

A case report of critical limb ischemia in diabetes mellitus patient aggravated by COVID-19

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Abstract

Peripheral artery disease (PAD) was one of COVID-19 complications, especially in diabetes mellitus (DM) patients. This case report illustrated a multidisciplinary therapeutic in critical limb ischemia (CLI) due to DM aggravated by COVID-19. A 59-year-old woman came to hospital due to pain and bluish in her left foot, which aggravate in 2 weeks. She also had pain and redness in her left foot. She had uncontrolled DM background. Her pulsation of tibialis posterior artery and dorsalis pedis artery were weakened, whilst the contra-lateral was not palpable. Her computed tomography angiography (CTA) found total occlusion due to thrombus in right and left popliteal arteries 6 cm and 12.7 cm long, respectively. After her COVID-19 converted negative, she had right popliteal artery thrombectomy (10 cm) and above knee amputation of the left inferior extremity, then she was getting better.

Conclusion: Therefore, comprehensive evaluation of claudication could be the first step to prevent morbidity and mortality in PAD.

Keywords: Critical limb ischemia, Covid-19, Diabetes mellitus

Introduction

Critical Limb Ischemia (CLI) is a severe form of chronic peripheral artery disease (PAD) and occurs as extremity metabolism needs exceed the arterial perfusion supply thus threatening extremity survival [1]. PAD prevalence was approximately 10 – 25% in people aged > 55 years, whilst 500-1000 new cases per 1 million people per year occur in Western Europe and United States, with 40% of morbidity (loss of extremity within 3 years) [2–4]. PAD is the most common complication of diabetes mellitus (DM), had intermittent claudication symptoms as far as amputation which often occurs in the distal inferior extremity blood vessels [5,20]. DM causes hyperglycemia, increased free fatty acid and insulin resistance which lead to increased stress oxidative, protein kinase C and Receptor for Advanced Glycation Endproducts (RAGE) activation thus provoking vasoconstriction, chronic inflammation and thrombosis, that is the main cause of PAD due to DM [6]. Therefore, PAD prevalence will increase along with increasing number of DM cases and older ages.

There was complex association between COVID-19,

DM and PAD, which is a slice of the complications from both diseases, approximately two-thirds of COVID-19 patients had PAD also had hypertension, DM and dyslipidemia background. Vascular abnormality and hemorheological disturbance in DM patients disturbed micro-circulation and provoked organ damage. Microvascular dysfunction in DM patients increases vascular permeability and interferes blood flow causing nephropathy, retinopathy, neuropathy, even cardiovascular complications, whereas atherosclerosis and vascular calcification cause macrovascular complication [7,8]. PAD management approach has two things that are related to each other, that is overcoming the specific symptoms and decreasing cardiovascular risk with the intention of preventing morbidity (amputation) and increasing the function and quality of live, thus requiring multidisciplinary therapy [1,9]. Thereof, PAD requires proper and immediate diagnosis in order to decrease morbidity.

This case report describes a 59-year-old DM woman having CLI and aggravated by COVID-19. It aims to illustrate the multidisciplinary management of the patient. This case report will hopefully assist clinicians determine a safe and appropriate

management modality for CLI and PAD patients, regardless their background.

Case presentation

A 59-year-old woman came to the Emergency Room (ER) due to pain in her left limb, felt for 5 years. This pain was felt when moving or walking and got better when resting. However, this pain got worse within last 2 weeks. The right limb was also in pain and reddish. She also had dry cough for a week, shortness of breath for 3 days and fever for 2 days. There was no decrease in appetite. She was referred from other hospital in Surabaya. She was admitted for 2 days due to COVID-19. She had 4 years background of uncontrolled DM. She was a housewife. She said there was no contact with any COVID-19 patients and there was no cardiovascular diseases background.

On physical examination, her blood pressure was 130/80 mmHg, pulse was 86 bpm, respiration was 24 times per minute, temperature of 36.7°C, oxygen saturation was 99% (room air). Her conjunctiva was anemic and appeared dyspneic. There were rhonchi in both of her lungs. Local status of her right pedis was reddish, warm, there were no necrotic tissue, the pulsation of the right tibialis posterior artery and dorsalis pedis artery were decrease. Meanwhile the local status of her left pedis was bluish, cold, there was necrotic tissue as high as her ankle, there was no pulsation of her left tibialis posterior artery and dorsalis pedis artery (Figure 1). Sensory examination of her right and left limbs were normal and numb, respectively. Meanwhile, her motoric examination of her right and left limbs were normal and immobile, respectively.



Figure 1. The clinical photo of patient's foot. (A) The photo was taken first time at her examination in the ER. (B) The photo was taken at the 9th day of treatment

She had leukocytosis ($24,460 \times 10^3/\mu\text{L}$), neutrophilia (88.1%) and thrombocytosis ($627,000 \times 10^3/\mu\text{L}$). Both her transaminase was increased, her *Serum Glutamic Oxaloacetic Transaminase (SGOT)* and *Serum Glutamic Pyruvic Transaminase (SGPT)* was 70 U/L and 93 U/L, respectively. Her kidney function was also decreased, her Blood Urea Nitrogen (BUN) and creatinine were 61 mg/dL and 1.3 mg/dL, respectively. Her random blood glucose was 289 mg/dL and her albumin was 2.89 g/dL. Her D-dimer was 3960 ng/mL and LDL was 95 mg/dL. Her electrolyte was normal. She had leukocyturia +2 and glucosuria +4. There was bilateral pneumonia on her chest x-ray (Figure 2). Her polymerase chain reaction (PCR) COVID-19 nasopharyngeal swab was positive. The inferior extremity computed tomography angiography (CTA) (Figure 3) showed right iliac artery, right femoris communis artery, right femoral profunda artery and right femoral superficialis were normal. There was total occlusion due to thrombus in right popliteal artery as high as ± 1 cm above right femorotibial joint, ± 6 cm to the inferior. Tibialis anterior artery received contrast flow from collateral artery. There was no contrast flow in the right tibialis posterior artery, right peroneus artery and right dorsalis pedis artery, left iliac artery, left femoris communis artery, left femoral profunda and left femoral superficialis were normal. There was total occlusion due to thrombus in left popliteal artery as high as ± 6 cm above left femorotibial joint, ± 12.7 cm to the inferior. There was no contrast flow in the left tibialis anterior artery, left tibialis posterior artery, left peroneus artery and left dorsalis pedis artery.

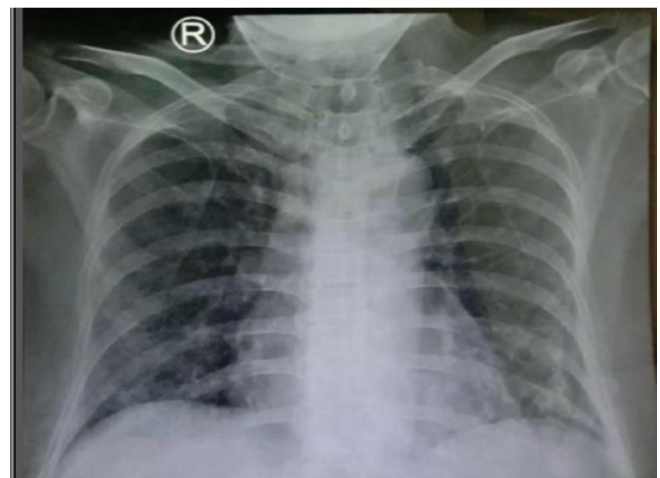


Figure 2. The patient's chest x-ray. It shows bilateral pneumonia due to COVID-19



Figure 3. The patient's CTA of her inferior extremity. (A, B, C) There was total occlusion due to thrombus in right popliteal artery as high as ± 1 cm above right femorotibial joint, ± 6 cm long to the inferior. Right tibialis anterior artery received contrast flow from collateral artery. There was no contrast flowing in the right tibialis posterior artery, right peroneus artery and right dorsalis pedis artery. There was total occlusion due to thrombus in left popliteal artery as high as ± 6 cm above left femorotibial joint, ± 12.7 cm long to the inferior. There was no contrast flowing in the left tibialis anterior artery, left tibialis posterior artery, left peroneus artery and left dorsalis pedis artery

Due to the patient was COVID-19 confirmed, she was admitted into Special Isolation Room (SIR). She was planned to have below knee amputation of her left inferior extremity (Figure 4) and doppler ultrasound (DUS) of left inferior extremity. At that time, the ultrasound, CTA and operation implementation protocol in the hospital was prioritizing the emergency one. The patient was not included; thus, she had to have negative conversion before the operation and ultrasound were implemented. She received heparin 5000 unit/12 hours subcutaneously and Cilostazol 100 mg/24 hour orally for her PAD. She also received rapid-acting and long-acting insulin to control her blood glucose and Remdesivir IV, Isoprinosine orally and Vitamin D orally to treat her COVID-19. Immediately after she was converted negative, at the 9th day of treatment, she had her CTA. In accordance with her CTA results, the Cardiothoracic Team performed antegrade right femoral artery thrombectomy (they received ± 10 cm thrombus) and above knee amputation of the left

inferior extremity. After the procedure, she had DUS. Her DUS result was triphasic flow of right femoral artery and right popliteal artery, biphasic flow of right tibialis posterior artery, no flow in right dorsalis pedis artery, a flow in left femoral artery and no flow in left popliteal artery, left tibialis posterior artery, left dorsalis pedis artery (amputation related).



Figure 4. The patient's left inferior extremity after above knee amputation.

Discussion

This case report highlights a DM patient having CLI and COVID-19 confirmed. She had pain in her right and left foot recurring for 5 years, aggravated within last 2 weeks. The pain is felt when moving or walking. While her physical examination showed necrotic tissue and numb sensation in her left foot, her inferior extremities CTA showed total occlusion due to thrombus in her right and left inferior extremities. In accordance with the data, she had Fontaine stage IV and Rutherford grade III category 6 of PAD [10]. A prior case also reported the same [7]. The patient was COVID-19 confirmed, prone to hypercoagulation state [11] and DM likewise [6]. Moreover she also had PAD risk factor, that was aged 50–64 years and other atherosclerosis factors (DM, hypertension and dyslipidemia) [12]. Therefore, holistic management is necessary to relieve symptom.

Increased blood viscosity causes deterioration of cardiovascular system, i.e. hypertension and DM causing atherosclerosis. Besides that, insulin resistance also decreased blood flow [13]. COVID-19 causes increased von Willebrand Factor (vWF) and Factor VIII leading to endothelial activation due to increase of inflammatory cytokine, complement activation as well as direct effect of SARS-CoV-2 infection on the endothelial cell through Angiotensin Converting Enzyme-2 (ACE-2) receptors, as in thrombosis related endothelitis [14,19]. Therefore, patients with claudication background could have aggravated PAD due to this mechanism.

During her treatment in SIR, she had anticoagulants and insulin, which is pharmacological management of PAD [12]. As the first approach to diagnose PAD was DUS to determine location and severity of obstruction. Then, CTA was more preferable in life-threatening PAD [15,16]. Authors used clinical approach to manage the PAD. Revascularization in PAD is an effort to restore blood flow as reduce ischemia and improve tissue viability [17]. As D-dimer shows hypercoagulopathy, often occurs as COVID-19 complication, anticoagulant also prevent worsening condition of the patient until she received definitive management [18]. In cases of necrotic gangrene or broad infection, amputation without revascularization was preferred [9]. Hence, this patient had above knee amputation of her left inferior extremity and thrombectomy of the right popliteal artery.

This case report has several limitations. The first diagnostic approach of PAD was not performed due to hospital protocol during COVID-19. Furthermore, the follow-up data of the patient was not reported as the authors focused on patient's management.

Conclusion

This case report illustrates CLI due to DM in COVID-19 patient. The patient has claudication background and uncontrolled DM. She received anticoagulant for her COVID-19 management, insulin for regulating her blood glucose, thrombectomy of her right popliteal artery and above knee amputation of her left inferior extremity for the CLI. This case was hoped to give consideration to the early symptoms of PAD that is claudication, as the patient could receive proper and immediate management to prevent morbidity and

mortality.

Consent for publication

Written informed consent for this publication was taken from the patient.

Conflict of interest

The authors declare no conflict of interest.

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Authors' contribution

FHR and HS managed the patient. FHR and HS designed the study. FHR collected the data. FHR analysed the data. FHR wrote the manuscript. HS confirmed the accuracy of the data and analyses.

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