

Case Report

## Symmetrical Gangrene, a Serious Complication from Infective Endocarditis

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### Abstract

**Case Description:** We present a case about a 42-year-old male with a history of opioid abuse. He developed acute infective endocarditis, secondary to his IV drug use (IVDU). Initially, he was non-compliant and left against medical advice. Nearly a week after his initial ER visit, he was readmitted with hemoptysis due to pneumonia secondary to a septic embolus from acute infective endocarditis (IE). He further developed a pneumothorax, empyema, and septic shock, and bilateral lower extremity gangrene.



**Discussion:** *the pathogenesis behind acute infective endocarditis in this patient includes the contamination from his known IVDU, which led to the bacterial colonization, which led to the formation of fibrin clots that encased the vegetation to the destruction and loss of function. Secondary to the development of an acute IE, septic shock and or cardiogenic shock can develop. This septic shock or cardiogenic shock can lead to the development of symmetric peripheral gangrene.*

**Assessment/Results:** *A complete review of symptoms, bloodwork, CT scan, echocardiography (echo) concluded that the patient had developed acute IE secondary to IVDU. Subsequently, he developed a pneumothorax, empyema, and septic shock, which ultimately led to bilateral lower extremity gangrene development.*

**Keywords:** *IV drug use, Infective Endocarditis, Gangrene, Acute Kidney Injury, Septic Shock.*

## Abbreviations

IV drug use (IVDU), infective endocarditis (IE), staphylococcus aureus (S. aureus), coronavirus-19 (COVID-19), clinical opiate withdrawal scale (COWS), pupils equal round reactive to light (PERRL), extraocular movements intact (EOMI), disseminated intravascular coagulation (DIC), Venous thromboembolism (VTE), hemodialysis (HD), peripherally inserted central venous catheter (PICC), acute kidney injury (AKI), pulmonary embolism (PE).

## Introduction

Acute IE, an infection of the endothelium, typically affects multiple valves and results from bacteremia. Some of the most common causes include dental procedures, surgery, distant primary infections, and non-steroid injections. Staphylococcus aureus (S. aureus) is the most common pathogen involved in acute IE. This is typically seen in patients with prosthetic valves or pacemakers and IVDU. They affect healthy valves, and if left untreated, can be fatal within six weeks. Patients typically develop constitutional symptoms, including fever, chills, tachycardia, generalized malaise, dyspnea, cough, pleuritic chest pain. Cardiac manifestations may develop in terms of a new heart murmur, heart failure, or arrhythmias. Extracardiac manifestations may include petechiae, Janeway lesions, Osler nodes, rough spots, acute renal injury, signs of pulmonary embolism, and neurological manifestations secondary to septic emboli.



IV drug users are at a 100-fold increase risk of developing infective endocarditis (IE) compared to that of the general population. With the increasing opioid epidemic in the United States, cases of acute IVDU-IE are on the rise. Additionally, some severe complications secondary to IVDU-IE are coming to light. They include but are not limited to acute kidney injury, neurological manifestations, signs of pulmonary embolism, splenomegaly, embolisms, and arthritis. Some notable potential predicting factors for embolic events (as seen in our patient) include *Staphylococcus* species, young age, skin manifestations, and sepsis-related organ failure.

## Case Report

We present a 42-year-old Puerto Rican male with a history of opioid abuse and tobacco use that presented to ER with vomiting complaints about five days. He stated that the vomit contained blood and was associated with some periumbilical abdominal pain. He had a Clinical Opiate Withdrawal Scale (COWS) score of 19 and was going through narcotic withdrawals. A consult for addiction medicine was sent and was placed on Hydromorphone 4mg every three hours for the time being.

In the Emergency Department, he had a workup that included blood work, CT scan of the abdomen, chest x-ray, and blood cultures. Bloodwork revealed that he had hyponatremia, and he had a temperature of 39.5°C. IV fluids and serial electrolytes were started, and nephrology consultation was ordered. He was referred for admission. A Coronavirus-Disease19 (COVID-19) infection was suspected, but the RT-PCR returned negative.

Overall, he was a poor historian but denied a prior history of abdominal surgery. He stated that he did have a cough, denied chest pain or shortness of breath. Upon further questioning, he admitted to injecting heroin and fentanyl and had recently been using up to six bags of fentanyl daily. He noted that his last use was the prior evening. He stated that his biggest complaint was not being able to walk because of severe pain in his right buttock and back. But he denied weakness, numbness, or tingling.

A review of systems revealed pupils were equal, round and reactive to light (PERLL), extraocular movements are intact (EOMI), with no photophobia. His neck was supple with a normal range of motion. There were course lung sounds throughout, and cardiac exam revealed a regular rate and rhythm, no murmurs, rubs, or gallops. His abdomen was soft and non-tender. He was alert and oriented x 3, with no gross motor or sensory deficits. Examination of his extremities showed skin needle marks on bilateral upper extremities. Right finger bent in flexion, and right hand and forearm painful to palpation. There was no ankle edema, but purple discoloration of the lower extremities bilaterally was noted. Straight leg



raising was equivocal on the right side, and he complained of right hip pain with right hip point tenderness.

A CT and MRI were then ordered for the back and right hip pain. The CT was negative, and the MRI ruled out osteomyelitis, discitis, and abscess. He then complained of abdominal pain, so a lipase, LFT, and abdominal CT were ordered, and all returned negative. He was started on Trimethoprim/Sulfamethoxazole. Later that day, he decided to leave against medical advice.

Six days later, he was readmitted to the hospital because of hemoptysis that was likely due to pneumonia, secondary to a septic embolus. A cardiac workup revealed that he had tricuspid MRSA endocarditis. He was monitored for further hematemesis. The next day he was admitted to the ICU for hypoxic respiratory failure secondary to multifocal pneumonia and septic shock secondary to tricuspid MRSA endocarditis. He was subsequently intubated. Infectious Disease consultation was ordered, and Vancomycin was started.

Bloodwork revealed thrombocytopenia likely due to sepsis, with normal fibrinogen making disseminated intravascular coagulation (DIC) less likely. Additionally, bloodwork also showed anemia that was likely anemia of chronic inflammation. Venous thromboembolism (VTE) Risk Assessment was Moderate, and he was given a heparin dose of 5,000 U. In the ICU, his urinalysis returned positive for opiates, marijuana, and cocaine in addition to signs of AKI. Nephrology consult concluded that the hyponatremia and acute kidney injury were secondary to sepsis and hypovolemia. Ultimately, his hospital course had been complicated by renal failure that required dialysis.

Tens days after admission into the ICU, he developed a right pneumothorax with subsequent chest tube placement. A left pleural effusion was noted the next day, and chest tube placement showed empyema. Pleuritic chest pain was reported, secondary to empyema and endocarditis. Three days later, thoracic surgery was consulted, and a right pigtail chest tube was placed. Thoracic surgery then decided that all of the other chest tubes should remain in place.

It was then noted that there was lower extremity ischemia, and anticoagulation was held. Vascular surgery and podiatry were consulted due to the potential risk of needing an amputation in the future. They said that there was no surgical indication or indication for anticoagulation at the time. Shortly after, he was extubated and was achieving adequate oxygen saturation on a 2L nasal cannula. NPO was continued due to encephalopathy. Pressors were discontinued and no longer required hemodialysis (HD).

Two days after he was extubated, his left foot was blue, and it was difficult to palpate a pulse. Although he achieved adequate oxygen saturation on the 2L nasal cannula, a chest CT was ordered and revealed

bilateral infiltrate and cavitory lesions consistent with septic emboli. Over the following days, he developed gangrene in his toes and feet bilaterally secondary to septic emboli. As seen in Figure 1.



**Figure 1:** Bilateral gangrene in toes and feet secondary to bacterial endocarditis.

## Discussion

Acute IE, an infection of the endothelium, typically affects multiple valves and results from bacteremia. It is associated with a high morbidity and mortality rate; increasing IVDU rates has led to an increasing number of acute IE secondary to IVDU. The most common pathogen associated with infective endocarditis is *S. aureus*, followed by the streptococci viridans group, other streptococci, and enterococci. Together, all of these pathogens account for nearly 90% of all cases of endocarditis. (1)

The modified Duke criteria are used in the diagnosis of infective endocarditis. (Table 1) Additionally, positive blood cultures are vital, and three blood samples should be obtained about 1 hour apart from separate or different access sites. Cardiac imaging in terms of a transthoracic echo may help assist in diagnosing infective endocarditis with a sensitivity of 70% in patients with native valves. However, a transesophageal echo may also be performed and has a sensitivity and specificity exceeding 90%. (1)



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## Modified Duke criteria

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### Major criteria

- Two separate blood cultures
  - typical microorganisms: Viridans streptococci, Staphylococcus aureus, Streptococcus gallolyticus, HACEK group, Community-acquired enterococci with absence of a primary focus.
- Persistently positive blood cultures with microorganisms that are consistent with endocarditis.
  - two or more positive blood cultures drawn more than 12 hours apart; or
  - all of the three or a majority of more than four separate bowl blood cultures (first and last samples more than one hour apart); or
  - single positive blood culture for Coxiella Brunetti or face IgG antibody titer greater than one:800
- Imaging
  - Echocardiogram positive for infective endocarditis
    - Vegetation
    - Abscess, pseudoaneurysm or intracardiac fistula
    - Valvular perforation or aneurysm
    - New partial dehiscence of prosthetic valve
  - Abnormal activity around the site of a prosthetic valve detected by PET/CT assuming more than three months after surgery or radiolabeled leucocyte-SPECT/CT
  - Paravalvular lesions by cardiac CT

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### Minor criteria

- Predisposing condition (e.g., IV drug use or underlying heart abnormality)
- Fever  $>38^{\circ}\text{C}$  ( $100.4^{\circ}\text{F}$ )
- Vascular abnormalities (Janeway lesions, septic infarction, arterial emboli, intracranial or conjunctival hemorrhages, splenic infarction, and mycotic aneurysm)
- Immunologic phenomena (positive rheumatoid factor, Osler nodes, Roth spots, glomerulonephritis)
- Microbiology: positive blood cultures that do not fulfill the major criteria or serologic evidence of infection with common organisms.

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**Table 1:** Modified Duke criteria for endocarditis. Definitive endocarditis is made by any one of the following: two major criteria, one major criteria, and three minor criteria, or five minor criteria.



Suspected infective endocarditis is made by either of the following: one major criteria and one minor criterion, or three minor criteria.

In the United States, over the past two decades, there has been a steady increase in hospitalizations due to IVDU IE. The hospitalization rate increased from 0.32 to 0.75 cases per 100,000. The percent of IE attributed to IVDU is anywhere from 8 to 37.8%, with an increased incidence of nearly 56% annually. IVDU IE typically affects the heart's right side compared to that of non-IVDU IE, which typically involves the left side. Roughly half of these patients will ultimately require operative intervention, especially if antibiotics failed to clear a systemic infection. Data has shown that surgeons are less likely to operate on patients with IVDU IE due to a concern for reinfection of the new prosthetic valves. (2)

Antibiotic treatment remains the cornerstone for IE as an essential adjuvant to surgical management but can be used as the sole therapeutic modality in a select number of cases. Abbreviated treatment with either oral or IV antibiotics, which is in uncomplicated right-sided IE. A two-week course of IV antibiotics in IVDU IE has about a 94% cure rate. A significant concern for the IVDU population is the fear of catheter manipulation and its possible use for illicit drug delivery; thus, peripherally inserted central venous catheters (PICC) are greatly limited. (2)

A study found that IV drug users were at a 100-fold increase risk of developing IE compared to the general population. Positive transthoracic echocardiogram rates were also higher amongst this group compared to the non-IVDU group. This is thought to be due to fewer overall morbidities in the IVDU group. Additionally, this study found that spondylitis and pulmonary septic emboli were more common in the IV drug use group. They also had a higher recurrence of infective endocarditis than the non-IVDU group. (3)

There are many complications due to IE, including acute kidney injury (AKI), neurological manifestations, signs of pulmonary embolism (PE), splenomegaly, embolisms, and arthritis. The most common complication is acute kidney injury that is estimated to occur in about 40% of cases, which was seen in our patient. It is also a predictive factor for mortality in IE. A study found that about 42% of patients with *S. aureus* IE developed AKI into an increase and then one-year mortality and chronic kidney disease development. (4)

Embolic events secondary to the bacteria carrying particles in IE can lead to various complications. In patients with right-sided IE, most embolic events will cause pulmonary embolism as seen in our patient, while left-sided IE will cause systemic embolic events. Miotic aneurysms, for example, typically occur in the visceral arteries, aorta, and cerebral arteries. These aneurysms are believed to occur because of septic emboli and possible hematogenous seeding. There has been some notable potential predicting



factors for embolic events, including the vegetation shape, late definitive echocardiography, a mean platelet volume greater than 8.6 fL, elevated troponin I, a matrix metalloproteinases-9 greater than 167 ng/ml, staphylococcus species, young age, skin manifestations, conduction abnormalities, and lastly sepsis-related organ failure assessment  $\geq$  two. (5)

Infective endocarditis is one of many causes that may be associated with limb ischemia. There are two very distinct syndromes of micro thrombosis-associated ischemic limb injury. The first is venous limb gangrene, and the second is symmetric peripheral gangrene. Venous limb gangrene occurs due to DIC disorders with deep vein thrombosis, all of which can be attributed to heparin-induced thrombocytopenia, adenocarcinoma, and anti-phospholipid syndrome. Some of the characteristics include deep vein thrombosis, protein C deficiency caused by vitamin K antagonist, acral skin necrosis in the limb with the deep vein thrombosis, and detectable pulses on palpation or Doppler signal. On the other hand, symmetric peripheral gangrene occurs due to DIC disorders, usually without deep vein thrombosis, and is attributed to septic shock or cardiogenic shock. Initially, in symmetric peripheral gangrene, the dermal abnormalities are often sharply demarcated, symmetric, initially gray, blue, or purple, and then progress to black as the skin dies. Other characteristics include non-acral skin necrosis, proteins C and antithrombin deficiency caused by acute ischemic hepatitis, metabolic acidosis, symmetric peripheral gangrene with reduced circulation to extremities associated with hypertension, and use of vasopressors. (6)

Hutchinson had first described symmetrical peripheral gangrene in 1891. He described a clinical case of sepsis with intravascular disseminated coagulation that led to symmetrical peripheral gangrene. Albano et al. Describe then described a case about a 45-year-old woman that also went into septic shock and developed symmetrical peripheral gangrene. They noted that this likely occurs due to decreased blood supply, consequently delivering fewer nutrients and oxygen to these peripheral regions for an extended time and has high morbidity and mortality rates. (7)

## Conclusion

Acute IE typically affects one or more of the heart valves due to the endocardium infection. The management of this condition is quite complex and typically involves many specialists, including infectious disease, surgery, and primary care physicians. Their diagnosis is based on the new criteria. Treatment with antibiotics and possibly surgery is sometimes needed. In some cases, septic shock may develop and lead to further complications such as symmetrical limb gangrene. If the infective endocarditis is left untreated, it is typically fatal.



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