CASE REPORT

Gasping the Death Throes: A Case Report and Review of Literature on Salmonella Empyema Among Malignancy Patients

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ABSTRACT

Salmonella infection typically manifests as gastroenteritis and enteric fever. The detection of *Salmonella* in empyema is rare, predominantly occurring in immunocompromised individuals. We report the case of a 68-year-old male with underlying lung adenocarcinoma who presented to the Emergency Department (ED) with right-sided pleural effusion. Pleural fluid aspiration was performed, and microbiological analysis of the sample identified the organism as *Salmonella enterica* serotype Kalamu (S. Kalamu). The patient was treated with parenteral amoxicillin-clavulanate for a total duration of five weeks. This case aims to highlight the potential role of non-typhoidal *Salmonella* (NTS) as a causative agent of pleural empyema, thereby enhancing clinical awareness and its implications in patient management, particularly in individuals with underlying malignancies.
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INTRODUCTION

Salmonella, a genus within the Enterobacteriaceae family, comprises gram-negative, non-spore-forming, facultatively anaerobic bacilli. Over 2,500 identified serotypes of the two primary species, *Salmonella bongori* and Salmonella enterica have been found. The serotypes most associated with human infections are *S.* Enteritidis and *S.* Typhimurium. (1,2) *Salmonella* infections are prevalent worldwide and present a significant public health challenge due to their diverse clinical manifestations and potential for severe disease in vulnerable populations. (1)

Salmonella infections (salmonellosis) often cause symptoms like gastroenteritis, enteric fever, bacteremia, vascular infections, and chronic carriers. (2,3) Extraintestinal *Salmonella* infections are frequently seen in *Salmonella* bacteremia and can be accompanied by enteric fever or gastroenteritis. (3) However, pleural empyema caused by *Salmonella* is rare. We present a case of *S.* Kalamu pleural empyema in a lung cancer patient with negative blood cultures and review the management of *Salmonella* pleuropulmonary infection in patients with malignancies. For NTS this serovar is rarely known pathogenic in humans.

CASE REPORT

This case involves a 68-year-old gentleman who was newly diagnosed with a right lung malignancy in October 2023. His histopathological examination (HPE) biopsy of the lung mass in the lower zone revealed non-small cell carcinoma, with features suggestive of adenocarcinoma. He was scheduled to receive intravenous (IV) carboplatin AUC 5 for six cycles; however, this was postponed due to the development of lung empyema. Initially, he presented with an intermittent cough and right lower chest pain during coughing. He also experienced shortness of breath, which worsened on the day of admission. He did not report any gastrointestinal symptoms, such as diarrhoea. Lung examination revealed reduced air entry over the right lung lower zone, accompanied by dullness on percussion.

His full blood count revealed anaemia with a haemoglobin (Hb) level of 9.5 g/dL. The white blood cell count (WBC) was slightly elevated at 12.5 x 10^3/ µL, with a differential showing 78.5% neutrophils, indicating a likely bacterial infection, and 15% lymphocytes. The platelet count was also increased at 575 x 10^3/ µL, possibly reflecting a reactive thrombocytosis. C-reactive

protein (CRP) was markedly elevated at 94.60 mg/L, consistent with significant inflammation or infection. Serum lactate dehydrogenase (LDH) was notably high at 1691 U/L, which could indicate tissue damage or malignancy.

A chest X-ray demonstrated a right pleural effusion (Figure 1). Pleural tapping was performed, draining 300 mL of pleural fluid for further analysis, including biochemistry, cytology, bacterial culture, and mycobacterium culture. Pleural fluid biochemistry revealed a very high LDH of 22,215 U/L, low glucose (0.1 mmol/L), low amylase (27 U/L), and elevated protein (100.3 mmol/L), suggesting an exudative effusion likely due to infection or malignancy.

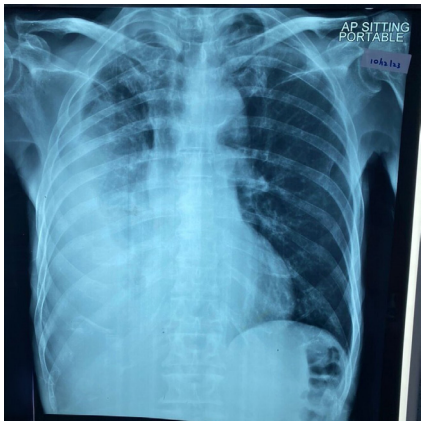

Figure 1: Anterior-posterior chest X-ray view.

Cytological analysis of the pleural fluid showed moderate cellularity with a predominance of neutrophils, indicating an inflammatory process, but was negative for malignancy.

Turbid pleural fluid was received in the microbiology laboratory. Gram-stain and Auramine-O immunofluorescent stain were done and numerous pus cells were seen but neither organism nor acid-fast bacilli were demonstrated. The pleural fluid was cultured on sheep blood agar (ThermoScientific, Melaka, Malaysia), Mac-Conkey agar, and *Shigella Salmonella* agar (SSA). The culture plates were incubated in 37°C aerobic incubation for twenty-four hours. The culture showed colonies with black centre on SSA (Figure 2), greyish colonies on blood agar and non-lactose fermenter colonies on Mac-Conkey agar. Triple sugar iron test (TSI) was done and incubated in 37°C aerobic incubation for 24 hours, revealing an alkaline slant and acid butt with H_2S (Figure 3). Further identification proceeded with matrix-assisted laser desorption ionization–time-of-flight mass spectrometry (MALDI-TOF MS) MS (Bruker, Germany), yielded *Salmonella* sp. with a high confidence identification log[score] value of 2.17, using the direct transfer method. The identification was confirmed via 16s RNA gene sequencing with the result of *S.* Kalamu. The sample was also cultured on Löwenstein–Jensen (LJ) media and Mycobacteria Growth Indicator Tube (MGIT) liquid broth medium and revealed no growth after forty-two days of incubation. A set of percutaneous blood cultures showed no growth following five days of incubation. No stool culture was sent.

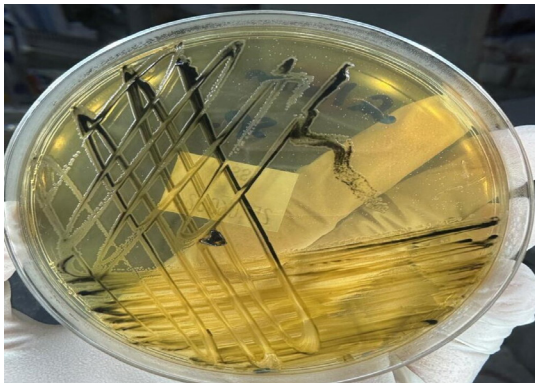

Figure 2: Black centre colony on *Shigella Salmonella* agar after incubated in 37°C aerobic incubation for 24 hours.

Figure 3: Triple sugar iron test (TSI) showed alkaline slant and acid butt with H2S incubated in 37°C aerobic incubation for 24 hours.

This case was presented to us at the end of 2023, during which the most recent Clinical and Laboratory Standards Institute (CLSI) M100, 34th edition had not yet been released. Antibiotic sensitivity testing was performed using the disc diffusion method and interpreted according to the CLSI M100, 33rd edition Enterobacterales breakpoints. The isolates showed susceptibility to ceftriaxone, ciprofloxacin, and amoxicillin-clavulanate, but resistance to ampicillin, ampicillin-sulbactam, trimethoprim-sulfamethoxazole, and cefoperazone. The difference between CLSI M100 34th edition and CLSI M100 33rd edition is that the recent CLSI has separated Enterobacterales breakpoints with the *Salmonella, Shigella* sp. breakpoints.

The patient was initially treated empirically with intravenous (IV) amoxicillin-clavulanate 1.2 g three times daily. Given his stable respiratory condition, he did not require oxygen support during the admission. The clinician decided to continue IV amoxicillin-clavulanate for ten days, followed by a switch to oral

amoxicillin-clavulanate 625 mg three times daily until discharge. The antibiotic treatment was continued until his follow-up appointment in the chest clinic on the 26th day of oral antibiotics. Unfortunately, the patient was readmitted during this follow-up due to shortness of breath. Pleural tapping was performed, and a pigtail catheter was inserted, draining 100 mL of pleural fluid. The pleural fluid was reported as exudative with pus cells and again yielded *Salmonella* sp., with a high-confidence identification log[score] value of 2.33.

The Infectious Disease (ID) team recommended continuing antibiotics for four to six weeks. The patient was treated with IV amoxicillin-clavulanate 1.2 g three times daily for fourteen days, followed by three days of oral amoxicillin-clavulanate 625 mg three times daily. No respiratory support was required during this admission. A follow-up appointment in the chest clinic was scheduled for one month later, to complete the six-week course of antibiotics. Unfortunately, the patient defaulted on the next follow-up.

DISCUSSION

Empyema is pus accumulation in the pleural cavity. It is often associated with pneumonia, but can be attributed to trauma, post-thoracic surgery complications, oesophageal rupture, and cervical infections.

Risk factor

Salmonella, an intracellular pathogen, often affects individuals with cell-mediated immunosuppression, such as those with acquired immunodeficiency syndrome (AIDS). (2) Although non-typhoidal Salmonella extraintestinal infections are relatively uncommon, they can cause a range of illnesses beyond enteritis, including meningitis, osteomyelitis, deep soft tissue infections, septic arthritis, pneumonia, and bacteremia. (1) The severity of NTS infections is often influenced by the host's immune response, which explains the increased mortality observed in newborns, the elderly, and immunocompromised patients. (1,2,4) Literature suggests that Salmonella empyema frequently affects individuals with comorbid conditions such as diabetes mellitus, sickle cell anaemia, iron overload, chronic renal insufficiency, pulmonary diseases (e.g., lung cancer), malignancies, and those undergoing corticosteroid therapy, antineoplastic treatment, or invasive procedures or as a sequelae of post-obstructive infection. (2-4)

Pathogenesis

Localised salmonellosis may result from seeding from the bloodstream, particularly in patients with positive blood cultures. The bacteria can lie dormant in the reticuloendothelial system and later reactivate, leading to hematogenous spread. (2) In cases where blood cultures are negative, as in our case, this may be due to a low bacterial load in the sample. A review of case reports indicates that *Salmonella* pleural empyema in malignancy sometimes shows no documented isolation in blood or stool is provided in Table I.

Table I: Cases of pleural empyema in malignancy patients

Year	Age	Sex	Comorbid	Species / serovar	Culture of blood or stool isolation	Antimicrobial agents and duration	Surgical intervention	Outcome	Country
2023 (2)	36	M	Low-grade B-cell Non-Hodgkin's Lymphoma Follicular (NHLF)	*Salmonella enterica* serovar Typhimurium	Blood culture negative.	Ceftriaxone therapy for 7 days then oral cefixime for 14 days.	Intercostal chest drainage.	Recovered	India
2019 (3)	60	M	Lung cancer, smoking	*Salmonella enteritidis*	Blood culture negative	Ampicillin for 14 days then oral ciprofloxacin ampicillin sulbactam for 28 days.	Intercostal chest drainage.	Recovered	Malaysia
2020 (4)	66	F	Lung cancer	*Salmonella* sp.	Blood culture negative	Levofloxacin, ceftazidime, and clindamycin for total 7 days.	Chest tube thoracostomy	Recovered	Egypt

Sex: Male (M), Female (F)

The frequency of lung infections caused by NTS is not well-documented, and *Salmonella* is not a common cause of pneumonia. In patients with lung cancer, empyema may arise from pneumonia, tissue damage from chemotherapy, post-invasive procedures, or post-obstructive infections. (3) Although the patient in our case had not yet received chemotherapy, the presence of lung cancer likely increased susceptibility to disseminated salmonellosis.

Laboratory Diagnosis

Leukocytosis is typical in nontyphoidal empyema, but patients with malignancy or those undergoing chemotherapy may not exhibit this due to weakened immune systems. This patient had a slight increase of leukocyte count. Therefore, CRP levels can be a better indicator of the immune response. (2) Diagnosing localised salmonellosis generally involves detecting the bacteria in sterile specimens, such as blood, joint fluid, pleural fluid, and cerebrospinal fluid. In our case, pleural fluid was obtained via pleural tapping.

A study conducted in Malaysia on salmonellosis in live rats and shrews found that out of thirty-two rats and four shrews, eight tested positive for *Salmonella*. Four serotypes were identified: *S. Kalamu , S. Typhimurium,*

S. Weltevreden, and *S. Brancaster*. Although *S. Kalamu* was reported as the fourth most common serotype in a study of stray dogs in Taiwan, there is limited information about its prevalence in rats. (5) In Malaysia, *S. Kalamu* is not well-known, but this finding, along with our case report, highlights the importance of understanding serovar distribution to assess the prevalence of different serovars causing salmonellosis in the region. Rawat *et al.* noted that various serotypes are linked to specific ecological roles and the extent of NTS infection. (1) Knowledge of the serovar is crucial not only for epidemiological purposes but also for managing NTS infections, identifying potential antimicrobial resistance, and anticipating associated morbidity and mortality.

Mortality

NTS invasive diseases can be fatal if not properly managed. *Salmonella* empyema, although rare, is associated with high mortality. Appropriate antibiotic therapy usually leads to clinical improvement in patients with *Salmonella*-associated pulmonary infections. (2)

Treatment

According to Malaysia antibiotic guideline, fluoroquinolones or ceftriaxone have been the drug of choice for NTS for human immunodeficiency virus (HIV) patient. While for lung abscess and empyema the guideline stated amoxicillin clavulanate acid and ampicillin-sulbactam are preferred drugs. Ceftriaxone is the alternative drug of choice. Review of the literature indicates that treatment with various antimicrobials can be effective based on susceptibility. In our case, the patient was treated with amoxicillin-clavulanate, which led to clinical improvement, and he was subsequently discharged with a course of oral antibiotics. For successful eradication of infection, it is advisable to administer antimicrobial prophylaxis for at least 14 days. However, since *Salmonella* species tend to linger in contaminated environments, a treatment duration of 4-6 weeks is generally recommended. (1)

The clinical course of non-typhoidal empyema often involves persistent positive pulmonary cultures and necessitates repeated drainage procedures and decortication. Besides antibiotics, optimizing nutrition, and drainage, surgical intervention is another treatment option for treatment. (3) Our case, like most cases of *Salmonella* pleural effusions, required drainage ranging from pigtail insertion for clinical resolution.

CONCLUSION

Pleural empyema caused by *Salmonella* can occur in immunocompromised hosts even in the absence of bacteraemia or gastrointestinal symptoms. Increasing awareness of this Gram-negative pathogen as a causative agent in pleural empyema, particularly in patients with malignancies, is crucial for early diagnosis and treatment. The choice of antibiotics should be guided by susceptibility testing, with options including ceftriaxone, fluoroquinolones, or amoxicillin-clavulanate, depending on local guidelines and patient-specific factors. Understanding serotype distribution is important for addressing future therapeutic challenges and for effective management of NTS infections. This awareness helps clinicians manage infections more effectively, monitor for antimicrobial resistance, and anticipate potential morbidity and mortality.

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