Emergency thrombectomy in acute upper limb ischemia patient with diabetes mellitus

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\textbf{ABSTRACT}

\textbf{Background:} Acute limb ischemia is a sudden decrease in limb blood perfusion with an onset of less than 14 days, most commonly occurs in lower extremities. Diabetes mellitus, one of diseases underlying peripheral artery disease, complicates the pathophysiology of acute limb ischemia. In this case report we present a patient with type 2 diabetes mellitus and acute ischemia in the left upper extremity that had successful thrombectomy treatment.

\textbf{Case presentation:} A 58-year-old female patient came to the Emergency Care Unit of Dr. Soetomo General Hospital with pain in the five fingers to the palm of the left hand for the past two days. The numbness spread from the elbow to the left fingers, making them weak and difficult to grip. Those five fingers were pale and cold as well. The left hand had no pulsated radial and ulnar artery, weak brachial pulse and undetected pulse oximetry result. The patient was diagnosed with type 2 diabetes mellitus since 2005 and has a controlled treatment. On the first day of hospitalization, the patient was scheduled for emergency thrombectomy at Dr. Soetomo General Hospital. Follow-up on the seventh-day post-surgery, the patient had no complaints of pain and pale in the left hand and the brachial, ulnar and radial arteries were palpable.

\textbf{Conclusion:} Acute limb ischemia is uncommon in the upper extremities but we found that it has an excellent prognosis with early revascularization, even in a patient with diabetes mellitus. The treatment must be in conjunction with aggressive diabetes mellitus treatment to avoid acute limb ischemia worsening.

\textbf{Keywords:} acute limb ischemia, revascularization, diabetes mellitus, peripheral artery disease, Indonesia.


\textbf{INTRODUCTION}

Acute limb ischemia (ALI) is a condition where there is a sudden decrease in limb blood perfusion within 14 days. It is one of vascular emergency cases that causes a decrease in extremity viability and even dead limbs if left untreated immediately. Most ALI cases involve the lower extremities. The incidence of acute upper limb ischemia (AULI) is only about $0.15\%$ of all ALI cases.\textsuperscript{1} The anticoagulation with the adjusted dose based on the severity of ALI may help, but revascularization therapy remains the treatment of choice in patients with ALI.\textsuperscript{2}

ALI is the part of peripheral artery disease (PAD) - a blood vessel disorder characterized by progressive narrowing and blockage of blood vessels mainly due to atherosclerosis, ranging from mild plaque formation to chronic vessel occlusion.\textsuperscript{3-5} Risk factors for PAD include smoking, diabetes mellitus (DM), obesity, high blood pressure, high cholesterol, aging, genetics, heart disease and stroke.\textsuperscript{3-5} DM is a major risk factor for PAD\textsuperscript{4} and associated with other diseases.\textsuperscript{7,8}

Epidemiological data show a strong relationship between PAD and DM with the prevalence of PAD in DM patients is $20\%$.\textsuperscript{6} Every $1\%$ increase in HbA1C level will increase the risk of PAD by $28\%$.\textsuperscript{6} A common symptom of PAD is the presence of intermittent claudication, which is felt as pain or cramp during activity and improved by resting. However, in patients with DM, PAD symptoms may be asymptomatic due to peripheral neuropathy and cause a delay of therapy.\textsuperscript{9}

In this case report, we report a case of AULI with DM that was treated with thrombectomy and resulted an immediate improvement.

\textbf{CASE PRESENTATION}

A 58-year-old woman, came to Emergency Care Unit of Dr. Soetomo General Hospital with pain in the five fingers of the left hand. The pain was continuously felt in the fingers, making them weak and difficult to grip. Those five fingers were pale and cold as well. The left hand had no pulsated radial and ulnar artery, weak brachial pulse and undetected pulse oximetry result. The patient was diagnosed with type 2 diabetes mellitus since 2005 and has a controlled treatment. On the first day of hospitalization, the patient was scheduled for emergency thrombectomy at Dr. Soetomo General Hospital. Follow-up on the seventh-day post-surgery, the patient had no complaints of pain and pale in the left hand and the brachial, ulnar and radial arteries were palpable.

From the previous medical history, the patient had no complaints of pain and pale in the left hand and the brachial, ulnar and radial arteries were palpable. The patient also complained of nausea and vomiting 2–3 times a day during the same days span. There was no history of fever, cough and shortness of breath. The patient had lack of appetite due to nausea.

When palpated, the five fingers were cold and blue with no swollen nor deformity. There was no stiffness nor trauma in the fingers. The patient also complained of nausea and vomiting 2–3 times a day during the same days span. There was no history of fever, cough and shortness of breath. The patient had lack of appetite due to nausea.
CASE REPORT

were: Hb 11.8 g/dL, leukocytes 13,320/μL, neutrophils 77%, platelets 275,000/μL, sodium 137 mmol/L, potassium 3.8 mmol/L, chloride 103 mmol/L, serum glutamic oxaloacetic transaminase (SGOT) 16 U/L, serum glutamic pyruvic transaminase (SGPT) 20 U/L, blood urea nitrogen (BUN) 20 mg/dL, serum creatinine 0.15 mg/dL, activated partial thromboplastin time (APTT) 25.4 sec, prothrombin time (PT) 9.8 sec and random blood glucose 300 mg/dL.

The chest radiography was normal. The electrocardiogram (ECG) showed sinus rhythm 92 x/min, inferior old myocardial infarct (OMI), anteroseptal ischemia with complete right bundle branch block (RBBB), right axis deviation (RAD) and counter-clockwise rotation (CCWR). The results of echocardiography showed the dimensions of all heart chambers were normal, systolic function of left ventricle (LV) was normal (ejection fraction; EF 68%), diastolic function of LV was abnormally relaxed, systolic function of right ventricle (RV) was normal, segmental analysis of LV was normokinetic, and left ventricle hypertrophy (LVH).

The CT-angiogram of the left upper extremity showed no contrast flow in the left radial artery at a distance of ±15 cm from brachial artery, ±5 cm long. The contrast flow was also not seen in the left ulnar artery at a distance ±0.9 cm from the brachial artery, ±3 cm long (Figure 2). The results of left extremity Doppler ultrasound showed soft plaque >50% on the left radial artery at wrist and left ulnar artery at mid antebrachial level to the wrist. The peak systolic velocity (PSV) and pulsatility index (PI) of the arteries outside the lesion was within normal limits. The Doppler ultrasonography of all arteries in the left upper extremities had triphasic waveforms which was normal.

The patient was consulted to Cardiology Department and the patients was diagnosed with ALI in the left superior extremity, Rutherford IIB. The patient was treated with aspirin 100 mg once a day, cilostazol 50 mg twice a day, beraprost sodium 20 mcg 3 times a day and atorvastatin 40 mg once a day. In 2018, the patient underwent surgery on her left toe due to a vascular blockage at Dr. Soetomo General Hospital. The patient’s father also had DM.

On physical examination, the general condition was weak, with Glasgow Coma Scale (GCS) 15, blood pressure 100/80 mmHg, heart rate 98x/min, respiratory rate 20x/min, body temperature 36.3°C, oxygen saturation 98%, visual analogue scale (VAS) score 6. Head and neck examination revealed no abnormalities, anemia, cyanosis, jaundice and dyspnea. The jugular venous pressure (JVP) was in normal range with no enlarged lymph nodes. Chest and abdominal examination showed no abnormalities. The examination of superior extremities showed that the left palm and fingers were pale, cold, no pulse on radialis and ulnar artery, weak brachial pulse and undetected pulse oximetry result (Figure 1). The patient was still able to move all five fingers. The ankle-brachial index (ABI) examination revealed 0.8 in the left side and normal in the right side. The results of laboratory examination near the patient’s house. The routine DM medications were glimepiride 2 mg once a day and metformin 500 mg 3 times a day. The patient also had hypertension but was not treated regularly, which was treated with amlodipine 10 mg daily. In 2018, the patient underwent surgery on her left toe due to a vascular blockage at Dr. Soetomo General Hospital. The patient’s father also had DM.

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cito thrombectomy and heparinization 10 mg/kg/hour.

After all examinations and consultation, the patient was scheduled for the examination of fasting blood glucose (FBG), 2 hours post-prandial blood glucose (2hppBG), HbA1C, lipid profile, PT/APTT (every 6 h) and fibrinogen. The patient was then injected with actrap for blood glucose regulation 4 units in 2 injections intravenously every 1 hour. After random blood glucose (RBG) was corrected to 187 mg/dL, the treatment was continued with insulin aspart (NovoRapid) injection 6 units sub cutaneous 3 times a day before meal, insulin detemir (Levemir) injection 10 units sub cutaneous once a day, diet for DM with cardiovascular diseases (diet-KV) 1900 kcal/day, tramadol injection 100 mg intravenously 3 times a day, lansoprazole injection 2 times a day intravenously, clopidogrel 75 mg orally once a day, ceftriaxone 1 gram intravenously twice a day, dorner 20 mg orally 3 times a day, metoprolol tartrate 100 mg orally once a day, atorvastatin 40 mg orally once a day.

On the seventh day of treatment, the patient had no complaints of pain in the left hand, the five fingers and the palms were red. The general examination showed GCS 15, blood pressure 120/78 mmHg, heart rate 94 x/min, respiratory rate 18 x/min, body temperature 37.2 °C, and VAS score 0. The left axillary, brachial, and ulnar artery were all palpated (+, +, +), respectively and the radial artery was still difficult to evaluate. The PT/APTT were 9.6 and 23.6 sec, respectively at 12:00 am, 9 and 27 sec at 06:00 pm, 9.2 and 30 sec at 00:00 am, fasting blood glucose 188 mg/dL, 2hppBG 236 mg/dL, potassium 3.3 mmol/dL, sodium 135 mmol/dL, chloride 97 mmol/L, RBG 196 mg/dL, Hb 12.7 g/dL, leukocytes 15900/μL, neutrophils 83%, platelets 340,000/μL, SGPT 129 mg/dL, SGPT 20 mg/dL, BUN 14 mg/dL, serum creatinine 0.69 mg/dL, total cholesterol 236 mg/dL, low-density lipoprotein (LDL) 180 mg/dL, triglycerides (TG) 129 mg/dL, high-density lipoprotein (HDL) 39 mg/dL. Dyslipidemia was added to the patient's diagnosis. The patient was injected with Novorapid 10 units sub cutaneous 3 times a day before meal, ceftriaxone 1 gram intravenously twice a day, atorvastatin 40 mg orally once a day, clopidogrel 75 mg orally once a day, ceftriaxone injection 1 gram intravenously twice a day, metformin 1000 mg orally three times a day, and pentoxifylline 400 mg orally three times a day, atorvastatin 40 mg orally once a day.

DISCUSSION

The mechanism of PAD is progressive narrowing and blockage of blood vessels mainly due to atherosclerosis, ranging from mild plaque formation to chronic occlusion of blood vessels. PAD symptoms’ severity depends on the blockage’s severity and the presence or absence of collateral vessels. ALI is a form of PAD that requires immediate treatment. The clinical features of ALI can occur within minutes, hours, or days and vary from intermittent episodes to sudden limb-threatening symptoms. The main clinical features of ALI include pain, pallor, and paresthesia in the affected limb, which can progress to tissue necrosis if left untreated. Early diagnosis and prompt intervention are crucial to prevent complications and improve outcomes.
of claudication to pain at rest, or sudden pain in the affected extremity, numbness of the extremity, absence of pulsations of the distal part to the occlusion, cold skin, pale and may be accompanied by motor impairment. These signs and symptoms are commonly abbreviated as 6Ps: paresthesia, pain, pale, pulselessness, poikilothermic and paralysis.\textsuperscript{12,11} The most common cause of AULI is embolic process (90\%) originating from the heart, trauma or embolism from aorta and its branches. AULI most often occurs in the brachial, radial and ulnar arteries.\textsuperscript{12}

In this case, the patient complained of pain in the five fingers to the palm accompanied by numbness to the left elbow, the left hand felt weak so it was difficult to grip. This complaint appeared for 2 days before she was admitted to the hospital. There was no history of such complaints. On physical examination, the left palm looked pale, cold, and there was no left ulnar and radial artery pulsation, and weak brachial artery pulsation.

ABI is a first-line examination in patients with suspected ALI accompanied by PAD symptoms. This test measures the systolic blood pressure of the arm (brachial artery) and ankle (dorsalis pedis and posterior tibial artery) in the supine position using a sphygmomanometer or Doppler ultrasonography. This test is non-invasive and easy to perform. Interpretation of ABI score was > 1.3 was non-compressible, 1-1.3 was normal, 0.9-1 was borderline, 0.71-0.9 was mild, 0.41-0.7 was moderate and 0.0-0.4 was severe PAD.\textsuperscript{11,13} If the result of ABI is positive for PAD (0.9 or lower), it is necessary to carry out further supporting examinations related to ALI. The patient in this study had ABI 0.8 for the left extremities, which means mild PAD, and 1 for another side.

The common scoring system used to determine the clinical state of PAD is Fontaine and Rutherford classification.\textsuperscript{14,15} This classification may help determining the right therapy for PAD patients. The Rutherford classification is most often used to determine the management of ALI. This classification may determine the prognosis of ALI, sensory function, motor function, and arterial and venous blood flow of the extremity.\textsuperscript{1,2} In this study, the patient had numb fingers of the left hand to the elbow. The motor function of the left hand decreased, the five fingers were difficult to move due to continuous pain and there was no tissue damage in the extremities. The Doppler ultrasonography showed soft plaque > 50\% on the left radial artery at wrist level and left ulnar artery at mid antebrachial to wrist level. The PSV and VI in Doppler ultrasound were normal in all arteries and the triphasic waveform was detected. Based on this classification, the diagnosis of the patient became ALI Rutherford IIB of the left superior extremities.

Among Vascular Doppler, Doppler ultrasound (DUS), Computed tomography (CT) angiography, magnetic resonance angiography (MRA), digital subtraction angiography (DSA), CT angiography is the gold standard for diagnosing ALI.\textsuperscript{10} Digital subtraction angiography (DSA) is the most accurate test to determine the anatomy and vascular abnormalities, but the examination is invasive so the risk of bleeding, infection, and rupture is high. Doppler ultrasound (DUS) is non-invasive, non-radiative, inexpensive and requires a relatively short time to examine. It also provides important information about hemodynamics (proximal and distal to obstruction) and patency of vascular flow. The limitation of DUS is its dependence on the operator and inability to provide a clear picture of the arteries. A more precise imaging technology is therefore required.\textsuperscript{2} The imaging modality of choice in ALI patient is CT angiography, with a 98\% specificity and 96\% sensitivity. It clearly shows calcifications, stents, location, level of occlusion and patency of blood vessels. Computed tomography angiography has a high enough risk in patients with renal impairment (glomerular filtration rate of less than 60 mL/min). Magnetic resonance angiography can still be used in patients with renal impairment with a filtration rate of less than 30 mL/min, but MRA cannot detect arterial calcification, thus providing limited information for anastomotic site selection and cannot be performed in patients with pacemakers and metal implants.\textsuperscript{1,10}

Blood tests that were examined including complete blood count, hemostatic function, LDH, D-Dimer, BUN, creatinine, lactic acid, potassium, blood gas analysis, blood glucose. However, laboratory examination does not really contribute in establishing the diagnosis of ALI. Laboratory examinations are only to assess general health status and assess comorbidities.\textsuperscript{2,10} Risk factors for PAD include smoking, hypertension, dyslipidemia, age, gender, and diabetes mellitus.\textsuperscript{6,14} DM is a very important risk factor for PAD due to abnormal conditions in DM such as hyperglycemia, insulin resistance and dyslipidemia, which may trigger the changes in the function and structure of blood vessels. Mechanisms of changes that occur such as increased oxidative stress, impaired intracellular signal transduction by protein kinase C (PKC) and receptor for advanced glycation end-products (RAGE) activation.\textsuperscript{17} As a result, there will be a decrease in nitric oxide (NO) and an increase in endothelin which are strong vasoconstrictors, activation of proinflammatory transcription factors such as nuclear factor kappa B, AP-1 and an increase in the prothrombotic factor plasminogen activator inhibitor.\textsuperscript{16,17,18} The risk factors in this patient were a history of T2DM since 2005, dyslipidemia and a postoperative history due to PAD on the left toe in 2018.

In all ALI cases, initial anticoagulant therapy such as unfractionated heparin (UFH) should be given immediately before and after the procedure to reduce thrombus propagation. Revascularization is the main therapy for ALI patients with the technique is based on the type of occlusion (thrombus or embolism), location, duration of ischemia, comorbidities and Rutherford classification.\textsuperscript{3}

There are some endovascular treatment techniques such as catheter-directed thrombolysis (CDT), percutaneous thromboaspiration (PAT) with or without thrombolytic therapy and percutaneous mechanical thrombectomy (PMT). Catheter directed thrombolysis is not recommended in ALI class IIB and III, because it takes a long time to reperfusion. In addition, ALI lasting longer than 14 days makes it challenging to insert the catheter through the thrombus, and this treatment is not advised in individuals who have thrombolysis contraindications. Approximately 25\% of patients with CDT
therapy require additional open surgical revascularization, despite the fact that this method is extremely effective. Although PAT, which has a 30% effectiveness rate, is extremely effective, some studies claim that using thrombolytic drugs in conjunction with this treatment may improve outcomes. Percutaneous mechanical thrombectomy is the first choice of therapy in ALI class IIb, because the time to reperfusion is shorter when compared to CDT. Patients with contraindications to thrombolysis and who are at high risk for surgery can undergo PMT. In patients with a high risk of bleeding, PMT can be used to remove thrombus masses before local thrombolysis and distal embolic complications that occur after CDT.\(^1\)\(^2\)

Open surgical revascularization is usually performed in severe ALI cases where the affected extremity is not viable, in ALI with onset of more than 14 days, or in which thrombolysis is contraindicated. This open surgical revascularization consists of: thrombectomy with a Fogarty balloon catheter, bypass surgery, and adjuncts such as endarterectomy, intra-operative thrombolysis and patch angioplasty. Patients with suspected embolism and no ipsilateral pulse of an ischemic extremity are best treated with Fogarty catheter balloon thrombectomy. This bypass surgery is usually performed in patients with ALI caused by thrombosis with underlying PAD. These patients are not suitable for balloon catheter thrombectomy, because thrombus may reoccur. Intraoperative thrombolysis, this procedure is rarely used and is only performed in special cases such as secondary ALI due to thrombus from popliteal artery aneurysm with tibial occlusion.\(^1\)\(^2\)

There are some treatments for ALI based on its classification. ALI class I, normal motor function without sensory loss and with intact capillary refill, usually only requires systemic anticoagulant therapy and stabilization of the patient in the early management phase. ALI class IIa, slow capillary refill with limited sensory loss and movement, must be revascularized. The treatment of choice for ALI class IIb, sensory loss spreading more than toe and rest pain, is also revascularization. Amputation is the primary option in ALI class III due to its permanent tissue damage or gangrene.\(^2\) A cytologic thrombectomy was performed with a Fogarty balloon catheter.

Other supportive therapies for PAD patients are cilostazol, pentoxifylline, lipid-lowering drugs and antiplatelet drugs. Cilostazol is a phosphodiesterase inhibitor that inhibits platelet aggregation and exhibits a vasodilating effect, administration of cilostazol 200 mg/day for 12 to 24 weeks increases the maximum walking distance without claudication.\(^14\) Pentoxifylline can reduce blood viscosity and increase erythrocyte flexibility. Antiplatelet effectively reduces the incidence of PAD.\(^14\)\(^9\) This patient was also given oral therapy with cilostazol 50 mg twice a day, pentoxifylline 400 mg once a day, clopidogrel 75 mg and atorvastatin 40 mg once a day. Management of PAD in addition so interventional and pharmacological therapy also includes controlling risk factors, for instance, blood glucose, blood pressure, cholesterol, smoking habits, and weight loss. The targets for blood glucose is HbA1C < 7, triglycerides < 150, LDL < 100, HDL > 35, low homocysteine, and blood pressure < 140/90.\(^20\)\(^21\)

The insulin is given in 0.5 – 1 unit/kgBW/day, with the targeted HbA1C < 7. In critical DM patients, the targeted blood sugar is 140 – 180 mg/dL.\(^2\)\(^2\) The patient in this study was given a diet-KV of 1900 kcal/day, injection of subcutaneous Levernir 10 units at night and subcutaneous NovoRapid 6 units every 8 h before meals. The insulin dose was titrated based on fasting and postprandial blood glucose levels.

Following the surgery, observations were conducted based on patient complaints, arterial pulsation, complete blood count, coagulation function, motor and sensory function, and CT angiography to determine the progression of ALI. In certain cases, reperfusion after revascularization was inadequate, necessitating amputation. The condition of the post-thrombectomy in this study showed that the pain was decreased, palpable radial and ulnar artery pulses, no numbness, warm with the last PT/APTT was 11.1 and 32.7, respectively.

CONCLUSION
Although ALI is uncommon in the upper extremities, we discovered that it has an excellent prognosis with early revascularization, even in diabetic individuals. The medication must be carried out in conjunction with intensive DM treatment to prevent disease development.

PATIENT CONSENT
The patient provided informed consent to include the case as case report.

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DISCLOSURE OF CONFLICTS OF INTEREST
We do not have no conflict of interest.

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AUTHOR CONTRIBUTION
Both authors contributed significantly to the case-report.

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