Case Reports

Journal of INTERNATIONAL MEDICAL RESEARCH

Journal of International Medical Research
50(7) 1–9

DOI: 10.1177/03000605221112019
journals.sagepub.com/home/imr
SAGE

Enterococcus faecalis-induced infective endocarditis: an unusual source of infection and a rare clinical presentation

Robert Seby[1], Christine Kim[1], Mahmoud Khreis[2] and Khaldoun Khreis[3]

Abstract

A 69-year-old woman was airlifted to the emergency department after awakening with angina, diaphoresis, and shortness of breath. She was found to have ST-elevation myocardial infarction with 100% occlusion of her left anterior descending artery, and aspiration thrombectomy was performed. Blood cultures confirmed *Enterococcus faecalis* bacteremia. Our team used a clinical tool to determine whether transesophageal echocardiography was warranted to investigate for infective endocarditis. The patient's transesophageal echocardiogram showed a large mobile vegetation on her mitral valve. Given the presence of infective endocarditis in the absence of known coronary artery disease, we determined that the patient had likely developed acute coronary syndrome from a septic embolus originating from her mitral valve vegetation. Further investigation for the source of the bacteremia revealed a perforation 20 cm from the anal verge at the rectosigmoid junction. After perforation repair, the patient became hypoxic and tachycardic with diffuse abdominal pain, guarding, rebound tenderness, and loss of pulse. Exploratory laparotomy revealed air in the mesentery consistent with extraperitoneal perforation of the rectum, and an end-colostomy was performed. Unfortunately, the patient subsequently died.

[1]Department of Infectious Disease, Eastern Virginia Medical School, Norfolk, VA, USA
[2]Department of Infectious Disease, Sentara Norfolk General Hospital, Norfolk, VA, USA
[3]Department of Internal Medicine, University of Pecs, Hungary

Corresponding author:
Robert Seby, Department of Infectious Disease, Eastern Virginia Medical School, 825 Fairfax Avenue, Norfolk, VA 23507, USA.
Email: SebyRM@evms.edu

Keywords
Enterococcus faecalis, transesophageal echocardiography, infective endocarditis, septic embolus, extraperitoneal perforation, mobile vegetation

Date received: 20 April 2022; accepted: 20 June 2022

Introduction

Enterococcus faecalis is a gram-positive, gamma-hemolytic streptococcus that grows in chains. Clinical presentations of *E. faecalis* infection include urinary tract infection, bacteremia, meningitis, and endocarditis.[1] *Enterococcus faecalis* is the third leading cause of infective endocarditis, accounting for 5% to 15% of all cases.[2] The genitourinary (GU) tract is the traditional source of infection in patients with infective endocarditis caused by *E. faecalis*, occurring mainly in men of advanced age.[2] However, *E. faecalis* is also part of the natural gut flora and has the potential, albeit rare, to translocate from the gastrointestinal (GI) tract to the heart and cause infective endocarditis.[3] Numerous patients with enterococcal bacteremia have concurrent infective endocarditis; population-based studies have shown that up to 25% of patients with community-acquired *E. faecalis* bacteremia have infective endocarditis.[4] Furthermore, because infective endocarditis has a high mortality rate, it is imperative to perform a bedside screening test with close to 100% sensitivity to rule out infective endocarditis.

The bedside screening test with the highest sensitivity (100%) to rule out infective endocarditis is the DENOVA scoring system.[4] The DENOVA system assesses the duration of symptoms lasting $\geq$7 days, embolization, the number of positive blood cultures (3/3 or the majority if >3), unknown origin of bacteremia, prior heart valve disease, and auscultation of a heart murmur, with each scored item assigned 1 point.[4] The DENOVA scoring system is used to determine whether to perform transesophageal echocardiography (TEE) if there is high clinical suspicion for infective endocarditis in a patient with enterococcal bacteremia. Specifically, if the patient attains a score of $\geq$3 on the DENOVA checklist, TEE is warranted to further investigate for infective endocarditis. Additionally, acute coronary syndrome (ACS) develops in only 1% to 3% of patients with infective endocarditis, making this a rare clinical presentation.[5] We herein present a case report of a patient with infective endocarditis due to *E. faecalis* with a known source of infection from the GI tract who developed ACS likely secondary to their infective endocarditis.

Case Presentation

This case is reported in accordance with the CARE guidelines.[6] The patient was a 69-year-old woman with a medical history of hypertension, type 2 diabetes mellitus, hypersensitivity pneumonitis, obesity with gastric band placement, and right breast cancer status post-lumpectomy. She was airlifted to the emergency department after waking up in the middle of the night with chest pain, shortness of breath, and diaphoresis. Upon arrival to the emergency department, a review of systems was positive only for chest pain (described as 4/10 in severity at onset) and shortness of breath. The patient's medical history was notably

negative for any cardiac disease. Her social history was also relatively unrevealing, with the patient denying tobacco use and describing herself as a social drinker of alcohol, although recreational drug use was unknown. Physical examination was grossly unremarkable. Cardiovascular examination revealed a regular heart rate and rhythm with no murmurs or gallops appreciated, and pulmonary examination revealed clear lungs on bilateral auscultation. An electrocardiogram was ordered in the emergency department, showing anterior ST elevation and an elevated troponin level of >10,000 ng/dL consistent with ST-elevation myocardial infarction (STEMI). The patient was immediately started on aspirin, heparin, and statin therapy and taken to the cardiac catheterization laboratory for percutaneous coronary intervention.

Investigations

Cardiac catheterization was performed through the radial artery. As shown in Figure 1, the patient demonstrated right dominant circulation with 100% occlusion of the left anterior descending (LAD) artery and no atherosclerosis in her other coronary arteries. Aspiration thrombectomy was performed.[7] The patient was started on dual antiplatelet therapy (prasugrel and aspirin), and discharge was planned for the following day.

That evening, however, the patient developed left upper quadrant abdominal pain. On day 2 of hospitalization, she became diaphoretic, short of breath, and spiked a fever of 103°F. She was tachycardic with a heart rate of 109 beats/minute and hypotensive with a blood pressure of 93/60 mmHg. A complete blood cell count with differential at that time showed leukocytosis with

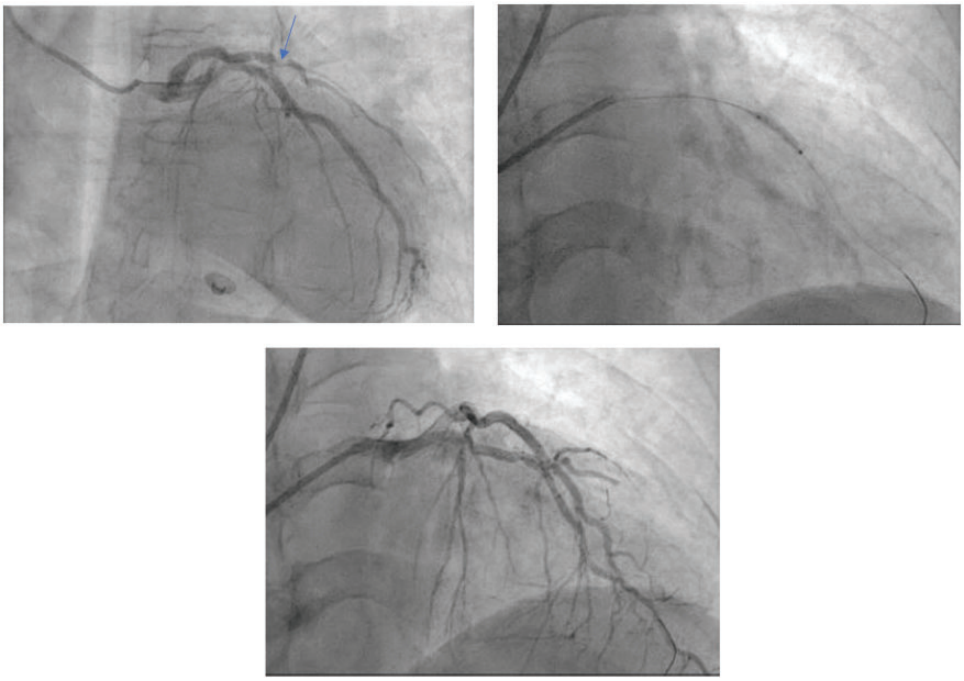

Figure 1. (Top) Stenotic lesion (blue arrow) in the left anterior descending (LAD) artery. (Middle) Stent placement in the LAD artery. (Bottom) Improved blood flow within the LAD artery.

a white blood cell (WBC) count of 16.5×10^3 cells/L, although her lactate concentration was only 1 mmol/L. Computed tomography (CT) of the abdomen showed a splenic infarct, high-grade stenosis of the celiac artery, and mild thickening of the splenic flexure. Transthoracic echocardiography was then ordered, which showed an ejection fraction of 40%, apical and mid/anteroseptal wall hypokinesia, trace pericardial effusion, and no significant valvular pathology. At this time, distributive shock, specifically septic shock, was ruled out because the patient's cardiac output was decreased and she had cold and clammy skin as opposed to warm and flushed skin. Hypovolemic shock was ruled out because the physical examination did not reveal dry mucous membranes and CT imaging showed no signs of hemorrhage. Obstructive shock was also ruled out because the patient had no signs of pleuritic chest pain or hypoxia typical of a pulmonary embolus or other causes of obstructive shock. The patient was therefore determined to have cardiogenic shock; she was started on milrinone, and a Swan-Ganz catheter was inserted. Two blood cultures were collected, and cefepime and metronidazole were initiated empirically for any potential source of infection. The vascular surgery department was also consulted; they recommended a heparin infusion and CT angiography, which revealed no emboli in her lungs.

On day 3 of hospitalization, the blood cultures exhibited growth of gram-positive cocci in pairs and chains (Table 1), and a complete blood cell count with differential showed an increase in the severity of leukocytosis with a WBC count of 26×10^3 cells/L. Therefore, vancomycin was added to the cefepime and metronidazole regimen, and two repeat blood cultures were collected. On day 4 of hospitalization, speciation identified *E. faecalis* as the causative organism. It was susceptible to ampicillin, gentamicin, and penicillin. The patient was placed on an antibiotic regimen of ceftriaxone at 2 g twice a day and ampicillin every 4 hours, and a urinalysis and urine culture were ordered. On day 5 of hospitalization, the patient was still afebrile and her WBC count continued to trend downward. Her urinalysis revealed trace leukocytes and negative nitrites, and her urine culture demonstrated no growth. However, repeat blood cultures grew gram-positive cocci in pairs and chains. Additionally, repeat

Table 1. Blood culture results throughout clinical course.

	Hospital day on which growth occurred/speciation was completed	Blood culture growth/findings	Speciation
Blood culture 1	3/4	Gram-positive cocci in pairs and chains	*Enterococcus faecalis*
Blood culture 2	3/4	Gram-positive cocci in pairs and chains	*Enterococcus faecalis*
Repeat blood culture 1	5/7	Gram-positive cocci in pairs and chains	*Enterococcus faecalis*
Repeat blood culture 2	5/7	Gram-positive cocci in pairs and chains	*Enterococcus faecalis*

The brand of blood culture device used was a BacT/ALERT 3D microbial identification system (bioMérieux SA, Marcy-l'Étoile, France). The method/automated system used for bacterial identification was matrix-assisted laser desorption/ionization–time of flight (MALDI-TOF) mass spectrometry.

abdominal and thoracic CT showed worsening bilateral pleural and pericardial effusion.

Our team used the DENOVA scoring system to determine whether to perform TEE to investigate for potential infective endocarditis. The patient attained a score of 3 because she likely had septic embolization to her spleen, an unknown origin of bacteremia, and four positive blood cultures. The DENOVA clinical scoring system indicates that any patient with enterococcal bacteremia who attains a score of $\geq$3 should undergo TEE to investigate for potential infective endocarditis. TEE was performed on day 6 of hospitalization and revealed a large 1.5- $\times$ 1.6-cm mobile vegetation with irregular borders on the mitral valve (Figure 2). There was mild mitral regurgitation and no mitral stenosis, and the ejection fraction was still 40%. The cardiothoracic surgery department was then consulted regarding the need for mitral valve replacement. On day 7 of hospitalization, speciation of the repeat blood cultures again identified *E. faecalis* as the causative organism; it was susceptible to ampicillin, gentamicin, and penicillin. A pre-cardiac surgery workup was also started on day 7, during which head CT notably showed a small asymptomatic focus of subarachnoid hemorrhage in the left frontal lobe. Head magnetic resonance imaging (MRI) revealed multiple emboli, likely septic, in the left frontal lobe. MRI of the left spine was concerning for discitis and osteomyelitis at L1/L2. Additionally, carotid duplex ultrasonography showed $<$50% stenosis and incidentally revealed a right internal jugular vein thrombus. Because of the patient's small focus of subarachnoid hemorrhage and high risk of bleeding, intravenous heparin infusion was withheld. The results of this work-up confirmed our suspicion that the patient's symptoms were likely due to septic emboli secondary to infectious endocarditis. However, the source of the infection leading to the infectious endocarditis remained unknown.

Treatment

Given the patient's persistent abdominal pain and the rare but documented possibility of *E. faecalis* translocating from the GI tract to blood vessels, we consulted our GI and general surgery clinicians to further investigate this theory. Fluid aspirated from the gastric band was clear and demonstrated no concerning findings with respect to infection. Esophagogastroduodenoscopy showed gastric mucosal atrophy, but there was no concern for infection. However, colonoscopy showed a perforation 20 cm from the anal verge at the rectosigmoid junction. This perforation was closed endoscopically with a suture and a hemoclip. The patient quickly became hypoxic and tachycardic after the colonoscopy and complained of abdominal pain. Physical examination revealed diffuse abdominal tenderness, guarding, and rebound tenderness with loss of pulse. She underwent noninvasive positive-pressure ventilation, and her poor circulatory status was quickly restored with an injection of epinephrine. The general surgery department was urgently consulted because of concern regarding a perforated viscus, and the patient was taken to the operating room. Exploratory laparotomy revealed no intraperitoneal contamination or rush of air upon entry. However, air was present in the mesentery, consistent with extraperitoneal perforation of the rectum as diagnosed by general surgery. The surgery team's assessment at that time was that the perforation appeared to be chronic in nature, with the omentum adhered to the descending colon. An end-colostomy was performed, and the patient was transferred to the intensive care unit. Because she remained persistently febrile and developed peritonitis secondary to extraperitoneal perforation of

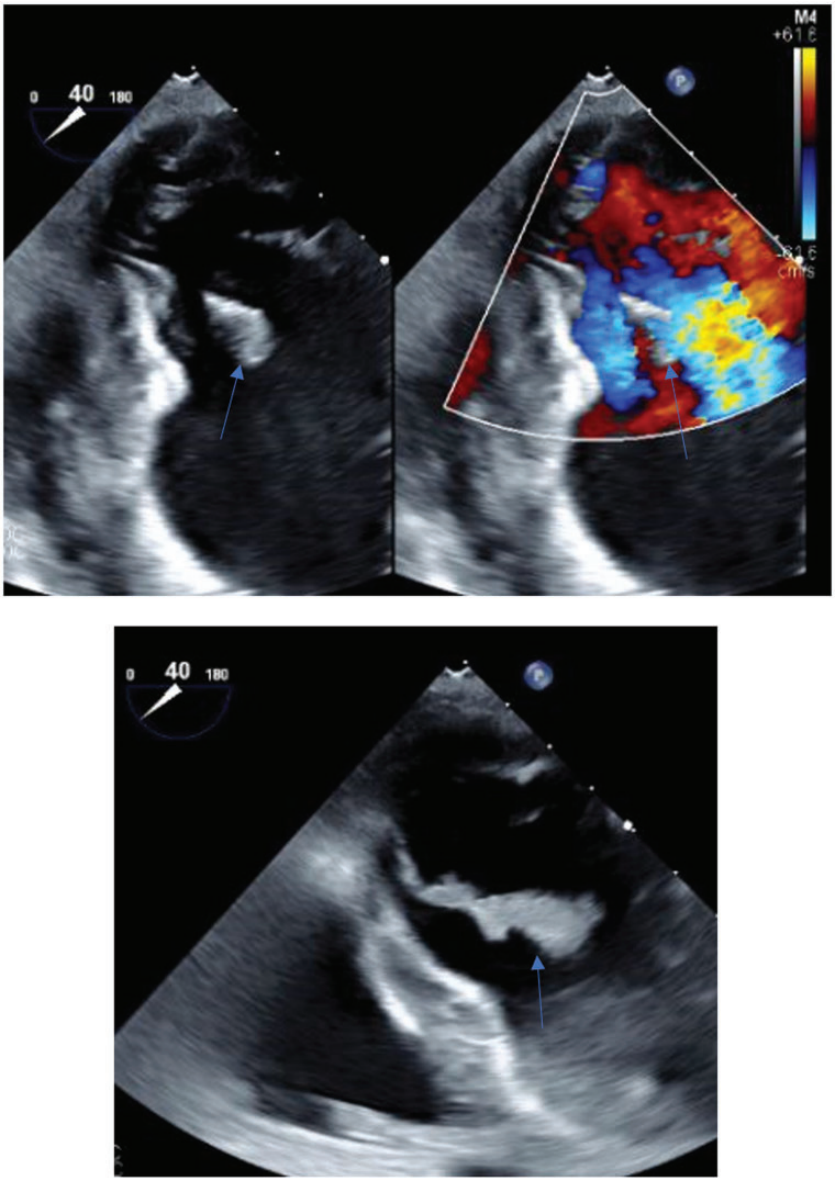

Figure 2. (Top left) Transesophageal echocardiography showing the mobile vegetation on the mitral valve (blue arrow). (Top right) Doppler ultrasound of blood flow through the mitral valve. (Bottom) Another view of the vegetation on the mitral valve (blue arrow).

the rectum, the cardiothoracic surgery department determined that the patient was not a good candidate for mitral valve replacement and signed off the service.

Postoperatively, the patient's WBC count increased to 23×10^3 cells/L and she spiked a fever to 102°F. She was given a stress dose of hydrocortisone and started

on hydrocortisone at 100 mg three times a day. Additionally, her antibiotics were changed to vancomycin and piperacillin/tazobactam. During the next 3 days, the patient's blood cultures and tracheal aspirate demonstrated no growth. Her fever did not recur, and her antibiotic regimen was switched back to ceftriaxone and ampicillin. However, she later developed ventilator-associated pneumonia caused by *Stenotrophomonas maltophilia* as well as acute kidney injury. She was later transferred to inpatient rehabilitation. During her hospital stay, however, she developed acute-on-chronic heart failure as well as cardiogenic versus septic shock with multiorgan failure and subsequently died.

Discussion

Enterococcus faecalis is the third leading cause of infective endocarditis. The source of *E. faecalis* bacteremia is often unknown, with most identifiable sources occurring in the GU tract.[2] However, because *E. faecalis* is part of the normal gut flora, it has the potential to translocate from the GI tract and cause bacteremia and infective endocarditis.[3]

Our case was unique for two distinct reasons. First, our patient potentially developed ACS secondary to infective endocarditis. This is rare because ACS only occurs in 1% to 3% of patients with infective endocarditis.[5] The two main mechanisms underlying the development of myocardial ischemia resulting in ACS are coronary embolism/external coronary artery compression and subclavian steal syndrome with severe aortic insufficiency. Our patient likely developed myocardial ischemia from a septic coronary embolus at the level of her LAD artery. Because the aspirated thrombus was not sent for pathologic examination or culture and no autopsy was performed, we cannot definitively say that the patient's infective endocarditis caused her STEMI. However, because she had no significant medical history or family history of cardiovascular disease or coagulative disease, and because she likely had septic emboli in her spleen and left frontal lobe on abdominal CT and head MRI, respectively, the 100% occlusion of her LAD artery was likely due to a septic embolus from her mitral valve vegetation. Additionally, our patient fit the classic presentation of electrocardiographic findings, anatomic location, and infectious source for a coronary embolus: Kariyanna et al.[8] found that 43.8% of patients with a coronary embolism presented with ST elevation on electrocardiography, 52.0% of the emboli were found in the LAD artery, and the main source of the coronary emboli was infective endocarditis (22.8%).

The second unique aspect of our case was the translocation of *E. faecalis* from the GI tract to the bloodstream.[3] Although the overall incidence of GI-associated sources of *E. faecalis* infections is unknown, GI-associated sources are far less common than GU-associated sources. Furthermore, the manner in which this patient developed *E. faecalis* bacteremia was unique. This patient had a silent perforation of her rectosigmoid junction that likely facilitated the translocation and caused the *E. faecalis* bacteremia. The *E. faecalis* bacteremia then seeded the mitral valve and caused infective endocarditis as well as subsequent septic emboli in the LAD artery, spleen, and left frontal lobe. The importance of this patient's clinical picture is that if a patient has enterococcal bacteremia with an unrevealing urinalysis and urine culture, imaging and/or colonoscopy of the GI tract should be considered to rule out a GI source of *E. faecalis* as a potential cause of the patient's enterococcal bacteremia.

The main clinical dilemma that we encountered in the management of this patient was when to order TEE to rule

out *E. faecalis* bacteremia-induced infective endocarditis. Currently, the most effective bedside clinical scoring system with which to address this question is DENOVA, as stated previously. According to the DENOVA clinical scoring guidelines, any score of $\geq$3 warrants TEE to further investigate for potential infective endocarditis.[4] Our patient's score was 3 because she likely had septic embolization to her spleen, had an unknown origin of bacteremia, and had four positive blood cultures. The DENOVA bedside clinical tool is 100% sensitive in ruling out potential infective endocarditis in patients with enterococcal bacteremia; therefore, it should be known and used by all clinical providers who encounter patients with enterococcal bacteremia to rule out infective endocarditis.

In conclusion, *E. faecalis* bacteremia due to translocation from the GI tract must be on the clinician's list of differential diagnoses when considering *E. faecalis* as a potential cause of infective endocarditis. Therefore, a thorough history, physical examination, and imaging when warranted should be undertaken to rule this out. Additionally, if a patient presents with ACS-like symptoms, infective endocarditis should still be on the list of differentials despite the fact that it is an unlikely cause. Finally, clinicians should use the DENOVA scoring system to decide whether to perform TEE to investigate potential infective endocarditis in patients with enterococcal bacteremia.

Learning points

- *Enterococcus faecalis* can cause infective endocarditis from both GU and GI sources. As a result, clinicians should perform an appropriate work-up for GU and GI sources of infection if clinical suspicion for infective endocarditis is high.
- ACS is a rare clinical presentation of infective endocarditis. Therefore, if a patient presents with ACS symptoms, infective endocarditis should be on the clinician's list of differentials.
- Clinicians should use the DENOVA scoring system to determine whether transthoracic echocardiography or TEE is indicated in patients with enterococcal bacteremia.

Compliance with ethical standards

This was a case report and did not involve any experiments on human or animal subjects; therefore, ethical approval was not required.

Declaration of conflict of interest

All authors declare that there are no conflicts of interest.

Informed consent

The deceased patient's spouse gave written consent to proceed with the publication of this case report.

Funding

No author received any specific grant or funding of any kind regarding the publication of this case report.

ORCID iD

Robert Seby https://orcid.org/0000-0002-1653-7916

References

1. Dubin K and Pamer EG. Enterococci and their interactions with the intestinal microbiome. *Microbiol Spectr* 2014; 5: 10. doi:10.1128/microbiolspec.BAD-0014-2016.
2. Khan Z, Siddiqui N and Saif MW. *Enterococcus faecalis* infective endocarditis and colorectal carcinoma: case of new association gaining ground. *Gastroenterology Res* 2018; 11: 238–240. doi:10.14740/gr996w.
3. Agudelo Higuita NI and Huycke MM. Enterococcal disease, epidemiology, and

implications for treatment. Enterococci: from commensals to leading causes of drug resistant infection. NCBI, https://www.ncbi.nlm.nih.gov/books/NBK190429/ (2014, accessed 8 January 2022).
4. Berge A, Krantz A, Östlund H, et al. The DENOVA score efficiently identifies patients with monomicrobial *Enterococcus faecalis* bacteremia where echocardiography is not necessary. *Infection* 2019; 47: 45–50. doi: 10.1007/s15010-018-1208-3. Epub 2018 Sep 3. PMID: 30178077.
5. Attias D, Lepage L, Messika-Zeitoun D, et al. Acute coronary syndrome in aortic infective endocarditis. *Eur J Echocardiogr* 2008; 9: 727–728, https://doi.org/10.1093/ejechocard/jen194.
6. Gagnier JJ, Kienle G, Altman DG, et al; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *Headache* 2013; 53: 1541–1547.
7. Maqsood K, Sarwar N, Eftekhari H, et al. Septic coronary artery embolism treated with aspiration thrombectomy: case report and review of literature. *Tex Heart Inst J* 2014; 41: 437–439. Published 2014 Aug 1. doi:10.14503/THIJ-13-3386.
8. Kariyanna PT, Ramalanjaona B, Al-Sadawi M, et al. Coronary embolism and myocardial infarction: a scoping study. *Am J Med Case Rep* 2020; 8: 31–43. doi: 10.12691/ajmcr-8-2-1.