CASEREPORT/OLGUSUNUMU



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Pleural Empyema Caused by *Salmonella* in a Immunosuppressed Patient: A Case Report and Literature Review

İmmünsupresif Bir Hastada *Salmonella*'nın Neden Olduğu Plevral Ampiyem: Bir Olgu Sunumu ve Literatürün İncelenmesi

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ABSTRACT

Salmonella is a gram-negative enteric bacillus primarily associated with gastrointestinal infections. However, it can also cause extraintestinal infections, including endocarditis, urinary tract infections, and septic arthritis following bacteremia. Although rare, pleural effusion or empyema are recognized focal complications of Salmonella infection. We report the case of a 74-year-old patient diagnosed with chronic myeloid leukemia who presented with chest pain and dyspnea. Salmonella spp. was isolated from pleural fluid cultures. The patient fully recovered after receiving levofloxacin 750 mg once daily for 21 days. No relapses or complications were observed following treatment.

Key Words: Empyema; Leukemia; Pleural; Salmonella

ÖZ

İmmünsupresif Bir Hastada *Salmonella*'nın Neden Olduğu Plevral Ampiyem: Bir Olgu Sunumu ve Literatürün İncelenmesi

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Salmonella, öncelikli olarak gastrointestinal infeksiyonlara neden olan gram-negatif bir enterik basil olup, bakteremi sonrası endokardit, üriner sistem infeksiyonları ve septik artrit gibi bağırsak dışı infeksiyonlara da yol açabilmektedir. Salmonella'nın neden olduğu plevral

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efüzyon veya ampiyem gibi odak infeksiyonlar oldukça nadirdir. Bu yazıda göğüs ağrısı ve nefes darlığı şikayetleri olan kronik miyeloid lösemi tanılı 74 yaşındaki bir hasta sunulmaktadır. Plevral sıvı kültürlerinde Salmonella species üremiştir. Hasta 21 günlük 750 mg levofloksasin tedavisi sonrası tamamen iyileşmiştir. Tedavi sonrası herhangi bir nüks veya komplikasyon görülmemiştir.

Anahtar Kelimeler: Ampiyem; Lösemi plevra; Salmonella

INTRODUCTION

Salmonella is a gram-negative enteric bacillus primarily associated with gastrointestinal infections^[1]. However, it can also cause extraintestinal infections such as endocarditis, urinary tract infections, and septic arthritis following bacteremia^[1,2]. Focal infections are particularly common in immunocompromised patients. While various extraintestinal infections due to Salmonella species have been documented, pleural empyema remains a rare complication, with fewer than 60 cases reported in the literature^[1,3]. This article presents a case of pleural empyema caused by Salmonella in a patient with chronic myeloid leukemia (CML).

CASE REPORT

A 74-year-old female with a history of CML presented with chest pain and shortness of breath. On examination, her vital signs were as follows: temperature, 38.0 °C; pulse, 124 bpm; blood pressure, 110/70 mmHg; and respiratory rate, 24/min. The patient was conscious, oriented, and cooperative, and bilateral crackles were noted on auscultation.

Laboratory examination revealed a white blood cell count of $8.9 \times 10^9/L$, creatinine of 1.07 mg/dL (reference range= 0.7-1.2 mg/dL), and a C-reactive protein level of 235 mg/dL (reference range= 0-5 mg/dL). Detailed laboratory findings are presented in Table 1.

Table 1. Evaluation of pleu	ral fluid and labor	atory findings			
	Day 1	Day 5	Day 10	Day 14	Reference value
Pleural fluid					
Aspect	Purulent	Clear	Clear	Clear	Clear
White blood cells (cell/mm ³)	12.343 leukocytes	2500 leukocytes	300 leukocytes	50 leukocytes	Negative
Gram stain	Negative	Negative	Negative	Negative	0-5
Giemsa stain	52% neutrophils	68% neutrophils	75% neutrophils	68% neutrophils	
Culture	Salmonella species	Salmonella species	Negative	Negative	Clear
AFB staining	Negative	Negative	Negative	-	Negative
Glucose (mg/dL)	34	40	60	80	≥60
Pleura protein/serum protein	0.6	0.8	0.5	0.3	< 0.6
Pleural LDH/serum LDH	3.3	6.0	0.6	0.4	< 0.6
ADA (g/L)	30.2	35	-	-	<30
Tuberculosis PCR	Negative	Negative	-	-	Clear
Blood culture	Negative	Negative	-	-	Clear
Laboratory findings					
White blood cells (10 ³ /µl)	8.9	10.7	7.3	4.1	4-10.5
Neutrophils (%)	89	82	60	54	40-75
Platelets (10 ³ /µl)	250	366	374	316	150-450
CRP (mg/l)	235	313	169	2	0-5
ESR (mm/h)	112	140	71	53	0-20
Creatinine (mg/dL)	1.07	1.6	1.1	0.84	0.7-1.2

AFB: Acid-fast bacilli, ADA: Adenosine deaminase, LDH: Lactate dehydrogenases, PCR: Polymerase chain reaction, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate.



Figure 1. Upon admission, chest X-ray showed increased opacity and effusion in the basal part of the left lung.

Chest X-ray revealed increased opacity and effusion in the basal region of the left lung (Figure 1). Thoracic computed tomography (CT) showed pneumonic infiltration in the lower and middle zones of the left lung, along with an increased density suggestive of bilateral pleural effusion. The pleural effusion measured up to 3 cm on the right side and 4.5 cm on the left side (Figures 2, 3).



Figure 2. Upon admission, thorax CT showed pneumonic infiltration in the lower and middle zones of the left lung.

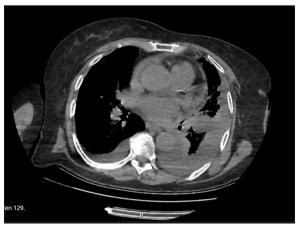


Figure 3. Upon admission, thorax CT showed increased density compatible with bilateral pleural effusion measuring up to 3 cm in the right lung and 4.5 cm in the left lung.

The patient was admitted with a preliminary diagnosis of pneumonia, and piperacillin-tazobactam 4.5 g intravenous (IV) every eight hours was initiated.

Blood and sputum cultures obtained on the first day of hospitalization no growth. Despite antibiotic therapy, the fever persisted, prompting sampling of the left pleural fluid, and a chest tube was inserted for fluid drainage. The pleural fluid sample was exudative, with the following characteristics: pH 7.2, glucose 34 mg/ dL, protein 37.5 g/L, and LDH 1054 U/L. The leukocyte count in the fluid was 12.343/ mm³. Gram staining did not reveal bacteria, but Giemsa staining showed abundant leukocytes (52% polymorphonuclear, 47% mononuclear). The adenosine deaminase level was 30.2 g/L (reference range= 0-30 g/L), and both acidfast bacilli staining and tuberculosis polymerase chain reaction were negative. Pleural fluid culture isolated a non-typhi Salmonella species (serovar not identified). Identification was performed using matrix-assisted laser desorption/ionization time-offlight mass spectrometry (MALDI-TOF MS) with the Bruker IVD MALDI Biotyper 2.3 system (Bruker Daltonik GmbH, Bremen, Germany) (Score: 2.146). Antimicrobial susceptibility testing was conducted using the fully automated BD Phoenix 100 system (Becton Dickinson, Sparks, United States of America). Antibiotic susceptibilities were interpreted based on the minimum inhibitory concentrations in accordance with the

Antimicrobial agent	Minimum inhibitory concentration (mg/mL)	Sensitivity
Amikacin	≤8	Resistant
Ampicillin	≤4	Sensitive, standard dose
Ampicillin/Sulbactam	≤1/8	Sensitive, standard dose
Cefepime	≤1	Sensitive, standard dose
Ceftazidime	≤1	Sensitive, standard dose
Ceftriaxone	≤1	Sensitive, standard dose
Ertapenem	≤0.25	Sensitive, standard dose
Gentamicin	≤2	Resistant
Imipenem	≤0.25	Sensitive, standard dose
Levofloxacin	≤0.5	Sensitive, standard dose
Meropenem	≤0.125	Sensitive, standard dose
Piperacillin/Tazobactam	≤4/4	Sensitive, standard dose
Trimethoprim/Sulfamethoxazole	≤2/38	Sensitive, standard dose

current European Committee on Antimicrobial Susceptibility Testing standards. The isolate was susceptible to ampicillin, ceftriaxone, cefepime, ceftazidime, ertapenem, imipenem, levofloxacin, and trimethoprim-sulfamethoxazole (Table 2). A stool culture for Salmonella did not yield any growth. Piperacillin-tazobactam was discontinued, and levofloxacin 750 mg IV once daily was initiated. The patient had no gastrointestinal complaints but had experienced gastroenteritis one month prior to hospitalization.

The chest tube was maintained for 14 days. On the 14^{th} day of levofloxacin treatment, pleural fluid and blood cultures showed no growth. A chest radiograph on the 14^{th} day of antibiotic treatment demonstrated a marked reduction in pleural fluid, and the chest tube was removed (Figure 4). The levofloxacin IV course was completed after 21 days. The patient's symptoms improved, and radiological resolution was noted (Figure 5).



Figure 4. On day 14 of hospitalization, chest X-ray showed a marked regression of pleural fluid.



Figure 5. On day 21 of hospitalization, chest X-ray showed marked improvement in pleural fluid.

Literature Review

A comprehensive search of the PubMed, Scopus, and Web of Science databases was conducted using the keywords "Salmonella" and "pleural empyema", with the search limited to adult patients (≥18 years). The review published by Saeed et al. in 2016 included cases reported between 1956 and 2015^[1]. Accordingly, our review focused on cases of Salmonella-related pleural empyema published between 2015 and 2024.

We included case reports published in English and excluded pediatric patients. Data analyzed included patient demographics, immune status, culture results, antibiotic treatment regimens, and clinical outcomes. Detailed information regarding the literature review is presented in Figure 6.

DISCUSSION

Pleural empyema is a rare complication of Salmonella infection^[2]. As of 2015, 40 cases of adult empyema caused by Salmonella had been reported^[1]. A review of the literature from 2015 to the present identified 21 additional cases of adult empyema caused by Salmonella, bringing the total number of reported cases

to 61, with this case representing the 62nd documented instance (Table 3)^[1,3-22]. Many of the reported cases involved patients with underlying conditions associated with immunosuppression, although nine cases occurred in individuals without any identifiable immunosuppressive conditions. The most frequently associated comorbidities included malignancies, human immunodeficiency virus infection, and cardiovascular diseases. In the present case, the patient had an underlying immunosuppressive condition, consistent with previously reported cases in the literature.

Impaired cellular immunity plays a key role in the pathogenesis of extraintestinal salmonellosis. In hematologic malignancies other than CLL and multiple myeloma, cellular immunity is primarily affected, making the eradication of intracellular microorganisms such as *Salmonella* more difficult in these patients^[23,24]. In the literature review, two cases were reported with lymphoma and one with myelodysplastic syndrome. In the present case, the diagnosis of CML suggests that this condition may also be a risk factor for the development of *Salmonella* empyema.

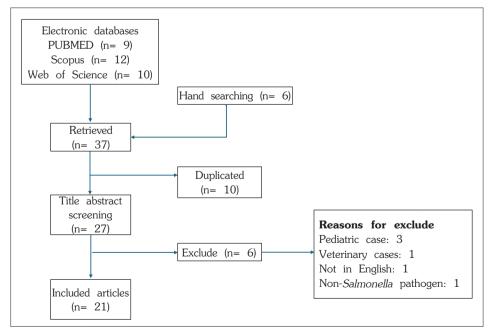


Figure 6. Summary of literature review.

	Age/	Age/			Blood		
Reference	Gender	Immune status	Underlying condition	Pleural fluid culture	culture	Treatment	Outcome
Saeed, 2016 ^[1]	20/M	Compromised	Hodgkin lymphoma	Salmonella enterica serotype Enteritidis	Negative	Ceftriaxone 14 days and cefixime 14 days	Cured
Davis et al., 2024 ^[3]	58/M	Compromised	Alcoholic cirrhosis, hepatocellular carcinoma, DM, HT	Non-typhoidal Salmonella	Z	Levofloxacin eight week + chest tube	Cured
Ali et al, 2015 ^[4]	57/M	Competent	None	Salmonella enteritidis	Negative	Piperacillin-tazobactam * and intrapleural streptokinase	Cured
Pathmanathan et al., 2015 ^[5]	81/F	Compromised	Ischemic heart disease, mitral valve stenosis, AF, HT, neutropenia	<i>S. enterica</i> serotype Typhi	Negative	Ceftriaxone two days (patient declined tube thoracostomy and antibiotic treatment)	Death
Woo et al, 2015 ^[6]	M/29	Compromised	Myelodysplastic syndrome	Salmonella enterica subspecies enterica	Negative	Ceftriaxone, followed by ciprofloxacin four weeks + Videoassisted thoracoscopic surgery (VATS)	Cured
Kojić et al., 2016 ^[7]	M/09	Compromised	Non-Hodgkin Iymphoma	Salmonella enteritidis	Negative	Ciprofloxacin and ceftriaxone two weeks + drainage	Cured
Xaplanteri et al., 2016 ^[8]	81/F	Competent	Congestive heart failure, pulmonary HT, AF, stroke	S. enterica serotype Enteritidis	S. enterica serotype Enteritidis	Ciprofloxacin10 days + tube thoracostomy	Cured
Pitiriga et al., 2016 ^[9]	26/F	Competent	None	Salmonella enterica subsp. enterica serotype Abony	Negative	TMP/SMZ + ciprofloxacin three weeks	Cured
Bretzing et al., 2018 ^[10]	40/M	Compromised	HT, HIV positivity, tobacco marijuana	Non-typhi Salmonella	Z Z	Ceftriaxone two weeks + video-assisted thoracoscopic surgery (VATS)	Cured
Mukai et al., 2018 ^[11]	M/9Z	Competent	chronic heart failure, AF, mitral valve regurgitation	S. enterica serotype houtenae	Negative	Levofloxacin six weeks	Cured
Nyanti, et al., 2019 ^[12]	M/09	Compromised	chronic smoker, lung adenocarcinoma	Salmonella enteritidis	Negative	Ciprofloxacin and ampicillin sulbactam four weeks	Cured
Johari et al., 2019 ^[13]	47/M	Competent	ΣΩ	Salmonella species	Negative	Ceftazidime two weeks, ampicillin sulbactam four weeks	Cured
Antony S et al., 2020 ^[14]	89/M	Competent	ΣΩ	Salmonella enterica	Z/A	Ceftriaxone two weeks + drainage	Cured
Samir Abdelhafiz et al., 2020 ^[15]	9/99	Compromised	Bronchogenic carcinoma	Salmonella spp.	Negative	Levofloxacin* + ceftazidime* + clindamycin +tube thoracostomy	Cured
Shima, et al, 2020 ^{[16}]	72/F	Compromised	SLE	S. arizonae	Negative	Levofloxacin* + tube thoracostomy	Death

Table 3. Studie	s reporting	Table 3. Studies reporting cases of pleural er	npyema due to Salmonel	empyema due to Salmonella in the last 10 years (continue)	ntinue)		
	Age/				Blood		
Reference	Gender	Immune status	Underlying condition	Pleural fluid culture	culture	Treatment	Outcome
Solanky D and Kwan, 2020 [17]	56/M	Competent	DM, alcohol	Salmonella enterica serotype Enteritidis	Salmonella enterica serotype Enteritidis	Ceftriaxone five weeks + Video-assisted thoracoscopic surgery (VATS)	Cured
Rôlo et al., 2021 ^[18]	83/M	Compromised	Myelodysplastic syndrome	Salmonella enterica serotype Enteritidis	Salmonella enterica serotype Enteritidis	Ceftriaxone + ciprofloxacin seven weeks + tube thoracostomy	Cured
Sullivan et al., 2022 ^[19]	57/M	Compromised	Rheumatoid arthritis, DMARD	Salmonella group D	Negative	Ceftriaxone and ciprofloxacin eight weeks + thoracotomy	Cured
Mehmood et al., 2023 ^[20]	M/9Z	Competent	ischemic cardiomyopathy, CRD	Salmonella enteritidis	Negative	Amoxicillin/clavulanic acid four weeks	Cured
Urlapu et al., 2024 ^[21]	57/M	Compromised	Glioblastoma	Salmonella enterica	Salmonella enterica	Ceftriaxone 12 weeks + Video-assisted thoracic surgery (VATS)	Cured
Grey et al., 2024 ^[22]	50/M	Competent	DM, ischemic heart disease,	Salmonella weltevreden	Negative	Amoxicillin four weeks + video-assisted thoracoscopic surgery (VATS)	Cured
Present case	74/F	Compromised	Chronic lymphocytic Ieukemia	Non-typhi Salmonella	Negative	Levofloxacin three weeks	Cured
N/A: Not available, DM: Diabetes mellitus, sulfamethoxazole, DMARD: Disease modifying *:The duration of treatment was not reported.	e, DM: Diabe DMARD: Disea reatment was	tes mellitus, HT: Hype Ise modifying anti-rheur not reported.	N/A: Not available, DM: Diabetes mellitus, HT: Hypertension, AF: Atrial fibrillation, SLE: Syst sulfamethoxazole, DMARD: Disease modifying anti-rheumatic drugs, CRD: Chronic kidney disease. *:The duration of treatment was not reported.	. SLE: Systemic lupus erythem ey disease.	atosus, HIV: H	N/A: Not available, DM: Diabetes mellitus, HT: Hypertension, AF: Atrial fibrillation, SLE: Systemic lupus erythematosus, HIV: Human immunodeficiency virus, TMP/SMX: Trimethoprim sulfamethoxazole, DMARD: Disease modifying anti-rheumatic drugs, CRD: Chronic kidney disease.	Frimethoprim

enoxazole, Divizio: Disease moniying anu-meur uration of treatment was not reported.

In the pathogenesis of focal infections such as pleural empyema caused by *Salmonella* species, it is hypothesized that the infection may spread from either a nearby pulmonary focus or through hematogenous dissemination^[8]. The isolation of an enteric pathogen such as *Salmonella* from pleural fluid should prompt clinicians to consider an intra-abdominal source of infection.

In most reported cases, stool cultures showed growth of *Salmonella typhi*, supporting a gastro-intestinal origin for hematogenous dissemination, and many cases also presented with positive blood cultures^[1]. Blood cultures were negative in 14 of the 21 cases reported in the literature.

In the present case, neither blood nor stool cultures showed growth. Although the primary site of infection could not be definitively identified, the patient's lack of gastrointestinal complaints, combined with a recent episode of gastroenteritis, suggests that *Salmonella* bacteremia may have spread to the lungs via the bloodstream after a gastrointestinal infection. Prior antibiotic treatment for pneumonia may have contributed to the negative blood cultures in this case.

Diagnostic methods for pleural empyema include CT, magnetic resonance imaging, and ultrasonography. In addition to imaging, the analysis of pleural fluid is essential for diagnosis. Typical pleural fluid serology findings in empyema include a pH level below 7.2, glucose levels below 40 mg/dL, lactate dehydrogenase levels above 1.000 IU/L, positive gram staining and/or culture, and white blood cell counts exceeding 50.000 cells/ μ L[25].

Blood cultures and pleural fluid sampling play a crucial role in confirming the diagnosis and guiding antimicrobial therapy. Therefore, blood cultures should be obtained from all patients, and pleural fluid should be evaluated for microbiological examination. In all cases reported in the literature, the diagnosis of empyema was confirmed through imaging findings and pleural fluid sampling. In these cases, pleural fluid cultures showed bacterial growth, while bacterial growth in blood cultures was detected in 19% (n= 4) of cases. The most frequently isolated *Salmonella* species was *Salmonella enteritidis*, identified

in 43% (n= 9) of cases. In the present case, a bilateral pleural effusion was detected on the initial chest CT; however, due to the patient's heart failure, pleural effusion was initially attributed to this condition. During follow-up, persistent fever and negative sputum culture led to the decision to sample the effusion. The fluid was found to be exudative, leading to the diagnosis of pleural empyema. No bacterial growth was observed in the blood culture, but *Salmonella* growth was identified in the pleural fluid culture. However, due to the inability to conduct further identification, the pathogen was reported as *Salmonella* spp.

Treatment for empyema caused by Salmonella species does not differ from treatment for other microorganisms. Preferred antibiotic regimens include third-generation cephalosporins or fluoro-quinolones for 14-21 days, with surgical drainage recommended for pulmonary infections caused by S. typhi. Alternative treatment options for susceptible strains include co-trimoxazole, ampicillin, or chloramphenicol for 14-21 days^[2].

Drainage procedures were performed in nearly all reported cases, and a chest tube was inserted for fluid drainage. The duration of treatment ranged from 2 to 8 weeks. In this case, surgical drainage was performed, and the patient was treated with levofloxacin 750 mg IV for 21 days. Among the cases reviewed in the literature, one progressed to chronic pulmonary infection, and three resulted in death. One fatal case was complicated by lung cancer, another by Nocardia co-infection, and the third by refusal of treatment^[5]. In the present case, the patient improved with appropriate treatment, and no recurrence was observed within the first three months.

CONCLUSION

It is important to recognize that Salmonella can lead to focal infections, particularly in patients with immunosuppression, malignancies, or alcohol dependence. Early diagnosis and prompt initiation of appropriate antibiotic therapy are critical for effective treatment. Source control through chest tube insertion or surgical intervention is often necessary.

CONFLICT of INTEREST

The authors declare that they have no conflicts of interest.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: YÇK Analysis/Interpretation: MÖ

Data Collection or Processing: MÖ

Writing: All of authors

Review and Correction: YÇK Final Approval: All of authors

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