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Subject/Topic: Microbiology

Case report

Unusual *Serratia marcescens* pleural infection in secondary spontaneous pneumothorax: a case report

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Running title: Unusual *Serratia* infection in pneumothorax

Abstract

Serratia marcescens is an opportunistic gram-negative pathogen that causes pneumonia, bloodstream infections, and urinary tract infections, particularly in individuals who are immunocompromised. Although commonly associated with pulmonary infections, its involvement in pneumothorax-related infections is exceedingly rare. Secondary spontaneous pneumothorax (SSP) is a life-threatening condition that can complicate underlying lung diseases, such as chronic obstructive pulmonary disease (COPD). This case report describes a rare presentation of *S. marcescens* infection in a patient with SSP complicated by a bronchopleural fistula. A 64-year-old male with a history of COPD, chronic smoking, and alcohol use presented with progressive dyspnea, cough, and left-sided chest pain. Clinical evaluation revealed tachypnea, tracheal deviation, and reduced breath sounds in the left lung. Laboratory investigations revealed leukocytosis with marked neutrophilia and an elevated erythrocyte sedimentation rate. Chest imaging confirmed pneumothorax, necessitating intercostal drain (ICD) placement. Pleural fluid cultures identified multidrug-resistant *S. marcescens*, prompting antibiotic escalation to intravenous meropenem and oral faropenem. Despite prolonged antimicrobial therapy and ICD placement, persistent pneumothorax with a bronchopleural fistula was noted. Bronchoscopy with Fogarty balloon placement and cyanoacrylate closure was performed. However, owing to financial constraints, the patient declined follow-up cultures and high-resolution computed tomography imaging, and was discharged with an ICD *in situ*. This case underscores the need for heightened clinical awareness of *S. marcescens* in pneumothorax-associated infections. Early microbiological identification and targeted therapy are crucial for the management of rare yet challenging presentations, particularly in resource-limited settings.

Keywords: Antimicrobial resistance; Enterobacteriaceae; MALDI-ToF; Pleural infection; *Serratia marcescens*

Introduction

Serratia marcescens is a gram-negative, motile, facultatively anaerobic bacillus belonging to the Enterobacterales order [1,2]. It is widely distributed in the environment, including in soil, water, plants, and air [2,3]. Although typically considered as an environmental organism, *S. marcescens* has emerged as a significant nosocomial pathogen, particularly in individuals who are immunocompromised [1,3].

The virulence of *S. marcescens* is attributed to multiple factors, including biofilm formation, motility, production of the red pigment prodigiosin, and secretion of extracellular enzymes, such as nucleases, hemolysins, proteases, and lipases [4]. These factors facilitate cytotoxicity in human epithelial cells, leading to vacuolization and subsequent cell lysis [3]. Clinically, *S. marcescens* is associated with severe infections, including pneumonia, meningitis, bloodstream, urinary tract, surgical site, and ocular infections [1,2]. Notably, its intrinsic and acquired resistance mechanisms make treatment increasingly challenging [1].

Although *S. marcescens* is a well-documented pathogen in pneumonia, abscess formation, and empyema, its involvement in pneumothorax-related infections is exceedingly rare and poorly characterized. Pneumothorax is defined as the accumulation of air within the pleural space, leading to the disruption of negative intrapleural pressure and subsequent lung collapse [5]. Recognized risk factors include smoking, preexisting pulmonary diseases, such as chronic obstructive pulmonary disease (COPD), and barotrauma [5]. Secondary spontaneous pneumothorax (SSP) is a life-threatening cardiopulmonary emergency without an iatrogenic or traumatic etiology [6]. Given the increasing incidence of multidrug-resistant *S. marcescens* in respiratory infections, its potential role in pneumothorax-associated infections requires further investigation.

This case describes a rare presentation of *S. marcescens* infection in a patient with SSP complicated by a bronchopleural fistula. Given the increasing antimicrobial resistance of *S. marcescens* and the potential for severe pleuropulmonary infections, clinicians should maintain a high index of suspicion when managing atypical or persistent pneumothorax cases. Early identification through microbiological analysis and targeted antimicrobial therapy are critical for optimizing patient outcomes, particularly in resource-limited settings where repeat microbiological assessments are not always feasible. Further studies and case reports are warranted to elucidate the full spectrum of *S. marcescens* involvement in pleuropulmonary infections.

Case

Ethics statement: Written informed consent for publication was obtained from the patient. This case report was conducted in accordance with the ethical guidelines of K S Hegde Medical Academy (KSHEMA), Nitte (Deemed to be University) and the principles outlined in the Declaration of Helsinki, and was determined by the KSHEMA Institutional Ethics Committee (IEC) to not require full IEC review.

A 64-year-old male with a history of COPD, chronic smoking, and alcohol use presented to the Department of Pulmonary Medicine with progressive dyspnea, cough, and left-sided chest pain over the previous 3 days. The symptoms had an insidious onset and gradually worsened from grade 1 to grade 4 dyspnea, becoming more pronounced in the evening and during routine daily activities, with no identifiable ameliorating factors. The patient also reported orthopnea.

The patient's medical history did not include prior antibiotic treatment for the current condition because this presentation marked the first episode of pneumothorax. There was no history suggestive of a recurrent pneumothorax or prior pulmonary intervention. He was directly referred to our institution from a rural healthcare facility because of the progression of his clinical symptoms. Furthermore, the patient was unable to provide any details regarding previous antibiotic use because he did not have access to medical records at the time of admission.

Upon examination, he appeared tachypneic (respiratory rate, 27 breaths/minute) with tracheal deviation to the right and decreased vesicular breath sounds over the left lung. Initial laboratory investigations revealed leukocytosis (white blood cell count, 15,250 cells/μL; range, 4,000–10,000 cells/μL). Differential leukocyte analysis revealed marked neutrophilia (93.1%), with 4.6% lymphocytes, 2.2% monocytes, 0.1% eosinophils, and 0.0% basophils (ranges: neutrophils, 40%–80%; lymphocytes, 20%–40%; monocytes, 2%–10%; eosinophils, 1%–6%; and basophils, 0%–2%). Additionally, the erythrocyte sedimentation rate was elevated at 42 mm/hour (range, 0–14 mm/hour), indicating a significant infectious or inflammatory response consistent with the patient's clinical presentation. Given the strong clinical suspicion of pneumothorax, an intercostal drain (ICD) was inserted, and pleural fluid was sent for microbiological analysis.

Gram staining of a pleural fluid smear revealed numerous gram-negative bacilli with a few pus cells. The specimen was inoculated into a BACT/ALERT Aerobic Culture Media bottle (BioMérieux, Marcy-l'Étoile,

France), and a broth smear confirmed the presence of gram-negative bacilli upon growth detection. MacConkey agar (HiMedia, Mumbai, India) and 5% Sheep Blood Agar (HiMedia) cultures revealed pale pink colonies, as seen in **Fig. 1**.

Species identification using a matrix-assisted laser desorption/ionization-time of flight mass spectrometer (BioMérieux) confirmed that the isolate was *S. marcescens*. Antibiotic susceptibility testing (AST) was performed using an automated turbidimetric VITEK 2 system (BioMérieux). The minimum inhibitory concentrations were interpreted based on Clinical and Laboratory Standards Institute (CLSI) guidelines [7]. The antibiotic susceptibility profile revealed resistance to amoxicillin-clavulanate (≥32 μg/mL), cefuroxime (≥64 μg/mL), cefuroxime axetil (≥64 μg/mL), ceftriaxone (≥64 μg/mL), cefoperazone/sulbactam (≥64 μg/mL), cefepime (≥32 μg/mL), gentamicin (≥16 μg/mL), ciprofloxacin (≥4 μg/mL), colistin (≥16 μg/mL), and trimethoprim/sulfamethoxazole (≥320 μg/mL). However, the isolate was sensitive to ertapenem (0.25 μg/mL), imipenem (0.5 μg/mL), meropenem (≤0.25 μg/mL), tigecycline (≤0.5 μg/mL), and fosfomycin (32 μg/mL). Additionally, the culture exhibited intermediate susceptibility to amikacin (8 μg/mL).

The patient had been initially administered intravenous ceftriaxone (1 g, twice daily). However, based on the AST results, the regimen was adjusted to intravenous meropenem (1 g, thrice daily) and oral faropenem (200 mg, thrice daily). Supportive care included administration of intravenous fluids, analgesics, nebulization therapy, intravenous steroids, and chest tube management.

Mild clinical improvement was observed on day 3 of therapy, with a slight reduction in dyspnea and chest pain by day 7. No significant adverse drug reactions were reported during the course of antibiotic treatment, and the regimen was well tolerated by the patient. On the 11th day of admission, a follow-up chest radiograph (**Fig. 2**) revealed persistent pneumothorax and the development of a bronchopleural fistula, despite some clinical improvement. The patient underwent bronchoscopy with Fogarty balloon placement and cyanoacrylate gel closure of the left lower lobe bronchopleural fistula. Despite 1 month of inpatient care, repeat imaging demonstrated minimal radiological improvement with persistent pneumothorax. A high-resolution chest computed tomography scan was advised for further evaluation; however, the patient declined due to financial constraints.

Owing to financial constraints, the patient requested discharge, and as a result, a repeat pleural fluid culture was not performed to assess bacterial clearance. Consequently, further microbiological evaluations, including

follow-up culture, were not feasible. This limitation underscores the challenges in managing multidrug-resistant infections in resource-limited settings and highlights the need for tailored treatment approaches based on clinical responses when follow-up testing is not possible. Eventually, the patient was discharged with an ICD *in situ* (**Fig. 2**) with instructions for ICD care and regular follow-up.

To provide a comprehensive overview of the patient's clinical progression, therapeutic interventions, and microbiological findings, a concise timeline summarizing the key events over the 1-month inpatient stay is illustrated in **Fig. 3**.

Discussion

Human infections caused by members of the genus *Serratia*, particularly *S. marcescens*, were not well recognized until the latter half of the 20th century. This was probably because of the challenge of taxonomically describing the genus and the fact that several species were not identified until the 1970s and 1980s [8]. Currently, *S. marcescens* is recognized as an important human pathogen and the second most frequently isolated pathogen in healthcare-associated infections [8,9]. Its occurrence is largely linked to prolonged hospitalization, invasive procedures, and the use of indwelling medical devices such as intravenous, urinary, and intraperitoneal catheters, as well as respiratory instrumentation [3]. In our case, the patient underwent ICD implantation and had a prolonged hospital stay, both of which are recognized as risk factors.

Although *S. marcescens* is not a common cause of primary bacterial infections, it can colonize the gastrointestinal and respiratory tracts, particularly in individuals who are immunocompromised [10]. In our case, the patient had a preexisting respiratory condition (i.e., COPD) and was receiving intravenous steroids, both of which increased the susceptibility to opportunistic infections. Several studies have identified *S. marcescens* transmission through contaminated intravenous fluids and healthcare personnel, highlighting the critical importance of rigorous infection control measures [4]. To provide a clear overview of the various infection routes and environmental reservoirs associated with *S. marcescens* in healthcare settings, Table 1 outlines key sources and their relevance [11].

Although *S. marcescens* has been frequently implicated in pneumonia, bloodstream infections, and urinary tract infections, its involvement in pleural infections is rare. A recent study by Saleh et al. [12] analyzed 414

clinical specimens and identified *S. marcescens* in 3.1% of the cases, predominantly from urine, sputum, and blood. Notably, no isolates were recovered from pleural fluid, further emphasizing the rarity of our case.

Two of the earliest case reports of empyema caused by *S. marcescens* described its association with pneumonia, lung abscess, and pleural infection in pediatric patients who were immunocompromised [13,14]. However, a case report by Sharma et al. [15] marked a notable deviation, documenting the first known instance of *S. marcescens*-induced empyema thoracis in a child who was immunocompetent at that time.

In a retrospective study by Ulu-Kilic et al. [16], 378 patients colonized or infected with *S. marcescens* between January 2008 and December 2012 were identified. Notably, *S. marcescens* was isolated from the pleural fluid of 36 patients (9.5%), highlighting the ability of this organism to cause pleural infections.

A case report by Kumaran et al. [17] described an unusual case of infected chylothorax in a patient after cardiac surgery, in which *S. marcescens* was the causative agent. That report emphasized the rarity of *S. marcescens* infection in spontaneous chylothorax and highlighted the clinical challenges posed by its multidrug-resistant nature, which can lead to prolonged hospitalization and increased treatment costs.

Sethi et al. [18] examined the microbiological profile of indwelling pleural catheter (IPC) infections and reported that *Staphylococcus aureus* was the most prevalent pathogen. *S. marcescens* accounted for 3.2% of the IPC-associated infections, underlining its occasional yet significant role in pleural space infections.

S. marcescens is a well-recognized nosocomial pathogen that colonizes moist environments such as medical equipment, disinfectants, commercial fluids, and dispensers. Its ability to survive in the hospital milieu is a persistent threat to critical care settings [19]. In a documented outbreak in the intensive care unit of the Division of Thoracic Surgery at a university hospital, Ulu-Kilic et al. [20] reported six cases of postoperative empyema attributed to *S. marcescens*. The investigation revealed that, although suction catheters were replaced between patients, the drainage system and its contents were not decontaminated according to standard infection control protocols. Prompt implementation of rigorous infection prevention and control measures, including decontamination of chest tube drainage systems between patients, successfully curtailed the outbreak.

These findings highlight the uncommon nature of *S. marcescens* as a causative agent of pneumothorax-related infections and underscore the significance of our report in expanding the existing limited literature.

SSP is a known complication in 50% to 70% of COPD cases, especially in patients over 60 years old [6]. Individuals who are chronic smokers are also at an increased risk [5]. Persistent or prolonged pneumothorax,

defined as an air leak persisting for >48 hours after chest tube insertion, often necessitates intervention to seal the leak [6]. These risk factors are closely aligned with those observed in our case. Although *S. marcescens* is commonly associated with pneumonia, empyema, and lung abscesses, its involvement in pneumothorax infections is exceedingly rare, making this case particularly noteworthy.

S. marcescens exhibits intrinsic resistance to multiple antibiotics, including ampicillin, amoxicillin, ampicillin-sulbactam, amoxicillin-clavulanate, first- and second-generation cephalosporins (e.g., cefazolin and cefuroxime), macrolides, tetracyclines, nitrofurantoin, and colistin [10]. This resistance is mediated by plasmid-encoded R-factors that facilitate horizontal gene transfer and further complicate treatment strategies [3,10].

The emergence of extended-spectrum beta-lactamase (ESBL)-producing *S. marcescens* has significantly reduced the therapeutic options [10,11,21]. A study by Mayorga et al. [9] indicated ESBL production in >80% of *S. marcescens* isolates, with >50% demonstrating multidrug resistance. Additionally, a study analyzing pleural fluid samples by Khan et al. [21] found 100% resistance to multiple drug classes, further highlighting the therapeutic challenges posed by *S. marcescens*.

Currently, ciprofloxacin is the most frequently prescribed first-line antibiotic for *S. marcescens* infections, followed by amikacin and gentamicin [11]. Carbapenems are the preferred treatment for ciprofloxacin-resistant cases, and fourth-generation cephalosporins and piperacillin-tazobactam are also considered viable options [1,11]. Given the increasing resistance trends, combination therapy is often recommended to enhance treatment efficacy [10,11]. In our case, the patient had a multidrug-resistant ESBL-producing *S. marcescens* infection and was managed with intravenous carbapenem (meropenem) and oral faropenem.

Carbapenems are typically considered “last-resort” antibiotics for the treatment of severe and life-threatening infections, particularly those caused by multidrug-resistant pathogens. Intravenous carbapenems are widely available in most countries for the treatment of complicated or drug-resistant bacterial infections, including respiratory tract infections. However, the clinical role of oral penem antibiotics is less clearly defined [22,23].

Faropenem is an orally administered penem antibiotic with broad-spectrum activity against a range of gram-positive, gram-negative, aerobic, and anaerobic bacteria. Currently, it is approved for use only in Japan and India. In Japan, faropenem is not a first-line therapy and is reserved for specific scenarios, including infections caused by ESBL-producing organisms [22,23]. In India, faropenem has been approved for the treatment of

respiratory tract, urinary tract, skin, soft tissue, and gynecological infections. It is increasingly being considered as a potential alternative to fluoroquinolones or macrolides/ketolides, particularly where antimicrobial resistance is a concern. Despite this, the clinical efficacy of faropenem against invasive ESBL-producing Enterobacteriaceae infections remains inadequately established [23,24].

Routine antimicrobial susceptibility testing for faropenem is not commonly performed in clinical microbiology laboratories in India or Japan, largely because of the absence of standardized interpretive breakpoints from major guidelines, such as those from the CLSI, European Committee on Antimicrobial Susceptibility Testing, and Japanese Society of Chemotherapy. This highlights the need to further investigate the clinical utility of oral penems such as faropenem and their influence on resistance trends. Such insights could contribute to better antimicrobial stewardship and improved treatment strategies for infections, including community- and hospital-acquired respiratory infections [22].

This case highlights the rare occurrence of *S. marcescens* infection in a patient with SSP complicated by a bronchopleural fistula, emphasizing the challenges posed by multidrug resistance in pleuropulmonary infections. Early microbiological identification and targeted antimicrobial therapy are crucial for optimizing patient outcomes, particularly in resource-limited settings.

Article information

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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Conceptualization, Data curation, Formal analysis, Methodology: AAA, SN, VKK; Funding acquisition, Visualization, Supervision: AAA, VKK; Investigation, Resources: AAA, SN; Writing-original draft: AAA, SN; Writing-review & editing: AAA, VKK.

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Table 1. Potential sources and transmission routes of *Serratia marcescens* in healthcare settings, highlighting its ability to persist in moist environments and contaminate medical equipment and fluids

Potential infection route	**Description/example**	**Relevance to *Serratia marcescens***
Contaminated medical fluids	Intravenous solutions, parenteral nutrition fluids	Frequently implicated in outbreaks
Respiratory equipment	Nebulizers, ventilators, ventilator tubing, bronchoscopes, laryngoscopes	Supports growth in moist environments
Indwelling medical devices	Central venous catheters, urinary catheters, chest tubes	Common route of colonization in intensive care unit settings
Environmental surfaces and reservoirs	Washbasins, disinfectants, soap dispensers, air-conditioning systems, tap water	Can survive and proliferate in moist, nutrient-rich areas

Figure legends

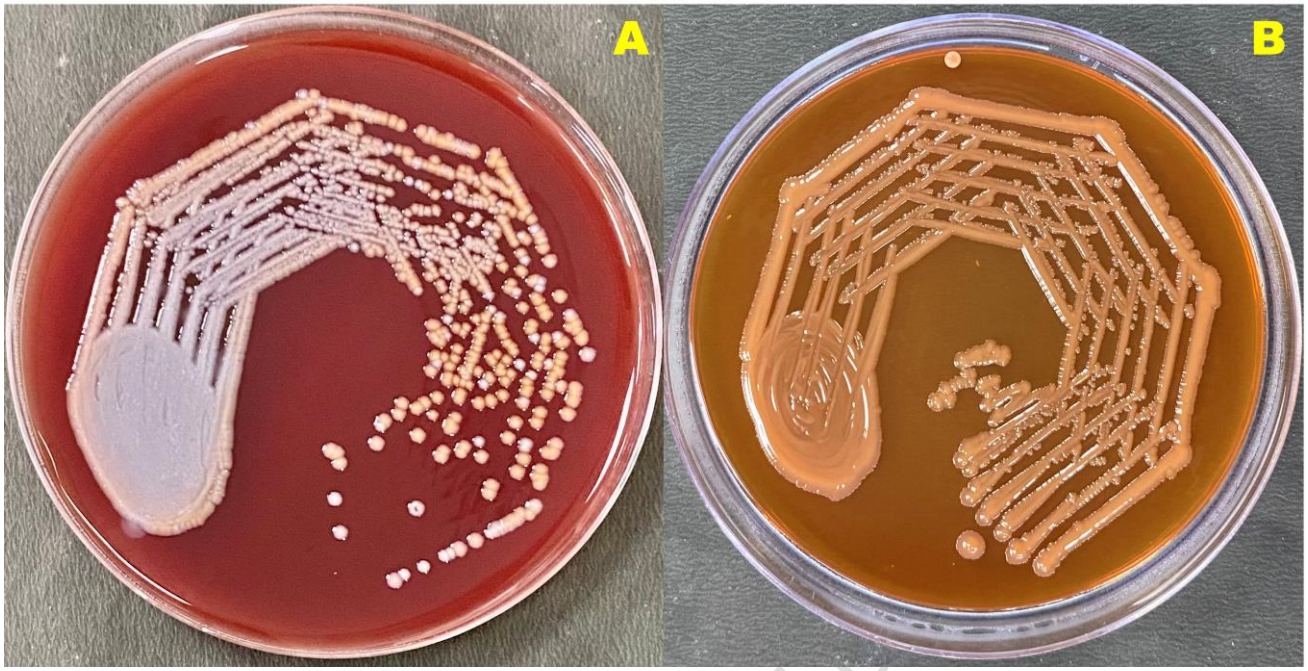

Fig. 1. Bacterial culture findings. (A) Moist, pale pink, non-hemolytic colonies observed on 5% Sheep Blood Agar (HiMedia, Mumbai, India). (B) Non-lactose-fermenting colonies detected on MacConkey Agar (HiMedia).

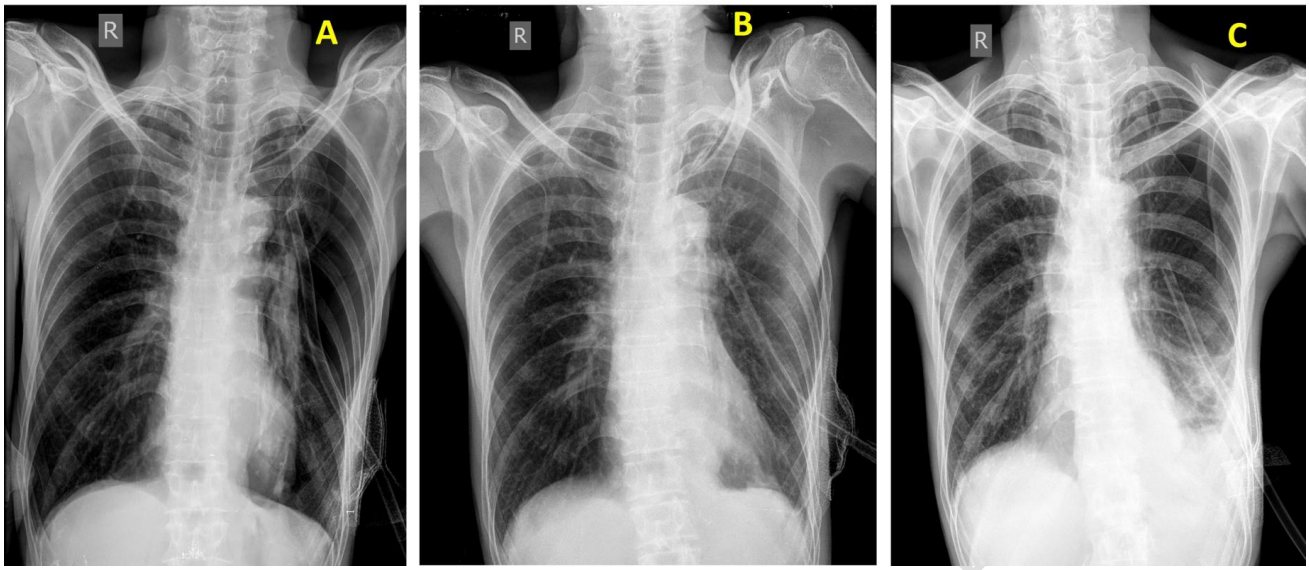

Fig. 2. Serial chest X-ray findings. (A) Initial chest X-ray at admission showing left-sided pneumothorax. (B) Follow-up chest X-ray on the 11th day of admission revealing persistent pneumothorax and a bronchopleural fistula. (C) Chest X-ray on the day of discharge demonstrating minimal residual pneumothorax with an intercostal drain *in situ*.

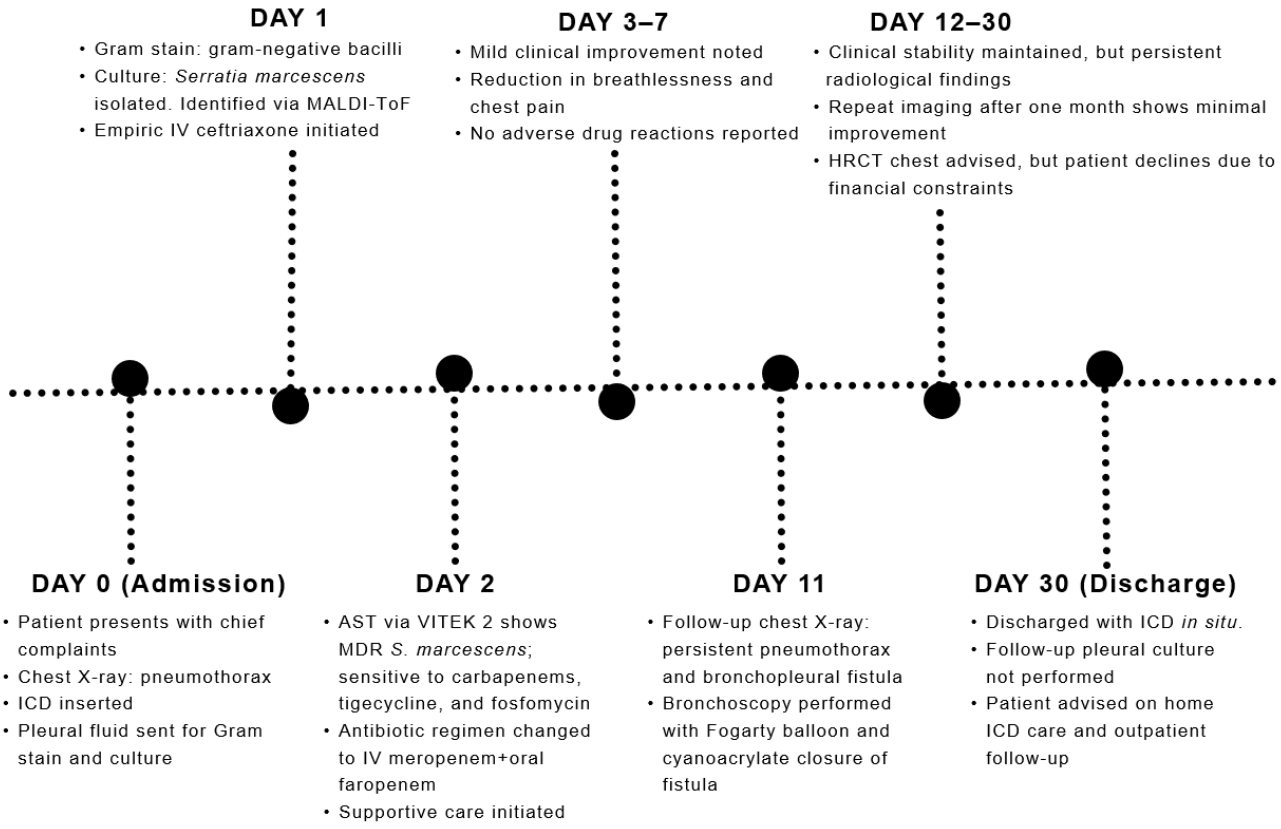

Fig. 3. Clinical timeline of the patient depicting a chronological overview of key clinical events from admission (day 0) to discharge (day 30). MALDI-ToF, matrix-assisted laser desorption/ionization time-of-flight; IV, intravenous; HRCT, high-resolution computed tomography; ICD, intercostal drain; AST, antimicrobial susceptibility testing; MDR, multidrug-resistant. VITEK 2: BioMérieux, Marcy-l'Étoile, France.