Complicated Thoracic Empyema of Serotype 23F *Streptococcus pneumoniae* in an Adult Patient

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ABSTRACT

We report a case of thoracic empyema in a 61-year-old male patient, a heavy smoker with malignancy undergoing chemotherapy. The patient's clinical symptoms included shortness of breath, productive cough, fever, and chest pain. This patient had never received antibiotics before. Streptococcus pneumoniae was isolated from a bedside culture of empyema fluid collected through thoracentesis. The empyema fluid was cultured on chocolate agar plates and in aerobic and anaerobic culture bottles. The isolate was identified as serotype 23F, a vaccine strain with sequence type 17532. The isolate was resistant to chloramphenicol, tetracycline, and cotrimoxazole. The patient clinically improved with the administration of combined intravenous ceftriaxone and levofloxacin antibiotics, along with chest tube drainage via thoracostomy. This is the first report of thoracic empyema caused by S. pneumoniae in an adult in Indonesia. Serotype 23F is multi-resistant with low invasiveness, typically causing infections in patients with comorbidities. It is covered by the pneumococcal conjugate vaccine; thus, it usually occurs in areas with low vaccine coverage. Our findings support the importance of improving adult pneumococcal vaccination coverage in Indonesia.

Keywords: *Streptococcus pneumoniae, thoracic empyema, adult patient, serotype 23F.*

INTRODUCTION

Data from the Global Burden of Diseases (GBD) 2019 showed that an estimated 7.7 million infection-related deaths were associated with 33 bacterial pathogens. *Streptococcus pneumoniae* was identified as one of the five leading pathogens, contributing to 54.9% of deaths.[1] Data regarding the worldwide burden of *S. pneumoniae* are primarily limited to children and the context of pneumonia or meningitis etiology.[2] Indonesia contributes significantly to the disease burden in Asia, accounting for an estimated 3% of global pneumococcal disease cases.[3] However, it does not have a national surveillance program to evaluate the impact of bacterial respiratory illnesses.[4] Consequently,

there is a shortage of necessary data for formulating suitable policies and strategies to manage pneumococcal disease.[5] These data are even scarcer for adults.[6] *S. pneumoniae* infection was detected in 13% and 14% of community-acquired pneumonia (CAP) patients in Semarang and Jakarta, respectively.[7,8] Here, we report a case of empyema caused by *S. pneumoniae* in an adult patient in Pekanbaru, Riau, Indonesia. Serotype 23F was found to be the cause in this case report. *Streptococcus pneumoniae* serotype 23F is known for often being multidrug resistant. This serotype also caused an outbreak in a daycare and has been reported to spread intercontinentally from Spain to the United States.[9,10]

CASE ILLUSTRATION

A 61-year-old man presented to the emergency department in Pekanbaru, Riau Province, with shortness of breath for approximately 1 month, accompanied by a worsening productive cough over the last 5 days. He lived in the Tampan sub-district, Pekanbaru Regency. Other symptoms included fever and chest pain. The patient reported a weight loss of 4 kg in the last 2 months. A week prior, he had visited the same emergency department with pleural effusion, and a thoracentesis yielded approximately 200 cc of clear yellow fluid. Six months prior, the patient had been diagnosed with gastric adenocarcinoma and had undergone two rounds of chemotherapy with the oxaliplatin regimen. He had comorbidities of smoking (Brinkman index 800) and uncontrolled hypertension for the past 10 years. No history of prior antibiotic administration was present.

A physical examination revealed a blood pressure of 138/85 mmHg, a respiratory rate of 24/minute, a heart rate of 101/minute, and a temperature of 36.8 °C. Oxygen saturation was normal. Chest examination and chest X-ray results were consistent with empyema (**Figure 1A**). The patient's leukocyte count was 33.5 × 10^3/mcL, hemoglobin level was 10.8 g/dL, neutrophil count was 70, and albumin level was decreased to 2.2 mg/dL. In the medical ward, a diagnostic thoracocentesis yielded 10 cc of turbid yellow fluid. The pleural fluid was cultured on a chocolate agar plate and inoculated into aerobic and anaerobic blood culture bottles at the bedside. Pleural fluid analysis revealed increased glucose (111 mg/dL), 197 U/L LDH, and 4.7 g/dL protein. Gram staining of the pleural fluid showed gram-positive cocci. Bacterial growth was not observed directly on chocolate agar, but both blood culture bottles showed positive bacterial growth the next day. The morphology and optochin test results were consistent with *S. pneumoniae*. Bacterial identification and antibiotic sensitivity testing with the VITEK 2 Compact (VK2C19207, Biomerieux, Marcy-l'Etoile, France) indicated *S. pneumoniae* susceptible to benzylpenicillin, ceftriaxone, levofloxacin, moxifloxacin, clindamycin, erythromycin, gentamicin, linezolid, teicoplanin, vancomycin, tigecycline, and rifampicin. The strain was resistant to chloramphenicol, tetracycline, and cotrimoxazole.

Genomic DNA was extracted from the *S. pneumoniae* isolate and sequenced using the Illumina platform. Sequencing data in the form of fastq output files, Illumina sequencing disassembly de novo using a unicycler, which is part of the automatic bacterial isolate assembly, annotation, and analysis pipeline (ASA3P; https://github.com/oschwengers /smoke).[11] The assembly results were then annotated using Prokka (https://github.com/tseemann/prokka), which is also part of ASA3P. Visualization of circular genomes and identification of clusters of orthologous groups of proteins using Genome Visualizer Software (GenoVi; https://github.com/robotoD/GenoVi). *The S. pneumoniae* isolate derived from the patient had a genome length of 2,178,456 bp (2.18 Mb) with a GC content of 39% (**Figure 1C**). The *S. pneumoniae* strain showed serotype 23F with sequence type 17532 (https://pathogen.watch/). The antibiotic resistance analysis was consistent with the phenotypic testing results.

The patient underwent closed-tube thoracostomy-based drainage and received intravenous levofloxacin (750 mg) and ceftriaxone (2 g) every 24 hours. Within 3 days, laboratory tests showed a decrease in leukocytes and neutrophils, with a further reduction in leukocyte count over the next 4 days. Chest X-ray revealed a significant reduction in homogeneous

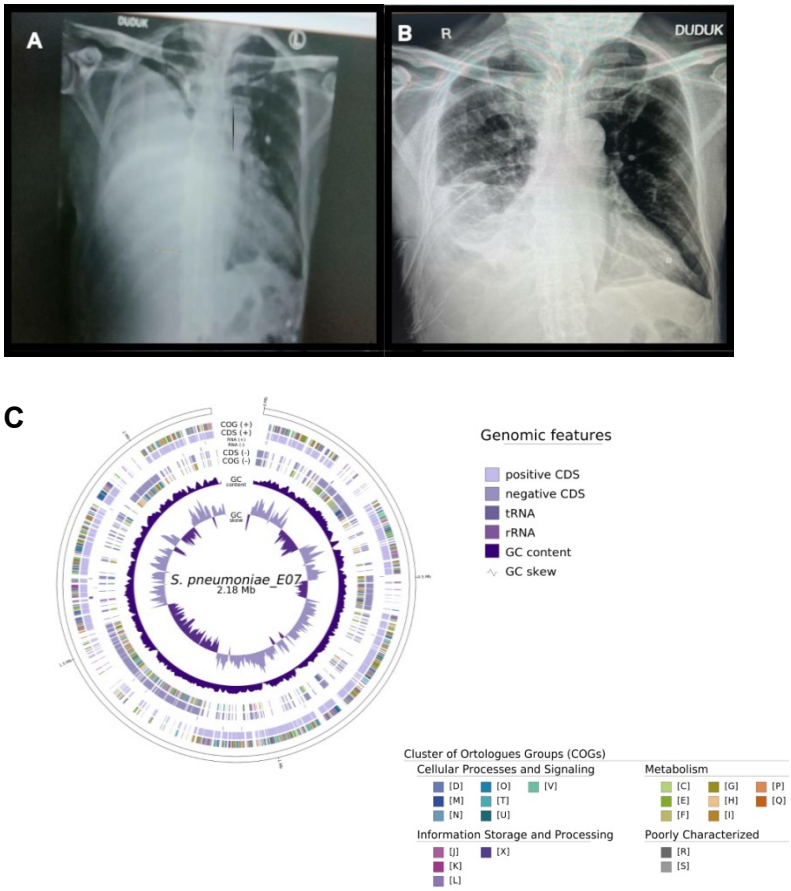

Figure 1. (**A**) Shows homogeneous sheathing in the lower and middle lung fields of the right hemithorax; (**B**) Showed improvement, right homogeneous sheathing is reduced, only in the lower field of the right lung, with the meniscus sign. **(C)** Genomic features of isolate. Circular genome contains all information related to the genome, such as coding sequences (CDS), RNA, Clusters of Orthologous Groups of proteins

opacity within 4 days of treatment (**Figure 1B**). After 7 days of treatment, the patient was discharged without breathing difficulties, productive cough, fever, or localized pain at the chest tube insertion site.

DISCUSSION

S. pneumoniae is frequently responsible for complicated pneumonia, including empyema, in both children and adults.[12] However, the reported cases of thoracic empyema caused by *S. pneumoniae* among adults in Indonesia are still very limited. Research on adult CAP patients in Semarang found that *S. pneumoniae* infection was identified in only 13% of cases, primarily through urinary antigen tests.[7]

Here, we report a case of thoracic empyema caused by *S. pneumoniae* in an adult patient. The culture was examined using an optimal technique at the bedside before antibiotic treatment. The addition of blood culture bottles for infected pleural fluid also enhanced microbial yield beyond that of the standard culture method.[13] Pneumococcal disease surveillance in Indonesia is crucial and should be carried out using locally applicable laboratory methods. Enhancing the infrastructure for laboratory-based diagnostic techniques, such as culture-based detection, urinary antigen detection, and polymerase chain reaction-based assays, is crucial to achieving this goal.[13]

The serotype of *S. pneumoniae* in this patient was 23F. The predominant serotypes observed among patients with empyema include serotype 1 (25%), 3 (12%), 7F (6%), 23F (4%), and others. Serotype 23F, known for its multidrug resistance as well as low invasiveness and disease potential, tends to infect or colonize patients with comorbidities more frequently.[15] This patient had the comorbidities of adenocarcinoma and

smoking. Studies in Indonesia showed high resistance rates to tetracycline (44–62%) and cotrimoxazole (15–29%), with a rate of 4–8% for chloramphenicol.[8,14]

Serotype 23F was identified as a vaccine serotype. The prevailing serotypes causing pneumococcal pneumonia in Indonesia indicate that vaccine serotypes frequently contribute to invasive pneumococcal diseases in regions where pneumococcal vaccination has not been implemented.[5] In Indonesia, the 13-valent pneumococcal conjugate vaccine (PCV-13) and the pneumococcal polysaccharide vaccine (PPSV23) are available. However, since these vaccinations are not yet mandatory, their coverage remains limited.

The patient experienced improvements in clinical and laboratory outcomes after being treated for 7 days with chest tube placement and a combination of two intravenous antibiotics. In contrast, research conducted in the United States of America showed that cancer patients with empyema had to undergo surgery and longer treatment, with an average of 12–21 days of treatment.[16] Antibiotics are given to patients for approximately 2–6 weeks, depending on their response, source control, and causative organism.

CONCLUSION

Although published information on pneumococcal disease in Indonesia is limited, infection caused by *S. pneumoniae* should still be considered in thoracic empyema cases, especially in patients with comorbidities. The prognosis is favorable with appropriate antibiotics and chest tube insertion. Increasing the implementation of *S. pneumoniae* vaccination and surveillance is crucial.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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