GSC Biological and Pharmaceutical Sciences
eISSN: 2581-3250 CODEN (USA): GBPSC2
Cross Ref DOI: 10.30574/gscbps
Journal homepage: https://gsconlinepress.com/journals/gscbps/

(CASE REPORT)

Check for updates

Case report: Infective endocarditis caused by *Streptococcus pneumonia* at Prof. Ngoerah Hospital, Denpasar, Bali

I Komang Putra Adnyana [1], Ni Made Adi Tarini [2, 3] and Komang Januartha Putra Pinatih [2, *]

[1] *Clinical Microbiology Specialist Program, Faculty of Medicine, Udayana University, Bali, Indonesia.*
[2] *Clinical Microbiology Department, Faculty of Medicine, Universitas Udayana, Bali, Indonesia.*
[3] *Clinical Microbiology Laboratory, Prof. Dr. dr. N.G.N.G Ngoerah Hospital, Bali, Indonesia.*

GSC Biological and Pharmaceutical Sciences, 2024, 29(01), 207–213

Publication history: Received on 04 September 2024; revised on 17 October 2024; accepted on 19 October 2024

Article DOI: https://doi.org/10.30574/gscbps.2024.29.1.0378

Abstract

Introduction: Infective endocarditis (IE) is a rare infection of the endocardial surface that can be caused by *Streptococcus pneumoniae* (pneumococcal endocarditis/PE), with an incidence of between 1.4–12.7 per 100,000 people each year, and a mortality rate of <3%. Infective endocarditis is associated with several complications including stroke and congestive heart failure. Here we report a case of IE in an adult caused by *S. pneumoniae*.

Case Description: A 27-year-old woman complained of swelling in both legs, red spots, and a history of fever since 2 days before admission. Physical and supporting examinations including echocardiography and three-sided blood culture were carried out using VITEK-2. *Streptococcus pneumoniae* was identified from the culture which sensitive to Benzylpenicillin group including Cefotaxime, Ceftriaxone, Levofloxacin, Erythromycin, Clindamycin, Tetracycline, and Trimethoprim/Sulfamethoxazole. Infective endocarditis due to S. pneumoniae in adult is very rare. The attachment of S. pneumoniae to the heart valve, may be facilitated by its capsule, which is considered essential in bacteremia. Patient received empirical intravenous antibiotics with 3 grams Ampicillin every 6 hours and 150 mg Gentamicin every 24 hours. The patient improved and treatment was continued by intramuscular injections of 1.2 million IU Benzathine Penicillin G were given every 28 days until age 40.

Conclusion: Infective endocarditis cases in adult patients are associated with high morbidity. Pneumococcal vaccination and adhering to rational antibiotic administration guidelines provide good prognosis to the patients.

Keywords: Infective endocarditis; *Streptococcus pneumoniae*; Ampicillin; Blood culture; Sensitivity test

1. Introduction

Streptococcus pneumoniae, is a gram-positive bacterium upper respiratory tract as a commensal bacterium in healthy individuals. This highly virulent pathogen responsible. For 50% of otitis media cases and approximately 27% of pneumonia cases globally1, is largely preventable through vaccination. Despite its potential to cause a range of diseases, from mild to fatal, including pneumonia, infective endocarditis (IE), septicemia, and meningitis, the prospect of prevention offers hope.

Infective endocarditis (IE) is a rare infection of the endocardial surface structures of the heart that can be caused by bacteria, viruses, or fungi. It can occur acutely or sub-acutely.3 The portal of entry for this infection is generally through the lungs. Although rare, cases of IE caused by *S. pneumonia* a bacterium typically residing in the upper respiratory tract as a commensal bacterium in healthy individuals, have been reported., with an incidence ranging between 1.4 and 12.7 per 100,000 people yearly. The mortality rate within thirty days is high, reaching 30%.4,5 Studies on the prevalence of

* Corresponding author: Pinatih, Komang Januartha Putra

IE in patients with streptococcal bloodstream infections (BSI) have shown that species such as *S. mutans, S. gordonii, S. sanguinis, S. gallolyticus,* and *S. mitis/oralis* have a higher prevalence of IE and associated risk compared to *S. pneumoniae*. The overall prevalence of IE in streptococcal BSI is 7.1%.6

In recent years, cases of IE caused by *S. pneumoniae* have become rare due to the development of antibiotics and vaccines. Pneumococcal endocarditis (PE) is a severe condition with a high mortality rate, accounting for less than three percent.7 Pneumococcal endocarditis typically manifests as an acute illness often accompanied by meningitis, rapid valve destruction, or congestive heart failure. The high mortality rate is associated with significant complications including stroke and congestive heart failure. Due to the atypical initial presentation, there is often a delay in diagnosis and high mortality.3,5,7

This case report describes a 27-year-old female Balinese with IE caused by *S. pneumonia*. The patient presented with swelling of both legs and red spots. The report includes a detailed analysis of the patient's medical history, microbiological diagnostic procedures, drug sensitivity tests, and treatment processes. This case report is of significant importance as it provides a comprehensive understanding of the diagnosis and treatment of IE caused by *S. pneumonia*, which can assist clinicians in identifying and managing similar cases effectively. Relevant literature related to this topic is also reviewed and discussed.

2. Case Report

A 27-year-old Balinese female was referred to Prof. I.G.N.G. Ngoerah Central General Hospital with a chief complaint of swelling in both legs and reddish spots one day before admission. The patient also had a fever for two days. At the previous hospital, the patient was referred to a cardiologist, who performed an echocardiography examination and diagnosed possible infected endocarditis (IE). The patient's journey to diagnosis began with these initial symptoms, and she was then referred for further management. The patient denied experiencing any other complaints, such as tightness, chest pain or palpitations. Previous history of diseases such as hypertension, diabetes mellitus, kidney disease, stroke or heart disease was denied. The patient was treated with levofloxacin 750 mg once a day.

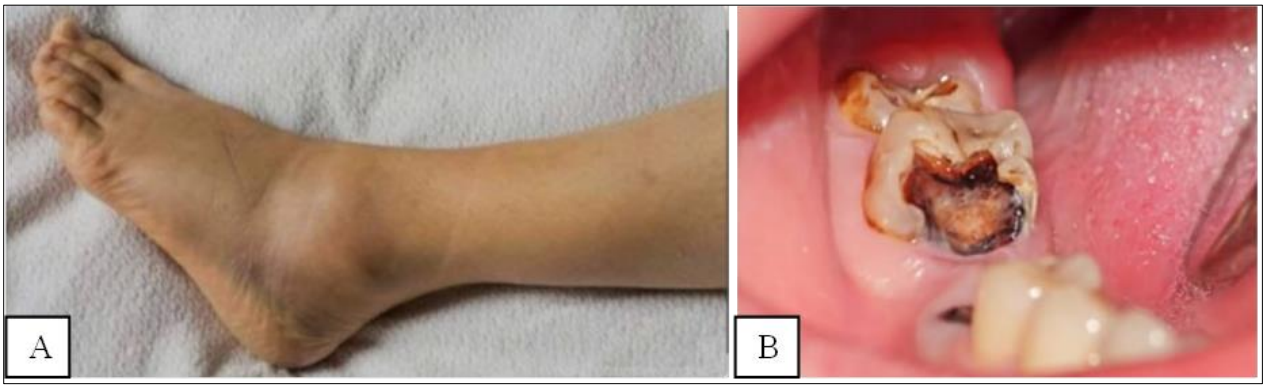

Figure 1 The picture shows swelling of the leg (A) and tooth decay (B) in the patient

The physical examination was thorough and revealed a blood pressure of 97/63 millimeters of mercury (mmHg), pulse rate of 66 beats per minute (bpm), body temperature of 38.1°C, respiratory rate of 20 times per minute, and oxygen saturation 99% (oxygen was given by nasal cannula at 3 liters per minute). Examination of the neck revealed an increased jugular venous pressure (JVP) of PR + 5 cmH2O. Dental and oral examinations found cavities with tartar on the lower jaw. The cardiac examination revealed one and two regular heart sounds with a grade IV/VI systolic murmur at the apex, without gallop. The auscultatory examination of the lungs found vesicular sounds in all lung fields, without rhonchi or wheezing. The abdominal and limb examinations were within normal limits. detailed physical examination results provide a comprehensive view of the patient's condition, aiding in the diagnosis of infective endocarditis.

The electrocardiogram examination revealed a sinus rhythm of 78 bpm. The laboratory examination showed leukocytosis with a white blood cells (WBC) count of 12.58 × 103/UL, mild normocytic anemia (hemoglobin level 10.3 g/dL), hypoalbuminemia (albumin level 2.8 g/dL), hypokalemia (serum potassium level 3.29 mmol/L), and hypocalcemia (calcium level 7.7 mg/dL). The renal function, as seen from urea and serum creatinine levels, is within normal limits, as is the liver function. Upon examination of the anteroposterior (AP) thorax photo, a CTR of 62% was obtained, indicating cardiomegaly. The lungs appears normal. The echocardiography examination revealed left atrium

(LA) left ventricle (LV) dilatation; left ventricular hypertrophy (LVH) (+) eccentric hypertrophy; normal LV systolic function with an ejection fraction (EF) blood pressure (BP) of 72.4%; undetermined LV diastolic function due to severe mitral regurgitation (MR); normal right ventricle (RV) contractility, tricuspid annular plane systolic excursion (TAPSE) of 1.8 cm; and global normokinetics. The valve shows severe MR et causa suspect flail anterior mitral leaflet (AML) et causa suspect IE related, with mobile structure consistent with IE attached to AML; mild mitral stenosis (MS) et causa suspect rheumatic cardiac disease (RHD); mild tricuspid regurgitation (TR), with low probability of pulmonary hypertension (PH); estimated proper atrial pressure (eRAP) is 8 mmHg.

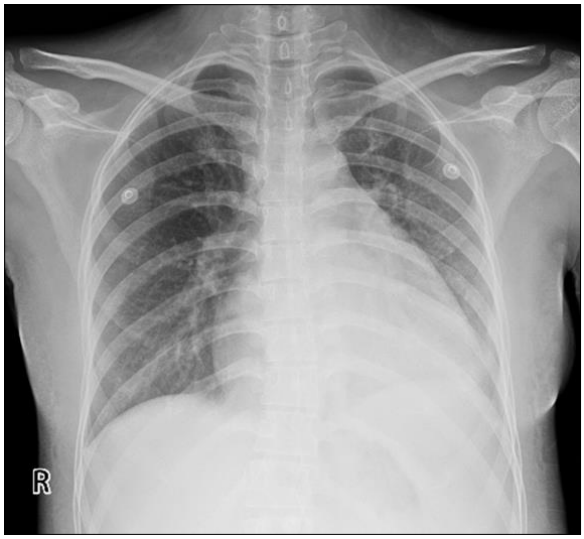

Figure 2 Antero-posterior thorax photo indicating cardiomegaly

During the examination of blood specimens and D84 indirect gram examination, specimens I to III consistently showed the presence of gram-positive cocci bacteria in Figure 3.

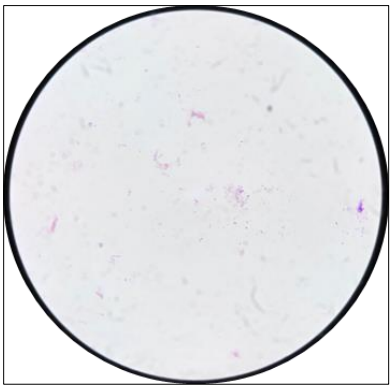

Figure 3 Gram-positive cocci bacteria were found on indirect gram examination (Gram stain, 100×)

After 21 hours, all three three-sided blood culture bottles gave positive results. The three positive samples were transferred to Blood Agar and MacConkey media respectively for further culture. The next day, a round, small, and white colony, an α-haemolytic colony, grew on Blood Agar medium (Figure 4). Identification and antimicrobial susceptibility testing were performed using the VITEK-2 Compact. *Streptococcus pneumoniae* was the result, with a 95% probability of analysis.

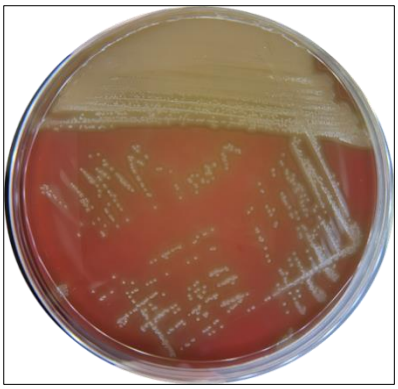

Figure 4 *S. pneumonia* exhibiting round-shaped, small-sized, and white α-hemolysis on Blood Agar medium

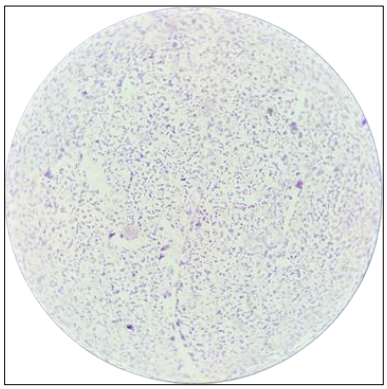

Figure 5 Under the microscope, cultured *Streptococcus pneumonia* appears as gram-positive cocci (Gram stain, 100×)

Antimicrobial susceptibility testing showed that the bacteria were sensitive to the Benzylpenicillin group, including Cefotaxime, Ceftriaxone, Levofloxacin, Erythromycin, Clindamycin, Tetracycline, and Trimethoprim-sulfamethoxazole. This sensitivity is crucial as it guides the selection of the most effective antibiotic for the patient's treatment, ensuring a higher chance of successful recovery

The patient was diagnosed with definite infected endocarditis with vegetation on the AML, congestive heart failure functional class II et causa RHD with severe MR et causa AML prolapse, tooth 46 pulp necrosis, and hypoalbuminemia. The patient received intravenous empirical treatment with 3 grams of Ampicillin every 6 hours and 3 mg/kgbb/day or 150 mg of Gentamicin every 24 hours. Gentamicin was administered for 14 days and Ampicillin for 28 days. The patients received intravenous fluid therapy with normal saline at eight drops per minute, Ramipril 2.5 mg, Bisoprolol 2.5 mg every 24 hours, and Spironolactone 25 mg every 24. The antibiotic therapy was continued once the pathogen and drug sensitivity were confirmed. Although surgery was planned, the patient and family opted for medication and routine check-ups instead. The patient's clinical condition improved during treatment. The patient was admitted to the cardiac and dental clinic as an outpatient, where Benzathine Penicillin G was prescribed until the patient reached 40 years of age.

During the patient's first post-hospitalization check-up, they reported no complaints. A physical examination of the heart revealed a systolic murmur at the apex, while all other vital signs and general status were normal. Additionally, abnormalities were detected during the echocardiography examination. The patient received intramuscular injections of 1.2 million IU of Benzatine Penicillin G every 28 days until the age of 40, while continuing to take Ramipril, Bisoprolol, and Spironolactone. After five follow-up visits, the patient was referred to the previous hospital to continue treatment.

3. Discussion

S. pneumoniae is a gram-positive, *alpha-hemolytic Streptococcus* with 97 known serotypes.8 In 2019, invasive pneumococcal disease was 8 cases per 100,000 in adults aged 19 to 64 and 24 cases per 100,000 in the elderly age group of 65 years and over.9 Previous studies by Chamat-Hedemand et al. found that the prevalence of IE in cases of pneumococcal bacteremia was 1.2%. Although *S. pneumoniae* is less commonly found in cases of IE than *S. mutans, S.*

gordonii, S. sanguinis, S. gallolyticus, and *S. mitis/oralis*, it is still a cause for concern due to its potential for significant morbidity and mortality.6 The main risk factors for *S. pneumoniae*-related IE disease that raise clinical suspicion include prosthetic valves, cardiac implant electronics, and previous endocarditis.3 Other risk factors for the development of the condition include underlying conditions such as lung disease and chronic heart disease, structural heart disease including bicuspid aortic valve, RHD, mitral valve prolapse, congenital heart disease (CHD), heart transplantation, dental infection, intravenous drug use, hemodialysis or use of a catheter attached to the patient's body, liver disease, smoking, alcoholism, old age, malnutrition, diabetes mellitus, and immunosuppressive conditions.9,10 The patient in this case report has not been identified with a specific risk factor. However, a potential risk factor associated with this case is the patient's dental infection.

The pathophysiology of IE involves the preparation of the heart valve for bacterial invasion, followed by infections and potential complications such as meningitis, embolism, and severe heart damage. The pathophysiology of IE involves three key elements, including cardiac valve preparation for bacterial adhesion, bacterial adhesions to the valve surface, and bacteria survival in infected vegetation. Valve trauma can cause changes in the endothelial cells, leading to surface disturbances, platelets and fibrines sedimentation. This can make the surface more susceptible to bacterial colonization. Certain bacteria adhere more firmly to the fibrin-thrombocyte matrix than others, and this is influenced by bacterial virulence factors and inherent survival on the vegetation surface. Pathogens such as certain streptococci, can interfere with valve cells and produce tissue factors (thromboplastin tissue). This can results in the sedimentation and growth of thrombocyte-fibrin clumps over rapidly growing bacterial colonies.11,12

The attachment of *S. pneumoniae* to the heart valve, which can result in endocarditis, may be facilitated by its capsule, which is considered essential in bacteremia. Although the specific mechanisms of adherence to the cardiac valve are not fully explained, the capsule plays an important role in the pathogenesis of pneumococcal endocarditis. In cases where the pneumococcal isolate has a reduced number of capsules, it can still cause infectious endocarditis. This suggests that other factors may also be involved in the adhesion process.13 Pneumococcal endocarditis presents clinically with symptoms such as fever, new heart murmur, pneumonia, meningitis, and/or Austrian syndrome, which is the triad of IE, meningitis and pneumonia caused by *S. pneumoniae*. This condition typically presents acutely as endocarditis, which manifests suddenly.9 The patient in the case report had an intermittent fever for two days prior to admission to the hospital. A new heart murmur was discovered during a physical examination of the heart, which was supported by abnormal findings on echocardiography. As a result, the patient was suspected of having IE. To determine the pathogen responsible for the infection, the patient underwent a three-sided blood culture examination.

The diagnosis of pneumococcal endocarditis is typically achieved through blood culture in 84.7% of cases or valve culture in a minority of cases.9 To increase the likelihood of detecting of bloodstream infections, most guidelines suggest obtaining at least 2 to 3 blood samples taken for culture over a 24-hour period. According to the American Heart Association (AHA) guidelines, at least 3 sets of blood cultures should be obtained from different venipuncture sites should be obtained, with the first and last samples taken at least 1 hour apart. Additionally, echocardiography should be promptly performed on patients suspected of having IE to assess the extent of valve damage and plan further treatment. It is important to note that blood culture results may be negative in up to 5% of patients diagnosed with IE using strict diagnostic criteria. Inadequate microbiological techniques, rapid infection with bacterial or nonbacterial microorganisms, or most importantly due to administration of antimicrobial agents before blood cultures are obtained can result failure to culture organisms in IE. To culture blood from patients suspected of having IE, it is recommended to use three sets, each set consisting of one aerobic bottle and one anaerobic bottle. The blood should be diluted at least one to five in the broth medium. When all blood cultures remain negative after 48 to 72 hours, the microbiology laboratory should incubate these cultures for a longer time of at least 2 to 3 weeks. After this period, the culture should be microscopically examined with acridine orange–stained aliquots of all vials, even if no growth was detected. On day 7, day 14, and at the end of the incubation period, subcultures were performed with aliquots on chocolate agar for further incubation from 3 to 4 weeks in an atmosphere with increasing carbon dioxide (candle bottles). These steps can facilitate the recovery of fastidious bacteria.4,5,14

The patient was diagnosed with definite IE due to meeting three major criteria in the form of positive blood culture results and evidence of endocardial involvement from echocardiography examination, and one minor criterion of experiencing a fever with a temperature above 38°C.3 For suspected *S. pneumoniae* as the infectious etiology, penicillin class antibiotics are the first line treatment. According to the AHA, in cases of IE cause by *S. pneumoniae*, antimicrobials such as penicillin, cefazolin, ceftriaxone, or vancomycin should be administered. For native valve endocarditis, a 4-week course of antibiotics is recommended, while prosthetic valve endocarditis requires a 6-week course of therapy.9,14 In cases of IE caused by penicillin-resistant *S. pneumoniae* without meningitis, high-dose penicillin or third generation cephalosporins can be administered. However, if meningitis is present, high doses of ceftriaxone or cefotaxime are recommended.14,15 According to drug sensitivity tests, the patient in this case report did not exhibit resistance to

penicillin class antibiotics. Therefore, the patient was prescribed a combination of penicillin class antibiotics as the first-line antibiotic therapy based on the etiology. The recommended duration of antibiotic therapy for the patient was 28 days or 4 weeks.

A multicenter study conducted over a 15-year period assessed the prognosis of IE caused by *S. pneumoniae*, which accounts for less than 2% of all IE cases. Out of 3886 patients with IE, only 1.3% had pneumococcal IE, with a majority being men (76%) with a mean age of 60 years. Predisposing conditions for invasive pneumococcal disease (IPD) were identified in 78% of cases. The survival rate at 90 days and 2 years after diagnosis is 67%. Mortality is mainly observed before 90 days, with age 65 years or older being a risk factor. To improve compliance, it is necessary to increase the proportion of patients receiving pneumococcal vaccination and adhering to antibiotic guidelines. Cardiac surgery significantly improves survival.16

4. Conclusion

This case report discusses IE caused by *S. pneumoniae* in a 27-year-old Balinese female. The report highlights the importance of early recognition and efficient treatment of this bacterial infection. Although cases of IE caused by *S. pneumoniae* have become rare due to the development of antibiotics and vaccines, they still result in significant morbidity and mortality. The diagnosis of this condition is made through a combination of anamnesis, physical and supporting examinations that are adjusted to major and minor criteria. These criteria include positive results of blood culture and echocardiography. It is important to select appropriate and wise antibiotic therapy according to guidelines and adjust it to blood culture results. Routine monitoring is also necessary to ensure good results for patients. This case presentation aims to provide clinicians with a deeper understanding of the clinical presentation, diagnosis and management of IE caused by *S. pneumoniae*. The goal is to enable clinicians to provide appropriate, effective and efficient management for patients with similar conditions in the future.

Compliance with ethical standards

Acknowledgments

We would like to thank all medical staff of Department of Clinical Microbiology and Internal Medicine, analyst and other colleagues in Prof. Ngoerah General Hospital who were involved in the management of this case. The completion of this case could not have been possible without the participation and assistance of so many people whose names may not all be enumerated.

Disclosure of conflict of interest

The authors state that this study was conducted without any commercial or financial ties that could be seen as a possible conflict of interest.

Funding

The authors declare that there was no financial support or sponsorship for this study

Author contribution

I Komang Putra Adnyana contributed to the study conception and design and drafted the manuscript; Komang Januartha Putra Pinatih and Ni Made Adi Tarini revised the manuscript critically for important intellectual content.

Statement of informed consent

Authors have secured informed consent from patient regarding this case report.

References

[1] Dion CF, Ashurst J V. Streptococcus pneumoniae. In: *NCBI Bookshelf*. StatPearls Publishing; 2023:1-5. doi:10.1016/B978-1-4377-2702-9.00125-2

[2] Dean KR, Koirala A, Samarasekara H. A case report of disseminated Streptococcus pneumoniae infection complicated by infective endocarditis, septic arthritis and epidural abscess in an immunocompetent patient. *Access Microbiol*. 2023;5(7):1-12. doi:10.1099/acmi.0.000611.v3

[3] Arockiam AD, Agrawal A, El Dahdah J, et al. Contemporary Review of Multi-Modality Cardiac Imaging Evaluation of Infective Endocarditis. *Life*. 2023;13(3). doi:10.3390/life13030639

[4] Rajani R, Klein JL. Infective endocarditis: A contemporary update. *Clin Med J R Coll Physicians London*. 2020;20(1):31-35. doi:10.7861/clinmed.cme.20.1.1

[5] Rezar R, Lichtenauer M, Haar M, et al. Infective endocarditis – A review of current therapy and future challenges. *Hell J Cardiol*. 2021;62(3):190-200. doi:10.1016/j.hjc.2020.10.007

[6] Chamat-Hedemand S, Dahl A, Østergaard L, et al. Prevalence of Infective Endocarditis in Streptococcal Bloodstream Infections Is Dependent on Streptococcal Species. *Circulation*. 2020;142(8):720-730. doi:10.1161/CIRCULATIONAHA.120.046723

[7] Yamazaki K, Miura T, Sunohara D, et al. Infective endocarditis caused by Streptococcus pneumoniae from sinusitis: A case report. *J Cardiol Cases*. 2022;25(5):279-281. doi:10.1016/j.jccase.2021.11.003

[8] National Centre for Immunisation Research and Surveillance. *Pneumococcal Vaccines for Australians.*; 2020.

[9] Ali S, Kim P, Dhar S. Pneumococcal Endocarditis, Rare but Not Forgotten. *Ann Intern Med Clin Cases*. 2023;2(6):2023-2025. doi:10.7326/aimcc.2023.0114

[10] Seo H, Hyun J, Kim H, et al. Risk and Outcome of Infective Endocarditis in Streptococcal Bloodstream Infections according to Streptococcal Species. *Microbiol Spectr*. 2023;11(4):1-9. doi:10.1128/spectrum.01049-23

[11] Yallowitz AW, Decker LC. *Infectious Endocarditis*. StatPearls Publishing; 2023. doi:10.1001/jama.1916.02590260043013

[12] Sheppard MN. Infective endocarditis. *Diagnostic Histopathol*. 2022;28(4):199-208.

[13] Henriet SSV, Langereis JD, Lo SW, et al. Endocarditis Caused by Nontypeable Streptococcus pneumoniae. *Clin Infect Dis*. 2022;75(4):719-722. doi:10.1093/cid/ciac079

[14] Baddour LM, Wilson WR, Bayer AS, et al. *Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications: A Scientific Statement for Healthcare Professionals from the American Heart Association*. Vol 132.; 2015. doi:10.1161/CIR.0000000000000296

[15] Tackling G, Lala V. *Endocarditis Antibiotic Regimens*. StatPearls Publishing; 2023. http://www.ncbi.nlm.nih.gov/pubmed/31194319

[16] Périer A, Puyade M, Revest M, et al. Prognosis of Streptococcus pneumoniae endocarditis in France, a multicenter observational study (2000–2015). *Int J Cardiol*. 2019;288:102-106. doi:10.1016/j.ijcard.2019.04.048