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Review Article

Streptococcus Pyogenes Infective Endocarditis: Case Report and Literature Review

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Abstract

Infective endocarditis (IE) is defined as an infection caused by microorganisms (bacteria or fungi) involving either the heart structures or the great vessels. The progression of IE can become complex due to heart dysfunction and bacterial particles spreading to almost any part of the body through embolization. Staphylococcus aureus and Viridians group streptococci are the predominant causative pathogens. Cases of IE caused by group A β-haemolytic streptococcus (Streptococcus pyogenes) are infrequently reported. Here, we present a case of native mitral valve endocarditis caused by Streptococcus pyogenes in a patient who is an intravenous drug user (IVDU), accompanied by a literature review. The patient had a native mitral valve endocarditis, complicated by brain, lung, spleen, and kidney septic emboli with septic arthritis and abscesses collections, improving after receiving a combination therapy (high dose penicillin with gentamicin). Unfortunately, the patient passed away after two weeks of antibiotic therapy due to a drug overdose.

Introduction

The term infective endocarditis (IE) refers to an infection affecting the inner surface of the heart, suggesting the actual presence of microorganisms within the lesion [1]. The progression of IE may lead to embolization affecting almost any organ, determined by whether the condition affects the right or left side of the heart [2]. IE is a rare entity, with a yearly incidence of about 3–10 per 100,000 people. The Gram-positive cocci of the Staphylococcus, Streptococcus, and Enterococcus species account for 80–90% of IE [3]. Infective endocarditis due to group A, B, C, G streptococci, and Streptococcus angriness group (S. constellates, S. angriness, and S. intermedia's) is relatively rare [4]. Cases of IE caused by group A β-hemolytic streptococcus (Streptococcus pyogenes) are infrequently reported. Here, we report a Streptococcus pyogenes native mitral valve endocarditis in an adult patient along with a review of the literature.

Case Presentation

A 48-year-old IVDU Lebanese male patient, known to have hepatitis C, working as a car mechanic, was admitted with a five-days history of fever, chills, abdominal pain, and right elbow and right knee pain. History goes back 15 days prior to presentation when the patient suffered from thermal burns with bilateral hand skin lesions while manipulating a car battery. He did not report any recent dental procedure or surgery. His past cardiac history was unremarkable. Initial vital signs were temperature 38.6°C, heart rate 80 beats/minute, blood pressure 120/80 mmHg, and respiratory rate18 breaths/min. On admission the patient was dyspneic and his cardiovascular examination revealed an apical systolic heart murmur 3/6. He also presented with multiple necrotic skin lesions on his thumb, index, and middle fingers on both hands, surrounded by minimal erythema. The initial laboratory assessment indicated evidence of disseminated intravascular coagulation (DIC) along with an elevated white blood cell count and an elevated C-reactive protein. He also had anemia and thrombocytopenia. Urine analysis was negative for infection. The electrocardiography (ECG) demonstrated sinus rhythm and the chest x-ray was normal. After taking 3 sets of blood cultures, he was empirically started on cefepime and vancomycin. CT scan of

the chest and abdomen showed findings suggesting pulmonary septic emboli, subtotal splenic infarctions, and bilateral renal infarctions. Blood cultures yielded positive results for gram-positive cocci arranged in chains, subsequently identified as Streptococcus pyogenes. Cefepime and vancomycin were stopped on the second day, and the patient was started on high-dose penicillin IV (18 million IU daily). The transthoracic echocardiogram (TTE) documented severe posterior mitral regurgitation with small hypoechoic mobile masses attached to the anterior valve highly suggestive of vegetations. On the second day, he developed an alteration of mental status, and magnetic resonance imaging of the brain showed findings suggesting recent subacute infarction that could be due to septic emboli. On the third day, the patient developed right elbow and knee swelling, erythema, hotness, and increasing tenderness. Magnetic resonance imaging of the left elbow and left knee showed subcutaneous abscess collections with no signs of osteomyelitis. He underwent incision and drainage. Blood cultures were repeated after 48 hours and showed persistent bacteremia with streptococcus pyogenes. Gentamicin IV (3m/kg daily) was added to penicillin on the third day. The trans-esophageal echocardiogram (TEE) documented severe eccentric mitral regurgitation with tiny hypoechoic mobile masse, highly suggestive of vegetations attached to anterior and posterior mitral leaflets (Figures 1 and 2).

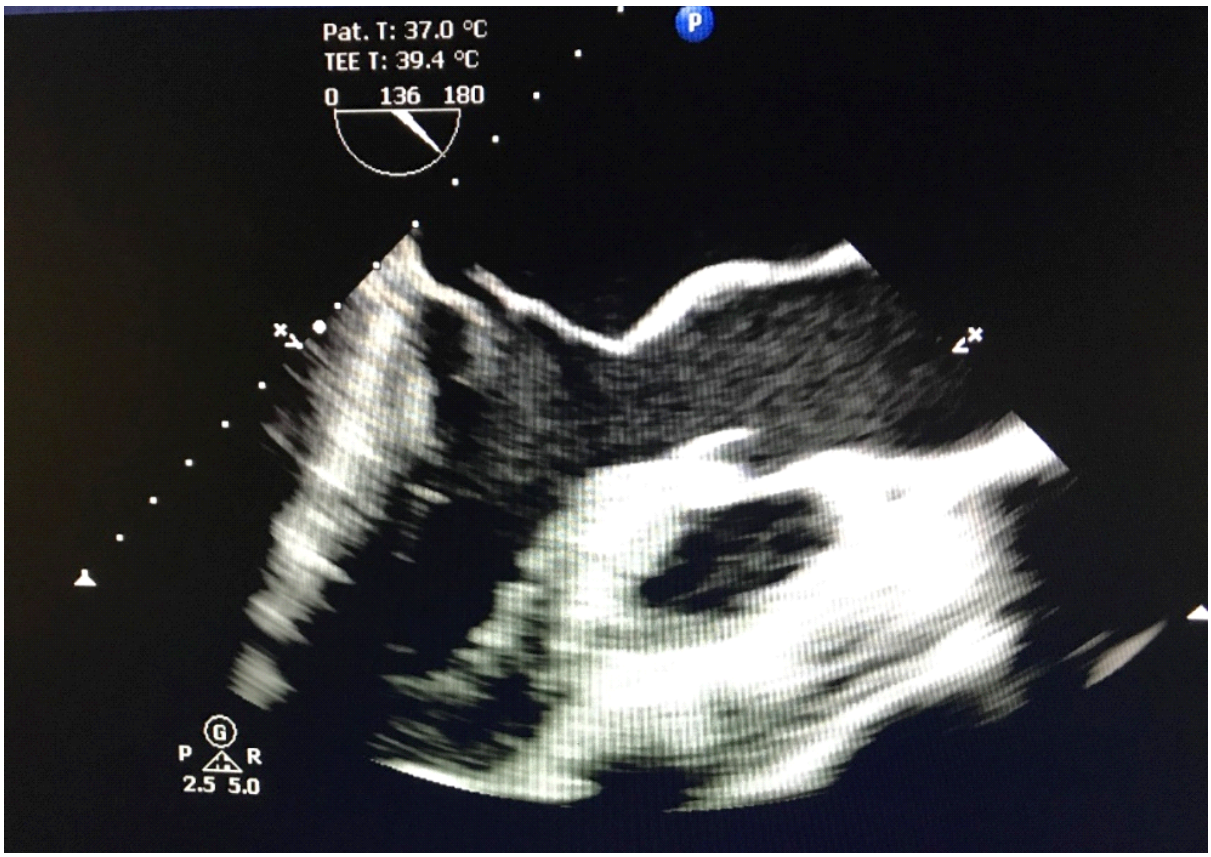

Figure 1: Tiny hypoechoic mobile masses, highly suggestive of vegetations attached to anterior and posterior mitral leaflets, were demonstrated with TEE, with a flail mitral valve leaflet.

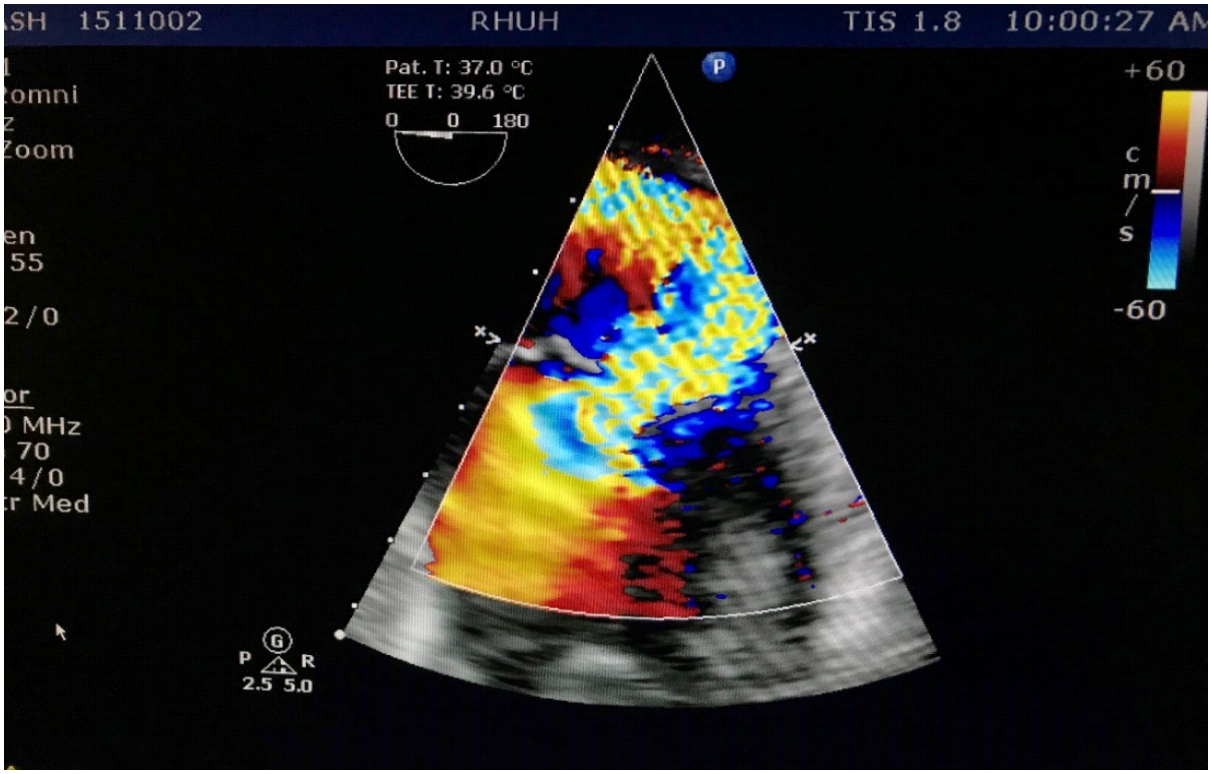

Figure 2: Moderate to severe eccentric mitral regurgitation with color Doppler echocardiography.

After adding gentamicin, the patient was clinically improving with no more fever or other complaints; new blood cultures were negative; laboratory tests showed improvement of fibrinogen and D-dimer, with decreasing in WBC count and CRP reactivity, and platelets were back to normal. The patient remained stable on penicillin and gentamicin for 14 days. TTE was repeated on the 12th day of antibiotic therapy and showed no major changes compared to the TTE performed on the second day. Unfortunately, on day 15, the patient developed cardiac arrest and passed away. His friend mentioned that the patient injected himself with a drug in the early morning. The toxicology screen showed a blood concentration of morphine equal to 0.35 mg/l. The cause of his death was assumed to be heroin intoxication.

Discussion

Streptococcus pyogenes are primarily associated with mild infections like pharyngitis and impetigo; however, they can also lead to severe conditions, such as bacteremia, cellulitis, necrotizing fasciitis, streptococcal toxic shock syndrome and infective endocarditis [4]. Studies showed a major role for fibronectin binding in the pathogenesis of S. pyogenes endocardial infection [9]. In our case, the source of bacteremia has been most probably a skin and soft tissue infection.

Infective endocarditis has rarely been reported, 41 cases of IE due to Streptococcus pyogenes in children and adults have been reported since 1940 [5]. A literature search was performed using PubMed covering published cases between 1940 and 2023. Reports were identified using the following keywords in Pubmed: ‘infective endocarditis and Streptococcus pyogenes’ or ‘Streptococcus pyogenes infective endocarditis’. Studies not available online were excluded. This review showed 39 cases published before 2023 and only 2 new cases published after. Globally, including the present case, 42 cases of endocarditis caused by Streptococcus pyogenes in children and adults have been reported since 1940 (table 1).

Case (Year of diagnosis) [ref]	**Gender (Age)**	**Previous cardiac abnormalities**	**Previous infections**	**Infected cardiac valve**	**Organ embolism**	**Complications**	**Treatment (medical vs surgical) + Duration**	**Outcome**
C-1 (1942) [6]	M (2y)	None	None	M	Brain Renal Spleen Skin	Splenomegaly Pneumonia	Medical therapy: ND Surgery: Not done	D
C-2 (1961) [7]	M (25y)	None	None	A + M	Spleen Liver	Kidney abscess HSM Hemopericardium	Medical therapy: sulfapyridine iv 25% glucose (Pen. was nav) Surgery: Not done	D at d21
C-3 (1975) [6]	M (6m)	None	Meningitis	A	None	AI CHF Microscopic hematuria	Pen. G	R
C-4 (1976) [6]	M (14y)	VSD AS	Tonsillitis	A	None	Myocardial abscess	Medical therapy: ND Surgery: Not done	D
C-5 (1980) [6]	M (16y)	None	Pharyngitis	A	Renal Peripheral	ARDS	Medical therapy: ND Surgery: Not done	R
C-6 (1984) [6]	M (2m)	PS	None	A + M	Brain Spleen	Pulmonary edema AI PGN	Pen G Nafcillin Gentamicin (28days)	D at d28
C-7 (1988) [6]	F (4m)	None	Varicella	A	None	Para-aortic abscess CHF Pulmonary edema	Cefuroxime Cefaclor Ampicillin Gentamicin	D
C-8 (1988) [6]	F (4y)	None	None	A	None	Polyarthritis AI	Cefotaxime Pen. G + Surgery	R

C-9 (1991) [8]	M (52y)	None	None	None	None	Toxic encephalopathy Involvement of 2 joints	Pen. G	R
C-10 (1991) [8]	F (63y)	None	Pharyngitis	None	None	Microscopic hematuria	Pen. G then oral Pen. V	R
C-11 (1991) [8]	F (65y)	None	Arthritis Cellulitis	M	Brain Skin	CHF Acute MI Janeway lesions	Pen. G	R
C-12 (1991) [8]	F (69y)	AVP PVP	None	AVP	Skin	None	Vancomycin Gentamycin	R
C-13 (1991) [8]	M (55y)	MR	None	M	None	MVP	Cefazolin then ampicillin then oral Pen. V	R
C-14 (1992) [6]	F (3y)	None	None	M	Brain Skin	L. hemiparesis Pericardial effusion MR	Pen. G	R
C-15 (1994) [27]	M (20y)	MVP	None	M	None	None	Medical therapy: ND Surgery: Not done	D
C-16 (1998) [6]	M (14y)	None	None	M	Brain	Cerebral infarction	Pen. 6w Gentamicin 3w	R
C-17 (1999) [6]	M (5m)	None	Varicella	M	Skin	Respiratory failure Purpura MR Aortic root abscess Toe amputation	Ceftriaxone Vancomycin Ampicillin Pen. + Surgery at d15 Discharged on Pen. for 6 weeks	R
C-18 (2000) [6]	M (3y)	None	Varicella	A	Peripheral Skin	Joint pain AI CHF	Pen for 2 weeks then Pen + gentamycin for 4 weeks (totally 6w) + Surgery at end of medical therapy	R

C-19 (2000) [6]	M (4y)	None	None	A	Skin	MR Necrosis of 2 toes requiring amputation	Medical therapy: antibiotic for 6w Surgery: done urgently	R
C-20 (2000) [6]	M (2y)	None	Varicella	A	Brain Skin	Aortic root abscess Aortic valve perforation -Focal seizure	Medical therapy: antibiotic for 6w Surgery: done at d2	R
C-21 (2001) [28]	F (16y)	Congenital cyanotic heart disease	No data	No data	Renal	CGN Vasculitis	Medical therapy: ND Surgery: ND	ND
C-22 (2004) [10]	M (11y)	Bicuspid aortic valve	Varicella	A	Brain Renal Spleen	-AI	Clarithromycin6d then another iv antibiotic for 6w +Surgery	R
C-23 (2008) [11]	M (68y)	None	None	A	Brain	Meningitis CHF Sepsis Stroke	Ceftriaxone Gentamicin	D
C-24 (2010) [12]	M (64y)	None	UTI Pharyngitis	None	-Skin -Renal	Splinter hemorrhage Janeway lesions CHF GN	Gentamicin and Benzyl Pen. for 6 days Then Benzyl Pen. alone for 6w	R
C-25 (2012) [13]	M (71y)	None	UTI	A + M	Renal Spleen	AI CAD Splenic infarct	Levofloxacin/ Vancomycin for 3d then Pen. G for 6w + Surgery at d22	R
C-26 (2014) [6]	F (6y)	PFO ASD	Erythematous rash Pharyngitis	A + M	-Skin -Brain	Aortic root abscess Arrythmia Stroke	Ceftriaxone (1 dose) Vancomycin Meropenem Gentamicin Then Pen. and clindamycin Then Pen. alone for 6w	R

C-27 (2014) [6]	F (8m)	PFO	Pharyngitis	T	Brain	Septic shock Multi-organ failure Respiratory failure Stroke Pleural effusion	Vancomycin Cefotaxime then Pen. and Clindamycin Then Pen. alone for 6 weeks	R
C-28 (2014) [14]	M (5y)	None	Gastroenteritis	M	None	None	IV Amoxicillin And Gentamicin For 2 weeks then oral amoxicillin for 4w	R
C-29 (2015) [15]	M (42y)	None	Vasculitis Arthritis	T	Lung Brain	Pulmonary thrombosis	Ceftriaxone Gentamicin	R
C-30 (2017) [16]	F (68y)	None	Skin and soft tissue infection Septic Arthritis	A	None	CHF Renal failure Pleural effusion Ascites	Ceftriaxone Meropenem Ampicillin Clindamycin Amoxicillin Cefazolin Levofloxacin +surgery d56	R
C-31 (2017) [17]	M (77y)	BMVP	Otitis Media	M	Brain	Meningitis	Ceftriaxone for 6 weeks	R
C-32 (2017) [26]	F (80y)	None	Meningitis	M	No data	Meningitis	Ceftriaxone and vancomycin then Ampicillin and Clindamycin for 6 weeks	R
C-33 (2019) [18]	F (14y)	None	Left foot cellulitis	M	Brain Spleen Kidney	Infarction of spleen, Kidney, and brain DIC Amputation of necrotic left toe at day 45	Ampicillin and Clindamycin Then Cefotaxime (due to skin rash) + Surgery at week 10	R

C-34 (2019) [18]	M (17m)	Previous spontaneous closure of VSD at 5m of age with residual mild MR	None	MSA	None	None	Ampicillin And Cefotaxime Then, ampicillin alone (total therapy: 5-6 weeks)	R
C-35 (2019) [5]	M (16y)	None	Pharyngitis	M	None	Osler nodes	Augmentin/ vancomycin empirically for 3 days Then, Ceftriaxone/ ampicillin for 7 days Then, Gentamycin/ Ampicillin (Genta for 2 weeks and ampicillin for 4 weeks)	R
C-36 (2019) [19]	M (5y)	None	Varicella superimposed skin infection Necrotizing fascitis of gluteal muscle	M	None	Rupture of chordae tendineae	Gentamycin and Ceftriaxone Then, IV amoxicillin For 4 weeks + surgery at d7	R
C-37 (2019) [22]	M (37y)	none	URTI	Mural (left atria)	None	Pericardial effusion Renal	Pen G then ceftriaxone for 4 weeks	R
C-38 (2019) [23]	F (63y)	Aortic valve replacement	ND	ND	skin	Splinter hemorrhage	ND	ND
C-39 (2020) [24]	M (30y)	ND	ND	M	Skin Eye	Janeway lesions Splinter hemorrhage Scleritis Endophthalmitis Roth spots Septic shock	Ceftriaxone for 6 weeks + surgery	ND

Case-40 2023 [21]	M (31y)	Bicuspid aortic valve	Pharyngitis	A	Liver Skin Renal Spleen Fingers Eye	Septic shock Respiratory failure AI Aortic root abscess Arthralgia HSM Pyelonephritis Janeway lesion Splinter hemorrhage Conjunctival hemorrhage Desquamative rash over palms	-vancomycin -cefepime -doxycycline Then ceftriaxone + surgery done urgently 6 weeks of ceftriaxone after negative blood culture	R
Case 41 2023 [25]	F (46y)	None	Gastroenteritis Pelvic infection	Normal TTE and TEE	Skin Renal	Janeway lesions Ascites Pleural effusion GN	Meropenem Vancomycin Then Penicillin (Total 5 weeks of therapy)	R

ref: reference; C: case; Gen.: Gender; M: male; F: female; y: years old; m: months; d: day; VSD: ventricular septal defect; AS: aortic stenosis; PS: pulmonic stenosis; CAD: coronary artery disease; AVP: Aortic valve prosthesis; PVP: pulmonic valve prosthesis; MR: Mitral regurgitation; MVP: mitral valve prolapse; HTN: hypertension; PFO: patent foramen ovale; ASD: atrial septal defect; BMVP: biologic mitral valve prosthesis; UTI: urinary tract infection; URTI: upper respiratory tract infection; TTE: transthoracic echocardiography; TEE: trans-esophageal echocardiography; LL: left lower; M: mitral; A: Aortic; T: tricuspid; AI: aortic insufficiency; CHF: congestive heart failure; ARDS: Acute respiratory distress syndrome; GN: glomerulonephritis; HSM: hepatosplenomegaly; PGN: proliferative glomerulonephritis; CGN: crescentic glomerulonephritis: MI: myocardial infarction; MVP: mitral valve prolapse; MSA membranous septal aneurysm; iv: intravenous; L: left; ND: no data; nav: not available; Pen: penicillin; D: death; R: recovered

Table 1: cases of streptococcus pyogenes endocarditis from 1940 to present for which clinical features are available.

Out of the 41 cases of Streptococcus pyogenes endocarditis, 27 were males (66%) and 14 were females (34%). Ages ranged from four months to 80 years with a median age of 31.25 years. Pre-existing heart defects were known in 31% of the cases. Skin lesions were the predisposing infection in 9 cases (21.95 %), while pharyngitis was described in eight patients (19.51%). In three cases (7.3 %), joint pain and arthritis were reported as the first manifestation. Thirteen cases (31.7 %) had no known preceding infections. The most common valves involved were mitral and aortic, with each accounting for approximately 43%. The tricuspid valve was affected in only 2 cases (4.8%). The embolic phenomenon occurred in 26 cases (63.41%) with the skin and central nervous system being the most frequent sites seen in 14 and 13 patients respectively, followed by the spleen, kidneys, and lung. Twelve patients (29%) had cardiac surgery, and none of them died after surgery. The mortality rate was 17% (71.42% before 1990 and 28.57 % after 1990) and was mainly due to cardiac failure and/or septic shock; most patients recovered after antibiotic therapy. Most patients treated with antibiotic therapy alone had a favorable outcome (71.4%). Combination therapy with gentamicin was recorded in 12 cases (29.26 %).

In 1928, a chance event in Alexander Fleming's London laboratory changed the fate of medicine forever. However, the first clinical use of penicillin for medical causes was not successful till 1943 [29]. Moreover, in 1944, Loewe introduced the effects of Penicillin in IE [30]. In the present case, gentamicin was added to penicillin when the patient had persistent fever and bacteremia. According to the available literature, intravenous administration of penicillin G, ampicillin, or Ceftriaxone for four weeks are suitable treatment for Streptococcus pyogenes IE. In the case of groups B, C, and G streptococcal IE, combining gentamicin with penicillin or ceftriaxone for at least the initial two weeks of a four-week antimicrobial regimen is an alternative option [20]. Alternatively, depending on the severity of the disease, daptomycin in combination with ampicillin could be considered. Vancomycin is justified only for patients who are unable to tolerate a beta-lactam antibiotic [20].

Conclusion

In summary, we present a rare case of Streptococcus pyogenes endocarditis in an adult patient with a history of IVDU and skin lesions, complicated by brain, lung, spleen, and kidney septic emboli with septic arthritis and abscesses collections, improving after receiving a combination therapy (high dose penicillin with gentamicin). Unfortunately, the patient passed away after two weeks of antibiotic therapy due to a drug overdose. When treated with appropriate antimicrobial therapy and supportive care in a timely manner, even severe presentations of streptococcus pyogenes endocarditis can have excellent outcomes.

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