Mishra S et al., 2004 [6] | 35 years | Male | Competent | No | *Salmonella* typhi | Left hydropneumothorax | - | - |
| Kömüs N et al., 2005 [7] | 65 years | Female | Compromised | Hepatic cirrhosis secondary to autoimmune hepatitis and hepatocellular carcinoma | *Salmonella* typhi | Right pleural empyema | Right tube thoracostomy was performed and sulbactam- ampicillin 6 g/day therapy | Improved |
| Genzen JR et al., 2008 [8] | 55 years | Male | Competent | Alcoholism, bronchitis, and oesophageal dysmotility | *Salmonella typhimurium* | Right upper lobe pneumonia with areas of cavitation | Antibiotic therapy | Improved |
| Kam JC et al., 2012 [9] | 66 years | Female | Compromised | Diabetes+Smoking-induced lung pathology | *Salmonella* group D | Pleural empyema | Decortication+Antimicrobial treatment | Improved |
| Nale SS et al., 2013 [10] | 30 years | Male | Compromised | Chronic alcoholic and Diabetes type II, HSM | *Salmonella typhi* | Left-sided pleural effusion with sub-diaphragmatic collection. | Antibiotic ceftriaxone for 30 days along with intercostal drainage | Initial failure then improved |
| Chao CT 2014 [11] | 61 years | Male | Competent | Intravenous drug abuse, major depression, suicide attempt and mycotic saccular abdominal aortic aneurysm | *Salmonella enterica* serotype Enteritidis | Left pleural empyema | Video-assisted thoracoscopic surgery and endovascular repair of the abdominal aortic aneurysm and six weeks of ciprofloxacin | Improved |
| Thompson Bastin ML et al., 2016 [12] | 33 years | Male | Competent | Intellectual disability, hypertension, depression and seizures | *Salmonella enteritidis* | Multifocal pneumonia | Antimicrobial treatment | Improved |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Rôlo Silvestre C et al., 2021 [13] | 83 years | Male | Myelodysplastic syndromw | No | *Salmonella enteritidis* | Pleural effusion | Antibiotic therapy with intercostal drainage, | Improved |
| Elnour S et al., 2022 [14] | 27 years | Male | Sickle-cell disease | No | *Salmonella* species | Multifocal pneumonia | Antimicrobial treatment | Improved |

**[Table/Fig-2]:** Reported studies in adults with pulmonary Salmonellosis [4-14].

## CONCLUSION(S)

The present case report demonstrated the importance of non typhoidal *Salmonella* infection in immunocompromised patients particularly cancer patients. In many cases of localised Salmonella infection, the initial source of infection cannot be identified, especially when there is a lack of gastrointestinal symptoms, absence of raised leucocytes and negative stool or blood cultures to confirm the source. But, with the initiation of appropriate antibiotic therapy, the fatality rate can be minimised. The authors believe that, more research is necessary to better in understanding the pathogenicity of the bacterium in these patients.

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