Infecitve Endocarditis Caused by Streptococcus alactolyticus and Kocuria kristinae Complicated with Severe Thrombocytopenia: A Rare Case

SUMMARY: Introduction: Infective endocarditis (IE) is a focus infection caused by bacterial, viral, or fungal microorganisms within the heart that involves the endocardium and heart valves. Streptococcus alactolyticus, classified under DNA cluster IV of the S. bovis/S. equinus complex, is a sparse isolated bacterium that rarely cause IE in humans. Kocuria kristinae is a gram-positive bacteria. Until now, there have been only six IE cases caused by K. kristinae infections reported in the literature. Thrombocytopenia and platelet dysfunction can manifest in IE cases and are related to the clinical outcome. Different mechanisms have been hypothesized to explain thrombocytopenia in IE.

Case report: We report the case of a 25-year-old female patient who complained of palpitation two weeks before admission. Initially, the patient complained of fever arising six months before admission. Blood cultures showed S. alactolyticus and K. kristinae. Echocardiography examination showed vegetation on anterior and posterior mitral valves with severe mitral regurgitation. During hospitalization, the patient also suffered from severe thrombocytopenia without bleeding signs. On day 16 after hospitalization, the patient suddenly complained of abdominal pain and dyspnea. The patient was declared deceased with cause of death to septic emboli.

Conclusion: We reported a case of IE caused by rare bacterial pathogens, S. alactolyticus and K. kristinae, which were aggravated by thrombocytopenia. Management of IE with thrombocytopenia requires caution because it is associated with poor outcomes. In this case, poor outcomes can be connected to thrombocytopenia coupled with the presence of specific bacteria, S. alactolyticus, which is known as a bacterium that often causes septic embolism.

KEYWORDS: infective endocarditis, valve disease, Streptococcus alactolyticus, Kocuria kristinae, thrombocytopenia.

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SAŽETAK: Uvod: Infektni endokarditis (IE) fokalna je infekcija uzrokovana bakterijskim, virusnim ili glijivičnim mikroorganizmima, koja unutar srca zahvaća endokard i zalistke. Streptococcus alactolyticus, klasificiran po IV DNA klasterom S. bovis / S. equinus kompleksa, bakterija je koja se rijetko nalazi u izolatu te koja malokad uzrokuje IE u ljudi. Kocuria kristinae je gram-požitivna bakterija. Dosad je objavljeno samo šest slučajeva IE-a uzrokovanih infekcijom bakterijom K. kristinae. Trombocitopenija i disfunkcija trombocita mogu se pojaviti u IE-u te su povezani s kliničkim ishodom. Postoje različite hipoteze o mehanizmima kojima se objašnjava trombocitopenija u IE-u. Prikaz slučaja: Predstavljamo slučaj dvadesetpetogodišnje bolesnice koja je žalila na palpitacije dva tjedna prije primitka u bolnici. Prvi je simptom bila povišena temperatura šest mjeseci prije primitka. Hemokulture su utvrdile S. alactolyticus i K. kristinae. Echokardiografskom su pretragom pronadene vegetacije na anterijornom i posteriornom lističu mitralnog zalistka uz tešku mitralnu regurgitaciju. Bolesnica je tijekom hospitalizacije imala tešku trombocitopeniju bez znakova krvarenja. Šesnaestog dana hospitalizacije naglo se počela žaliti na abdominalnu bol i zaduhu. Bolesnica je umrla, a uzrok smrti bili su septicki emboli. Zaključak: Prikazan je slučaj IE-a uzrokovana rijetkim bakterijskim patogenima (S. alactolyticus i K. kristinae) koji je pogoršala trombocitopenija. Liječenje IE-a s trombocitopenijom zahtijeva oprez jer je to stanje povezano s lošim ishodima. U ovom se slučaju loši ishodi mogu povezati s trombocitopenijom uz prisutnost specifične bakterije, S. alactolyticus, koja je poznata kao bakterija koja često uzrokuje septičku embolijs.

KLJUČNE RIJEČI: infektivni endokarditis, valvularna bolest, Streptococcus alactolyticus, Kocuria kristinae, trombocitopenija.

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**Uvod**

Infektivni endokarditis (IE) infekcija je mikroorganizmi - ma u srčanom endotelu (zalasti i endokardijalna membrana). Karakteriziraju ga tipične lezione – vegetacije koje su fibrinska masa s trombocitima različitih oblika i veličina. *Streptococcus alactolyticus* je podvrsta *S. bovis / S. equinus* kompleksa (SBSEK). Taj kompleks sadržava nebata-hemo- litičke streptokoke i streptokoke Lancefieldove D grupe, koji su opurtunistički bakterijski patogeni ljudskih i životinjskih probavnih sustava. Infekcije koje uzrokuje *S. alactolyticus* sporadične su u ljudi. *Kocuria* je gram-pozitivna bakterija, ak- tinobakterija u kokoidnim tetradama iz porodice Micrococcus, podred *Micrococcineae*, red Actinomycetales. *Kocuria* se u ljudi i drugih sisavaca često može naći u usnoj šupljinji i na normalnoj koži. *K. kristinae* može uzrokovati bakteriemiju i infektivni endokarditis koji se mogu povezati s ulaznim mje- stom postavljenog katetera.

Trombociti imaju ključnu ulogu u patogenezi endokardi- tisa te su osjetljiva na boljim odgovora organizma na infekciju. *Kocuria* infekcija postavljenog katetera. Pri simptomima umjetnog odgovora organizma na infekciju.*Kocuria* infekcija postavljenog katetera. *Kocuria* je glavni patogen, a prvi simptomi mogu postati kardiomegaliju i izražena hepatomegalija.

**Prikaz slučaja**

Prikazat će slučaj dvadesetpetogodišnje bolesnice koja se javila u bolnicu žaliva u funkciji srca. Kliničkim je pregledom utvrđeno dobro opće stanje, sa norma- lima vitalnih znakova. Hemoglobin je 12 g/dl, leucociti 8000, pluća, abdomena i udovi su uredan. Elektrokardiogram pokazuje sinusnu stabilitetku bez nepropisućih simptoma.

**Case report**

We report the case a 25-year-old female patient presenting with complaints of palpitation two weeks before admission. The patient was referred from a private hospital with a suspi- cion of IE. Initially, the patient had complained of fever arising during the next two months. At the time, the patient was admitted by a primary health care center and received paracetamol as medication. Reportedly, the patient’s complaints increased and the patient was diagnosed as allergic to paracetamol.

**Introduction**

Infective endocarditis (IE) is a microorganism infection of the heart endocardium (heart valves and endocardial membrane). Infective endocarditis is characterized by a typical lesion called vegetation, a mass of fibrin, and platelets with various shapes and sizes. *Streptococcus alactolyticus* is a subspecies of *S. bovis / S. equinus* complex (SBSEK). This complex contains non-beta hemolytic streptococci and Lancefield group D streptococci, which are opportunistic pathogenic bacterial pathogens of human and animal digestive tracts. *Kocuria* is a gram-positive bacterium, actinobacteria in coccosid tetrad from the Micrococcus family, suborder Micrococcineae, order Actinomycetales. *Kocuria* is often found in the oral cavity and normal skin in humans and other mammals. *K. kristinae* is known to cause catheter-related bacteremia and infection endocarditis.

Platelets have an essential role in the pathogenesis of en- docarditis and are a sensitive monitor of systemic host re- sponses to sepsis. About 20-25% of patients with bacterial endocarditis have thrombocytopenia, even though it is usually mild to moderate. However, very severe thrombocytopenia can be observed, which in some cases is associated with reactive platelet autoantibodies or syndromes that resemble thrombocytopenia purpura (TTP). Thrombocytopenia is one of the guideline criteria used by WHO as a potential indicator of clinical severity.
1. Flail anterior mitral valve leaflets (AML) with moderate mitral regurgitation (MR) (MR ERO 0.3 cm²; MR RV 29 mL), CARPENTIER type II. Mild tricuspid regurgitation (TR) (TR max PG 46.92 mmHg). Trivial aortic regurgitation (AR).

2. Cardiac chamber dimension: dilated left atrium (LA) (LA major 6.4 cm; LA minor 4.5 cm), normal left ventricle (LV) (LVIDd 4.8 cm), normal left atrium and left ventricle (RA and RV) (RVDB 2.2 cm). There is vegetation at the AML valve (2.0 cm × 1.0 cm) without thrombus.

3. Normal systolic LV function (LVEF 67%). Normal RV systolic function (tricuspid annular plane systolic excursion (TAPSE) 1.8 cm).

4. Normokinetic segmental analysis.

5. Concentric LV.

**FIGURE 1.** (A) Electrocardiography showed sinus tachycardia 119 bpm and normoaxis (B) Chest X-ray showed cardiomegaly with cardio-thoracic ratio of 70% and mitral heart configuration.

**FIGURE 2.** The transthoracic echocardiography view of parasternal long axis and 4-chamber view shows the presence of left atrial dilatation and vegetation in anterior mitral valve leaflets.
The patient was diagnosed with possible IE, moderate MR, mild TR, thrombocytopenia pro-evaluation, normochromic normocytic anemia, and systemic lupus erythematosus (SLE) suspicion. As the initial therapy, we administered an intravenous (IV) infusion of saline 500 mL/24 hours, cefotaxime 3×1 g IV, gentamicin 1×150 mg IV, furosemide 2×20 mg IV te peroral spironolakton 1×25 mg, lisinopril 1×5 mg p.o., bisoprolol 1×1.25 mg p.o.

The blood culture examination carried out at 3 locations showed results positive for K. kristinae and S. alactolyticus, leading to the conclusion that they were bacteria isolated from 3 significant blood sample as infectious agents and true bacteremia. The blood cultures showed sensitivity to levofloxacin. The patient was diagnosed with definite IE and given levofloxacin 1×750 mg IV as a substitute for cefotaxime. Three days later, the platelets decreased to 20,000, and hypokalemia (potassium 2.6 mg/dL) was observed, and the patient was given additional therapy comprising potassium chloride 3×600 mg.

Transesophageal echocardiography (TEE) was performed (Figure 3), with the following results:

1. Valves: There is flail AML (A2) valves with severe MR (MR ERO 0.8 cm²; MR RV 71 ml), CARPENTIER type II, trivial TR.
2. No thrombus in the left atrium (LA), left atrial appendage (LAA), LASEC (-).
3. Intaktan interatrijski septum.
4. There was vegetation in the AML (A2) valve (1.3 cm × 0.6 cm) and posterior mitral valve leaflets (P3) (1.8 cm × 0.8 cm).

The patient was given an antibiotic and had a stable hemodynamic for two weeks while waiting for the scheduled surgery. On day 16 of hospitalization, the patient suddenly complained of abdominal pain and dyspnea. Systolic blood pressure decreased to 60–70 mmHg, and tachycardia, cold extremities, decreased consciousness, and lateralization to the right were observed. We provided hemodynamic support with norepinephrine 100 ng/kg BW/minutes and dopamine 5 mcg/
lesne težine/minutu uz povećanje doze prema kliničkoj slici. Pripremili smo je za intubaciju, no bolesničko se stanje naglo pogoršalo te je nastupio zastoj srca. Proveli smo kardiopulmonalnu reanimaciju te je dpvatu uspješno postignut povratak u spontanu cirkulaciju, no bolesnica je umrla u iduća dva sata, a uzrok smrti bili su septicni emboli.

**Rasprava**

Infektivni se endokarditis definira kao infekcija uzrokovanja bakterijskim, virusnim ili gljivim mikroorganizmima na endokardu srca, koja može uključivati jedan ili više zalistaka, stjeniku ili septalne defekte. Najčešći infektni endokarditis zalistaka jesu gram-positivne bakterije, koje uključuju *S. aureus*, *S. viridans* i enterokoke.

Podatci upućuju na to da je *Staphylococcus aureus* i dalje najčešća bakterijska infekcija u svim slučajevima IE-a u razvijenim zemljama (31%), a potom slijedi skupina *Streptococcus viridans* (17%), koagulazna negativni stafilokoki (11%), enterokoki (10%) i *S. bovis* / *S. equinus* kompleks (6%). Strepotokogi su još uvijek dominantni u zemljama u razvoju. Publikacije o slučajevima infekcija u ljudi koje uzrokuje *S. alactolyticus* i *Kocuria kristinae* uključuju nekoliko zalistaka, uključujući umjetne i mitralne zalistke. Embolijeski događaji za *S. bovis* / *S. equinus* kompleks u IE-u prisutni su na skupu od 9 do 55%.

*K. kristinae* je gram-positivna bakterija te je dio normalne flore usne šupljine i ljudske kože. *Kocuria* bakterije široko su rasprostranjene u prirodi. Tijel budak bakterija ima više od 18 vrsta, a samo pet smo identificirali kao oportunističke patogene. Postoji samo šest prikaza slučajeva u kojima je IE uzrokovana bakterija *K. kristinae*. Studije koje istražuju *K. kristinae* te IE također su vrlo rijetke. Najnoviji prikaz slučaja dali su Arif godine.

Discusión

Infective endocarditis is defined as bacterial, viral, or fungal microorganism infection on the endocardium, which can include one or more heart valves, endocardial murmurs, or septal defects. The most common infectious agents that cause infective valve endocarditis are gram-positive bacteria, including *S. aureus*, *S. viridans*, and enterococci.

Data indicate that *Staphylococcus aureus* is still the most common bacterial infection for all IE cases in developed countries (31%), followed by the *Streptococcus viridans* group (17%), staphylococci negative coagulase (11%), enterococci (10%), and SBSEC (6%). *Streptococcus* still dominates in developing countries. Reports of cases of *S. alactolyticus* infection in humans are still infrequent. *S. alactolyticus* is reported to be a causative agent for IE complicated by septic embolism. Cekmen et al. reported a patient with aortic valve endocarditis obtained the presence of *S. alactolyticus* bacteremia from the culture. On the other hand, there is a tendency for SBSEC bacteria to affect several heart valves, including prosthetic and mitral valves. The embolic events of SBSEC in IE range from 9% to 55%.

*K. kristinae* is a gram-positive bacteria and is part of the normal flora of the oral cavity and human skin. *Kocuria* are widely distributed in nature. The genus has more than 18 species, but only five are known to be opportunistic pathogens. There have been only six case reports of IE caused by *K. kristinae*. Studies that examine *K. kristinae* and IE are also very rare. The newest case report by Arif et al. reported a rare case of right-sided IE due to *K. kristinae* presenting with undiagnosed fever for 1 year. In our case, the patient also had a history of prolonged fever that increase suspicion for *K. kristinae* infection. IE is a possible cause of a prolonged fever, especially in the presence of congenital heart disease. Antibiotic susceptibility is required for adequate therapy for *Kocuria* infection. Until now, there have been no internationally accepted guidelines for antibiotic treatment of IE caused by *K. kristinae* infection.

Platelets are an essential component in pathogenesis of endocarditis. However, it is uncertain whether platelets may increase or limit disease progression. Thrombocytopenia tends to be a specific prognostic marker in endocarditis, rather than just a surrogate marker for acute phase reactions. Platelets play an essential role in local defense against endovascular infections. According to a study by Duran et al. thrombocytopenia is an independent predictor of death on days 1 and 8 of IE. Thrombocytopenia in patients with IE has an essential clinical implication. Firstly, patients with thrombocytopenia must receive empirical anti-staphylococcal therapy because of the strong relationship between early thrombocytopenia and *Staphylococcus aureus* infection. Secondly, thrombocytopenia can increase the risk of bleeding if anti-platelet agents are considered as adjunctive therapy. Thirdly, thrombocytopenia on day 8 indicates an impaired defense response to sepsis and predicts increased mortality. Therefore, patients with thrombocytopenia may require more intensive monitoring, specific treatment, and, if relevant, surgical considerations.
i infekcije bakterijama Staphylococcus aureus. Kao drugo, trombocitopenija može povećati rizik od krvena ako se antitrombocitni lijekovi uzmu u obzir kao dodatna terapija. Kao treće, prisutnost trombocitopenije u osmom danu upućuje na oslabljen obrambeni odgovor organizma na sepsu i predviđa povisenu smrtnost. Stoga bi bolesnicima s trombocitopenijom mogao biti potreban intenzivniji nadzor, specifično liječenje, uzimanje kirurških zahvata u obzir.

Predstavili smo slučaj IE-a uz trombocitopeniju kojemu su, kroz ljudski koži, S. alactolyticus i K. kristinae. S. alactolyticus je baktoria koja može uzrokovati septičku emboliju, koja je se u ovom slučaju može povećati s lošim ishodom. K. kristinae je dio normalne flore na ljudskoj koži, no može biti patogena bakterija. K. kristinae je povezana sa stalan bolesnikom koji su imunokompromitirani te s infekcijom urinarnih trakta u bolesnika s urinarnim kateterima. U prikazane bolesnice rezultati analize urina bili su pozitivni na bakterijsku infekciju. Trombocitopenija je povezana s lošom prognozom u bolesnika s IE-om. Dosad u literaturi nije opisana patogeneza tih dviju patogenih bakterija pronađenih u našem slučaju zajedno sa manjom trombocita. Početna terapija u bolesnika koji su suspektni na infekciju koju uzrokuje Staphylococcus aureus i K. kristinae je bakterija koja može uzrokovati septičku emboliju, koja se u ovom slučaju daje u obliku antitrombocitnih sprekka, cefotaksima i gentamicina.

Zaključak

Predstavili smo slučaj IE-a uzrokovana rijetkim bakterijskim patogenima, S. alactolyticus i K. kristinae, koji je bio pogoršan trombocitopenijom. Potrebna su daljnja istraživanja o liječenju IE-a uzrokovana bakterijama S. alactolyticus i K. kristinae. Liječenje IE-a uz trombocitopeniju zahtijeva oprez jer je povezano s lošim ishodima. U prikazane se bolesnice loš ishod može povećati s trombocitopenijom u kombinaciji s prisutnošću određene bakterije, S. alactolyticus, za koju se zna da često uzrokuje septičku emboliju.

In this case, we reported IE with bacteremia which resulted in culture showing S. alactolyticus and K. kristinae. Both are rare bacterial pathogens in IE. S. alactolyticus is a bacterium that can cause septic embolism, which can be associated with the poor outcome in this case. K. kristinae is a normal flora of flora on human skin but can be a pathogenic bacterium. K. kristinae is related to the condition of patients who are immunocompromising and to urinary tract infections in patients using urine catheters. However, urinalysis results were positive for bacterial infection. Thrombocytopenia is associated with a poor prognosis in patients with IE. So far there have been no descriptions in the literature the pathogenesis of the two pathogenic bacteria in this case with platelets depletion. Initial therapy in patients that are usually suspected of Staphylococcus aureus, as we administered in our case as well, is in the form of a broad-spectrum antibiotic, cefotaxime and gentamicin.

Conclusion

We reported a case of IE caused by rare bacterial pathogens, S. alactolyticus and K. kristinae, which were aggravated by the condition of thrombocytopenia. Further studies are needed in the management of IE relating to S. alactolyticus and K. kristinae as causative agents. Management of IE with thrombocytopenia requires caution since it is associated with poor outcomes. In this case, poor outcomes can be connected to the condition of thrombocytopenia coupled with the presence of specific bacteria, S. alactolyticus, which is known as bacteria that often causes septic embolism.

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