

# Acute Limb Ischemia: A Rare and Devastating Complication of Infective Endocarditis

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## Abstract

**Introduction:** In contrast to embolic events to the brain, lungs and spleen which have been comprehensively discussed in literature, acute limb ischemia (ALI) due to septic embolism (SE) from infective endocarditis (IE) are uncommonly reported. There have been no reported cases of ALI as a complication of IE among Filipinos to date making this case report the first in our country.

**Case Presentation:** We report two cases of community-acquired native valve endocarditis caused by *streptococcus spp.* and *enterococcus faecalis*. Both patients had large and mobile vegetations in the mitral valve and aortic valve respectively on transthoracic echocardiography. The first one developed ALI (IIa) on the R leg after the initiation of antibiotics. The second case presented with ALI (IIa) on the R leg on admission. They were given the appropriate antibiotics and received systemic anticoagulation with

heparin. The first case underwent successful emergency embolectomy on the R leg but developed new-onset ALI on the L leg and refused further intervention. Embolectomy was also recommended on the second patient who also re-fused any intervention. Despite maximal medical management, both patients subsequently expired.

**Conclusion:** Infective endocarditis (IE) patients are at risk to develop SE before or during the initiation of appropriate antibiotics. ALI is a life threatening extra cardiac complication of IE. Early recognition and prompt aggressive management are therefore imperative.

**Keywords:** infective endocarditis, acute limb ischemia, septic embolization, large vegetation, case series

## Introduction

Infective endocarditis (IE) is defined as a microbial infection of the endocardial surface of the heart which commonly involves one or more valves, mural endocardium damaged by aberrant jets of blood or foreign bodies, or intracardiac devices.<sup>1-2</sup> The annual incidence of IE among Filipinos in the largest tertiary referral center in the country was reported to be 10 cases per 10,000 person days, with an equal male to female distribution and a mean age of 30 years.<sup>3</sup> Complications may occur at the involved valve or at extra-cardiac locations that can result in serious morbidity and mortality if left untreated or inappropriately treated.<sup>1,2</sup>

Systemic embolization, a feared complication of IE, occurs in 22% to 50% of patients with IE which may occur

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prior to or during the initiation of antibiotics.<sup>4</sup> This significantly contributes to increased morbidity and mortality.<sup>1-5</sup> In contrast to embolic events to the brain, lungs and spleen which have comprehensively been discussed in literature, acute limb ischemia (ALI) due to septic embolization is uncommonly reported.<sup>1,4</sup>

To date, there have been no reported cases of ALI as a complication of IE among Filipinos in our institution and to the best of our knowledge, this may be the first local report to be published. This paper aims to increase awareness of this uncommon and devastating complication of IE which warrants aggressive intervention upon recognition in the hopes of decreasing morbidity and mortality.

## Case Presentation

### Case 1

A 27-year-old male with rheumatic heart disease had intermittent fever and myalgia for six months. He developed dyspnea for one month which progressively worsened prompting admission. He denied illegal drug use.

On admission, he was febrile (38°C). Blood pressure was 90/60 mmHg, heart rate was 98 bpm and respiratory rate

was 24 cycles per minute. He also had distended neck veins, bibasal rales, a grade 5/6 holosystolic murmur at the apex, and strong peripheral pulses on all extremities. Laboratory tests showed leukocytosis and thrombocytopenia (WBC 20,300/uL, neutrophils 76%, platelet count 40,000/uL, hematocrit 35%), normal renal function and electrolytes. A diagnosis of sepsis secondary to infective endocarditis was made, and blood cultures on three different sites were taken prior to initiation of empiric antibiotic therapy which were given intravenously (ceftriaxone 2.0 grams/24 hours and gentamicin 3.0mg/kg/24 hours). Transthoracic echocardiography (TTE) showed a dilated left ventricle, a thickened and calcified anterior mitral valve leaflet which flails into the left atrium during systole with fluttering echogenic densities attached to it with severe mitral regurgitation exhibiting a coanda effect and a dilated mitral valve annulus as seen in Figure 1. The left atrium was markedly dilated.

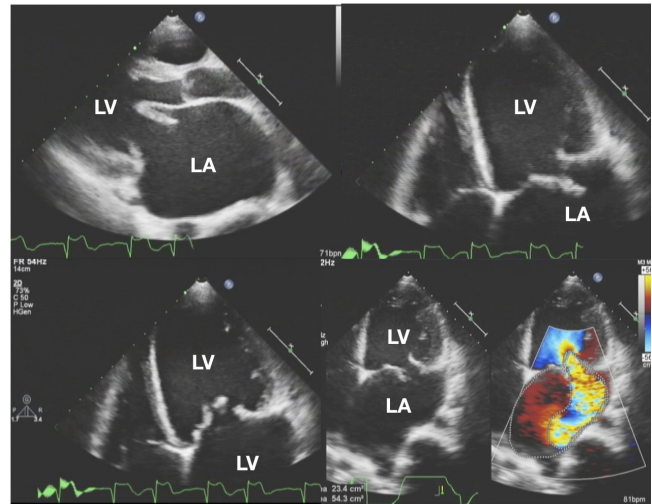
On the first hospital day, he had sudden onset of right leg pain with sensory loss. There were no palpable pulses on the right foot. On Doppler studies, biphasic pulses in the popliteal area were noted but there were none in the right dorsalis pedis artery (DPA) and posterior tibial artery (PTA) (Table I).

Acute limb ischemia (IIB) was considered. Heparin was given (1000U/hour after a bolus of 5,000U). A focused arterial duplex scan (ADS) showed monophasic waveforms at the deep femoral artery (DFA), proximal to distal SFA and at the trifurcation. Emergency embolectomy and profundoplasty were performed to restore blood flow in the affected extremity. A thrombus was visualized before the bifurcation of the proximal to distal superficial femoral artery (SFA) and DFA up to 32.0cm distal to the SFA. Operative findings include a friable femoral artery at the level of the bifurcation of the SFA and DFA. Good distal run-off was noted on completion angiogram. On the second hospital day, he developed septic shock. Norepinephrine was started. Both legs were mottled. On doppler studies, the following findings were noted on Table II.

Embolectomy was advised but no consent was given by the family. He continued to be hypotensive despite maximum medical management and expired on the third day.

## Case 2

A 43-year-old female with rheumatic heart disease who had been having exertional dyspnea for the past two weeks complained of sudden onset of right foot pain and numbness for two days. She was weak-looking, dyspneic, hypotensive (BP 80/50 mmHg), tachycardic (HR 150 beats per minute, irregularly irregular), tachypneic with a respiratory rate of 26 cycles per minute) and afebrile (37.6) at the time of admission. She had mottling of the right foot with no palpable pulses on the right posterior tibial artery and right dorsalis pedis artery. There were no sensory and motor



**Figure 1.** Parasternal long axis and apical four chamber views showing fluttering echogenic densities attached to the anterior mitral valve leaflet which flailed into the left atrium

**Table I.** Doppler studies on the lower extremities

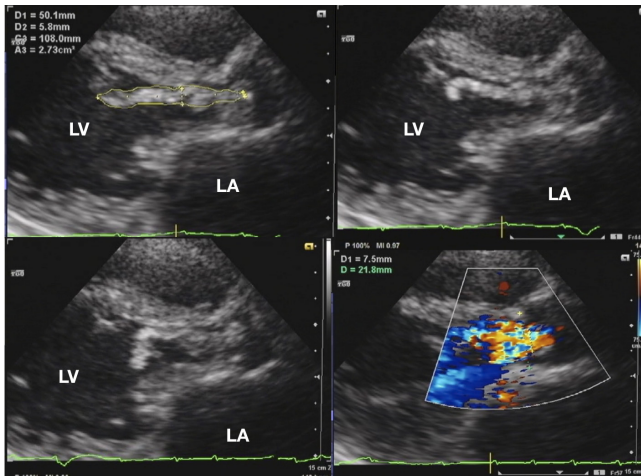
	R	L
Femoral artery	++	++
Popliteal artery	++	++
Posterior tibial artery	-	++
Dorsalis pedis artery	-	++

**Table II.** Doppler studies on the lower extremities on the second hospital day

	R	L
Femoral artery	++	++
Popliteal artery	++	-
Posterior tibial arteries	-	-
Dorsalis pedis arteries	-	-

deficits. She also had a grade 4/6 diastolic murmur at the right upper parasternal border which was new in onset. She was managed as a case of septic shock and septic embolism due to infective endocarditis. Norepinephrine was started. Blood cultures were taken. Empiric antibiotics were given (ceftriaxone 2.0grams/24 hours and gentamicin 3.0mg/kg/24 hours) intravenously. On doppler studies, there was a weak audible signal on the right popliteal artery and none on the PTA and DPA (Table III).

Acute limb ischemia (IIa) of the R-leg was considered. Heparin was started (18 units/hour after a bolus dose of 80 units/kg was given). There was leukocytosis and thrombocytopenia (WBC 29,900/uL, neutrophils 86%, hematocrit 0.35, platelet count 14), an elevated creatinine level (0.18 mmol/L), and hyponatremia (sodium 128 mmol/L). There was growth of *streptococcus spp.* on blood culture on all sites. ADS on the RLE showed a totally occluded proximal to distal posterior tibial artery and peroneal artery and a near total occlusion of the dorsalis pedis artery due to acute thrombosis. Transthoracic echocardiography showed a slightly dilated left ventricle, large echogenic serpentine fluttering density attached to the ventricular aspect of the right coronary cusp measuring 5.0cm x 0.6cm with severe aortic regurgitation (vena contracta of 1.0cm) (Figure 2).



**Figure 2.** Parasternal long axis views demonstrating the large echogenic serpentine fluttering density attached to the right coronary cusp. Color flow display showing severe aortic regurgitation

**Table III.** Doppler studies on the lower extremities on the second hospital day

	R	L
Femoral artery	++	++
Popliteal artery	++	-
Posterior tibial arteries	-	-
Dorsalis pedis arteries	-	-

**Table IV.** Doppler studies on the lower extremities on the second hospital day

	R	L
Femoral artery	++	++
Popliteal artery	++	-
Posterior tibial arteries	-	-
Dorsalis pedis arteries	-	-

The left ventricular size was only slightly increased (5.3cm) consistent with acute aortic regurgitation. The left atrium was normal in size.

Urgent surgical excision of the vegetation and aortic valve replacement was recommended. Due to thrombocytopenia, a decision to delay surgery was made. Growth of *enterococcus faecalis* after 13 hours was reported on all four sites. Antibiotics were then shifted to ampicillin 2grams + sulbactam 1gram every four hours intravenously based on antibiotic susceptibility testing.

On the second hospital day, there was progression of the right leg discoloration with motor loss. Mottling on the left foot was observed. New onset ALI on the left foot was considered (Table IV).

Embolectomy was recommended but patient refused any intervention. Despite maximal medical management, patient expired on the third day.

## Discussion

Despite advancements in the diagnostic and therapeutic management of infective endocarditis, morbidity and mortality of IE continues to be high, particularly in patients

with complications.<sup>1-9</sup> The mortality rate ranges from 29 to 35%.<sup>5-8</sup>

Although not common, ALI is a devastating complication of IE particularly if this is recognised late. In the setting of IE, this is caused by septic embolism which causes an abrupt occlusion of an artery causing cessation of blood flow on the affected extremity.<sup>2,4,9</sup> On our first case, the patient received appropriate antibiotics yet still developed ALI. In the second case, ALI developed prior to the initiation of antibiotics. Septic embolization can therefore occur before or during the initiation of antibiotics consistent with reported literature.<sup>2,4,10</sup> Depending on the acuteness and severity of ischemia, treatment may range from administration of anticoagulation and antimicrobial therapy to surgical embolectomy or amputation. Among those who have received antibiotics, the risk of embolic complications is highest during the first two weeks when the infectious burden is still high.<sup>2,4,9-12</sup> This then declines after source control with the initiation of appropriate antibiotics.<sup>4,13</sup>

Vegetations that are mobile or large (>10mm) are reported to carry the highest risk of SE<sup>9-10, 12-13</sup> Both our patients had large and mobile vegetations which placed them at high risk for embolism.

Aherera et al. prospectively studied 87 Filipinos with definite IE. Cardioembolic events to the brain, kidneys, spleen, eyes and mycotic aneurysm were described on admission. Twenty-nine percent had major embolic events after antibiotic initiation while 20% had these events before antibiotics were given. Forty-seven percent occurred during the first week of antibiotics.<sup>10</sup>

A more recent study by Kang et al. compared the outcome of early surgery (within 48 hours after randomization) and conventional treatment for IE, and the authors concluded that early surgery among those with large vegetations significantly reduced the composite end point of death from any cause and embolic events by effectively decreasing the risk of systemic embolism. Although the result of this study is promising, the sample size was not large enough (37 vs 39).<sup>14</sup>

The authors recommend early recognition and aggressive management of IE and its complications at the outset. Physical examination findings are summarized with the "six Ps": pain, paresthesia, pallor, pulselessness, poikilothermia and paralysis. These findings are expected when there is absence of pulses distal to the occlusion, pallor, cool skin, delayed capillary return and venous filling, and decreased or absence of sensory perception or motor function.

The treatment of infective endocarditis largely depends on the use of appropriate antibiotics which ideally must be culture-guided and prolonged (two to six weeks for native

valve endocarditis and at least six weeks for prosthetic valve endocarditis).<sup>1-2,4</sup> Treatment of complications such as acute limb ischemia is of equal importance since profound ischemia to an extremity can immediately threatens its viability, thus, will require emergent restoration of blood flow through endovascular or surgical revascularization to salvage the affected limb.<sup>2</sup> When this is not done promptly, morbidity rises, and loss of the affected limb or mortality may ensue.

The presence of a large vegetation that is >10mm on the aortic or mitral valve after one or more embolic episodes is a Class I indication for urgent valvular surgery to prevent embolism.<sup>4</sup> The presence of aortic or mitral valve endocarditis with severe acute regurgitation, obstruction or fistula causing symptoms of heart failure or echocardiographic signs of poor hemodynamic tolerance; refractory pulmonary edema or cardiogenic shock; and infection caused by fungi or multi resistant organisms are other Class I indications for surgery.<sup>4</sup> Other factors to be considered include the patient's hemodynamic status, nutritional status and comorbid illnesses which must be taken into account to optimize outcomes. Early recognition and prompt aggressive management of infective endocarditis and its complications are therefore imperative.

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