Case Report:

PERCUTANEUS AND SURGICAL TRANSLUMINAL ANGIOPLASTY AS COMPLEMENTARY THERAPIES FOR LEUKEMIC PATIENTS WITH ACUTE LIMB ISCHEMIC MANIFESTATIONS

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ABSTRAK

Leukemia dengan trombositosis dapat menyebabkan penyakit arteri perifer. Komplikasi trombotik arteri pada penyakit myeloproliferatif dapat terjadi dengan jumlah trombosit hanya sedikit meningkat. Wanita tua A-50-tahun dengan sejarah leukemia dan diabetes dikembangkan kaki kiri iskemik. Dia punya rasa sakit dan kelumpuhan sebagai gejala awal. Jumlah trombosit adalah 1004000/µL. Angiogram menunjukkan tersumbat salah distal ketiga arteri femoralis kiri superfisialis dan ada trombus. Pengobatan dengan trombectomy Forgaty ditemukan thrombus 15 cm. Kami lakukan Percutaneous Transluminal Angioplasty (PTA) dengan hasil jangka distal off sampai arteri tibialis anterior. PTA dan thrombectomi Forgaty dapat dianggap sebagai pengobatan komplementer untuk pasien dengan iskemia tungkai akut. ***(FMI 2015;51:59-65)***

Kata kunci: *iskemia tungkai akut, leukimia, percutaneous transluminal angioplasty, operasi*

ABSTRACT

Leukemia with thrombocytosis can cause peripheral artery disease. Arterial thrombotic complication in myeloproliferatif disease can occur with only mildly elevated platelet counts. A-50-years old woman with history of leukemia and diabetes developed ischemic left foot. She got pain and paralysis as initial symptom. Platelet count was 1004000/µL. An angiogram demonstrated occluded one third distal of left femoralis superficialis artery and there was thrombus. Treatment with trombectomy Forgaty found thrombus 15 cm long. We perfomed Percutaneous Transluminal Angioplasty (PTA) with the result distal run off until anterior tibialis artery. PTA and thrombectomi Forgaty can be considered as the complementary treatment for these patients. ***(FMI 2015;51:59-65)***

Keywords: *Acute limb ischemia, leukemia, percutaneous transluminal angioplasty, surgery*

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INTRODUCTION

Acute limb ischemia (ALI) is one of commonly-found vascular emergencies. ALI is a situation where there is blockage of the arteries that suddenly causes disruption of balance between supply and demand between blood flow, oxygenation of skeletal muscles and surrounding tissue is then threaten the viability of the limb. ALI has a high number of risk of death and amputation. In addition ALI also has a high mortality rate because patients with ALI have other comorbid diseases, heart, vascular, and cerebrovascular diseases (Micthell et al 2008, Hirsch et al 2006, Singh 2006, Rajan et al 2005).

Data in England and Wales states that the ALI has attacked nearly 5,000 patients annually with a mortality rate of 20% and a loss of one limb of the body by 40%. ALI patients with embolic causes of have high mortality while those with thrombus causes have high numbers of limb loss. National Health and Nutrition Examination Survey said that with age, the prevalence of ALI rose nearly 3-4 fold (Micthell et al 2008, Libby et al 2008).

ALI is the main cause of emboli and thrombi. Most emboli originate from heart, while thrombosis is largely due to the process of atherosclerosis. However, there is no less important other causes of thrombosis, that is the hypercoagulable state. Hypercoagulability is a common condition that occurs in malignancy. Manifestations of hypercoagulable state can be in both extremes, either bleeding or thrombosis. Presentation of coagulation abnormalities in leukemia, the thrombosis, is very rare. Thrombosis occuring in large blood vessels can be followed with impaired microvascular perfusion and vascular occlusion with ALI manifestation (Handa et al 2000, Callum & Bradbury 2000, Belizna et al 2009, Chang et al 2003). What can we do in leukemia patients with manifest-ations of ALI? The choice of therapy depends on the location, lesions degree and anatomic, long occlusion, type of blood clot, comorbidities and

risk of the surgical procedure. Intraarterial thrombolytic therapy is a viable alternative for the extremities. Thrombolytic therapy has extremely limited usefulness, depending on the degree, duration of ischemia as well as the length of time required to achieve the dissolution of thrombus. Moreover, it turns out that thrombolytic therapy is not a therapeutic option in ALI patients with leukemia. The threatened limb should be revascularized surgically. In nonviable extremity, the therapy of choice is amputation, but revascularization is still required to accelerate wound healing amputation or amputation on the lower level. Surgery, in this case is thrombectomy by Fogarty and PTA, can be performed in patients with ALI as a complementary therapy (Micthell et al 2008, Working Party on Thrombolysis in the Management of Limb Ischemia 2003, Gray et al 2008). We present a case of PTA therapy in leukemia patients with manifestations of ALI.

CASE REPORT

A 50-year-old woman presents with pain and weakness in left limb. About 2 weeks previously the patient felt a sudden weakness in the left limb along with pain. The pains is increasing, accompanied by tingling and left limb was numb. Then bluish color on the toes began to appear. The patient was suffering from diabetes since 10 years and leukemia since 2 years previously. The patient received therapy with Hidrea, Agrilin, glimepiride and fenofibrate.

The patient was presented with a fairly common condition, GCS 4-5-6, blood pressure 120/80, pulse 90x/m, respiratory 18x/min. Physical examination of the left inferior extremity pulses was not obtained in the popliteal artery and dorsalis pedis artery, touch was felt cold and there was bluish color on the tip of the toes. Laboratory results obtained Hb 13; 12590 leukocytes; Platelet 1004000; cholestrol 187; triglycerides 220; HDL 29.4; 99.8 LDL and others were within normal limits. Thoracic photo was within normal limits. Echo-cardiography was within normal limits. Arteriography was performed with results as high as 1/3 of total occlusion of the left distal superficial femoral artery and the presence of thrombus. Thrombus aspiration was attempted unsuccessfully (Figure 1).

The patient was consulted to Thorax and Cardiovascular Surgery for thrombectomy. Fogarty thrombectomy was done, obtaining thrombus with a length of 15 cm. One week later arteriography evaluation showed total distal occlusion as high as one third of the left superficial femoral artery and there are no distal run off. PTA was done with Plain Old Baloon Angioplasty (Poba) with balloon Powerline 2.5x20 mm, followed by a 4.5x8 mm Maverick balloon starting to 1/3 of left distal superficial femoral artery to the anterior tibial artery with distal run off to anterior tibial artery (Figure 2). Then we carried out the amputation of the left ankle.

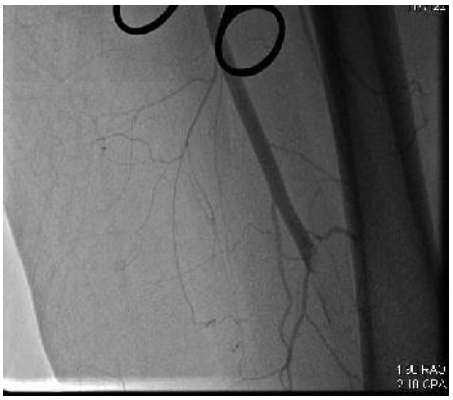

Figure 1. Total occlusion as high as 1/3 of the left distal superficial femoral artery, which is revealing thrombus.

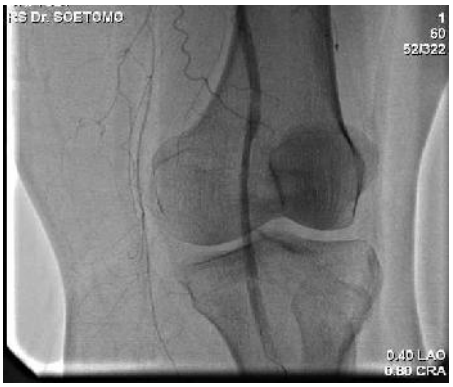

Figure 2. POBA was started 1/3 left distal superficial femoral artery to anterior tibial artery with distal run off up to tibialias anterior artery.

DISCUSSION

Based on Inter Society Consensus for the Management of Peripheral Arterial Disease, ALI is a condition where sudden decline is present in arterial blood flow in the extremities, usually accompanied by clinical symptoms and new or increased severity of existing sign and symptoms that endangers the viability of the affected extremity within a period of less than two weeks (Micthell et al 2008, Hirsch et al 2006).

Over the last 25 years there have been gradual changes in the ALI causes, thrombosis (60%) and embolism (30%). Thrombosis of narrowing blood vessels primarily due to atherosclerosis process is dominated

the cause of ALI. Medium embolism from blood vessels elsewhere. The severity of the ALI depends primarily on the location, the length of the obstruction and the presence of collateral vessels in the vicinity of the obstruction. ALI caused by embolism, thrombosis or both can cause obstruction (Micthell et al 2008, Handa et al 2000, Callum & Bradbury 2000).

Most embolism (80%) comes from heart (valves, mural thrombus) and 20% came from elsewhere (the aneurysm, atherosclerosis plaque). Most potential arterial embolism originates from thrombus in the left ventricle due to myocardial infarction and in the atrium due to atrial fibrillation by 75%. Emboli will head to the extremities, usually the lower extremities are more frequently affected than the upper ones. Parts that are often affected are femoral artery 28%, arm 20%, aortoiliac 18%, popliteal 17%, visceral and others 9%. Limb ischemia that occurs due to embolism is usually acute (Micthell et al 2008, Handa et al 2000, Callum & Bradbury 2000).

Arterial thrombosis occurs because previously there had been stenosis due to atherosclerosis. Stenosis occurs because of the mechanisms: (1) the progression of atherosclerosis itself that causes increased narrowing of arterial lumen so that blood flow becomes slow, static of blood flow, and thrombosis finally happens, (2) rupture of a plaque or local hypercoagulopathy. However, in arterial thrombosis, despite obstruction, usually there have been collateral blood vessels that can lighten the process of ischemia. Other thrombosis predisposing factors are dehydration, hypotension, malignancy, polycythemia or hypercoagulable state (Micthell et al 2008, Handa et al 2000, Callum & Bradbury 2000).

Hypercoagulability is a common condition that occurs in malignancy. Hypercoagulable state manifestations are in the form of two extreme circumstances ie bleeding to thrombosis. Leukemia is a malignancy involving hematological organ. As a result, complications of leukemia have blood clotting and fibrinolytic abnormalities with hemorrhagic manifestations until thrombosis. Hemorrhagic manifestations are more common than thrombosis. Extreme thrombosis in large blood vessels is a rare case. Therefore, caution should be increased by clinicians because thrombosis can also be a classic presentation of leukemia as blood disorders (Belizna et al 2009, Chang et al 2003).

When monocytes or macrophage interact with cancer cells, they will remove tumor necrosis factor, interleukin-1 and interleukin-6, causing endothelial damage and take off a layer of endothelial cells and alter vascular blood flow to a thrombogenic surface. The interaction between tumor cells and macrophages also activates platelets, factor XII and factor X, which plays a role in the formation of thrombin and thrombosis (Bick 2003, Heit 2005, Kalk et al 2003).

Malignant cells can activate coagulation via interaction with platelets or clotting and fibrinolysis system to form thrombin. The balance between coagulation and fibrinolysis system can shift into a prothrombotic state in malignancy, due to an increase in tissue factor (TF), procoagulant protein or plasminogen activator inhibitor (PAI-I) or molecule inhibitor deficiency (antithrombin, protein S, protein C) or fibrinolytic factors tissue plasminogen activator (T-PA) (Bick 2003, Heit 2005, Kalk et al 2003).

TF is a transmembrane protein that is expressed on the parenchyma and connective tissue of normal cells and malignant cells. Tumor cells express TF continuously. TF is the primary initiator of the extrinsic pathway of cellular blood coagulation system. TF procoagulant molecule expression in tumor cells have the ability to activate blood coagulation by systemic manifestations such as thromboembolism. TF acts on the surface of the receptor and the protease activating cofactor for coagulation factor (F) VIIa. TF and FVIIa complex activate coagulation protease cascade, leading to fibrin deposition and platelet activation (Bick 2003, Heit 2005, Kalk et al 2003).

In malignant tissue there is also cancer procoagulant (CP), a cysteine protease, which can directly activate FX into Xa, not depending on TF and FVIIa complex. Other CP, such as mucin that contain sialic acid, can also directly activates FX (Bick 2003, Heit 2005, Kalk et al 2003).

The incidence of thromboembolic episodes can occur in a variety of diseases both in periods of remission, during therapy or in patients who did not receive therapy. The hemopatic state itself, in combination with chemotherapy, leads to an increase of procoagulant activity and injury to the endothelium. Hyperviscosity syndrome is also common and can be followed microvascular perfusion and vascular occlusion disorders (Belizna et al 2009, Chang et al 2003, Kalk et al 2003).

The incidence of ischemia can occur in various types of leukemia and involving all the arteries. Clinical manifestations may include cerebral events, coronary or limb ischemia. Vascular lesions on the extremities are characterized by the presence in various degrees of limb ischemia caused by arterial thrombosis. Complications of arterial thrombosis in myeloproliferative disorders can occur in a mild increase of platelet count (Belizna et al 2009, Chang et al 2003, Kalk et al 2003).

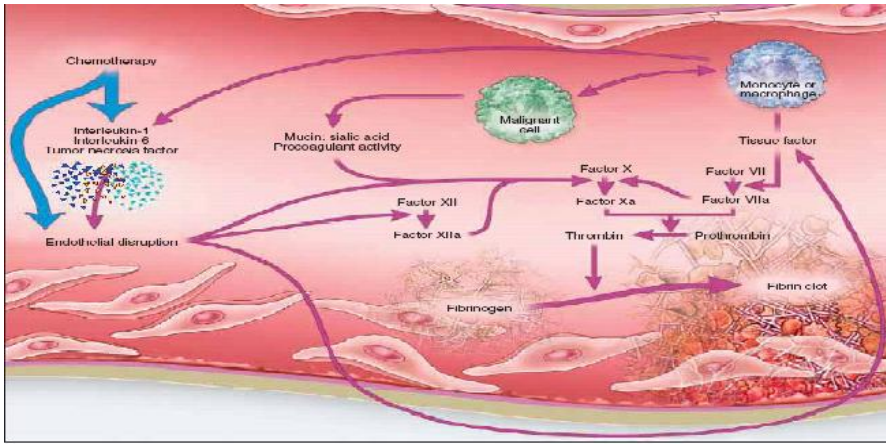

Figure 3. Mechanisms of thrombosis in cancer.

Markers often used for the ALI is 6P ie pain, paralysis, paresthesis, pallor, pulseless and poikhilotermi. Approximately 75% of ALI patients experience sudden pain and located on the site of occlusion, severe pain will increase along the course of ischemia process. Then the pain can decrease due to beginning of sensory nervous system destruction. In occlusion due to embolism usually the patient can say exactly when the pain occurs because it occurs suddenly, while the gradual increase in pain can be caused by a thrombus occlusion. Paresthesis is sensory loss in the form of tingling. Paralysis is the motor function disorders that shows advanced limb ischemia that threatens limb viability. This is related to the fact that the movement of the limbs is performed especially by proximal limb muscles. Pallor was discoloration in the extremities of the redness becomes cyanotic and bluish. Pulseless is a pulse deficit, by combining the extremity location decreased pulsation can be known location of occlusion of an artery with an accuracy approaching 90%. Poikilothermia is cold extremity because of occlusion (Micthell et al 2008, Hirsch et al 2006, Singh 2006). Classification of the severity of the ALI by the Society of Vascular Surgery/International Society of Cardiovascular Surgery can be used to determine the degree of severity and management of ALI (Hirsch et al 2006, Kasirajan & Ouriel 2002).

The degree of ischemia according to the above classification will determine the inspections to be carried out. Prior to heparinization, we carry out complete blood examination and testing of anticoagulation. Thorax and electrocardiogram should be performed in each ALI patient. When ALI is expected to cause embolism, echocardiography should be immediately performed. Nevertheless, ALI therapy should be a priority rather than examinations that take up time (Micthell et al 2008, Kasirajan & Ouriel 2002).

Table 1. Degree of ALI

Class	Category	Prognosis	Sensory Loss	Muscle Weakness	Arterial Doppler Signal	Venous oppler Signal
I	Viable	No immediate limb threat	None	None	Audible	Audible
IIA	Threatened: marginal	Salvageable if threated promply	Minimal-none	None	+ Audible	Audible
IIB	Threatened: immediate	Salvageable if threated immediately	More than just toes	Mild-moderate	Rare audible	Audible
III	Irreversible	Limb loss or permanent damage	Profound	Profound	None	None

Society of Vascular Surgery/International Society of Cardiovascular Surgery (SVS/ISCVS)

Currently clinicians have utilized vascular arteriography examination in patients with ALI. Arteriography may be used to determine subsequent therapy planning. This examination is very valuable to know the location of occlusion and can differentiate occlusion due to embolism or thrombus, because both have a similar profile. Arteriography is also helpful in determining whether a patient is better using percutaneous therapy or embolectomy therapy using embolectomy Fogarty catheter or open revascularization procedures. At arteriography sometimes we have problems with the induction of contrast media that can aggravate kidney damage. However, with the digital substraction angiography (DSA) this risk can be reduced and this angiography is still the gold standard for ALI examination (Kasirajan & Ouriel 2002).

The patient presented with pain and bluish on the fingers of the left foot with fatigue, tingling and numbness since 3 weeks prior to hospital admission. Past medical history revealed history of diabetes and leukemia. Physical examination of the left inferior extremity pulses was not obtained in the popliteal artery and dorsalis pedis, cold on palpation and a bluish color in the left toe. Arteriography performed with results as high as 1/3 of total occlusion of the distal superficial femoral artery thrombus left and obtained. The patient was diagnosed as having ALI.

In 1978, Blaisdell and his colleagues first introduced the concept heparinization to prevent thrombus propagation and prevent thrombosis distal to the arterial and venous system caused by slow flow and stasis. Time is critical, the decision to heparinization depends on clinical evaluation and diagnostic procedures should not wait to do. After heparinization, subsequent therapy depends on the degree of ALI (Kasirajan & Ouriel 2002, Clagett et al 2004).

ALI therapy duet to acute thrombosis resulting from leukemia is directed against basic diseases. Leukemia therapy includes therapeutic management of blood products, antibiotics and chemotherapy. ALI therapy itself, according to the Society of Vascular Surgery /International Society of Cardiovascular Surgery (SVS/ISCVS), depends on location, degree and anatomy of lesions, duration of occlusion, the type of blood clot, comorbidities and risk of the surgical procedure/ endovasculer, coupled with Doppler ultrasound examination. Grade I and IIA could subjected to endovascular/percutaneous revascularization or thrombolytic therapy, grade IIB to Fogarty embolectomy, early grade III to surgical thrombectomy while in grade III sometimes amputation is the treatment of choice (Micthell et al 2008, Hirsch et al 2006, Kasirajan & Ouriel 2002).

Intraarterial thrombolytic therapy is a viable alternative to the extremities. However, the usefulness of thrombolytic therapy is limited depending on the degree, duration of ischemia as well as the length of time required to achieve dissolution of thrombus. Moreover, thrombolytic therapy is not part of ALI therapy in patients with leukemia. For the threatened limb revascularization should be done surgically. The majority of patients experiencing events ALI embolism and irreversible changes may occur at least 4-6 hours after ischemia. Surgical embolectomy is required to liberate the blood vessels of occlusion and getting adequate blood flow to the extremities. When thrombolytic therapy is done it will accelerate the dissolution of thrombus but it takes a long time, so that thrombolytic therapy may be an alternative therapy in addition to surgery (Micthell et al 2008, Kasirajan & Ouriel 2002).

For nonviable extremity the therapeutic option is amputation. Revascularization is still needed to accelerate wound healing after amputation or amputation at lower level. Revascularization procedures should be adapted to the condition of the patient. Endovascular surgery can be performed on patients with ALI as a complementary therapy. Amputation level is determined clinically and tissue viability. Every effort is made to protect the joints as much as possible, thereby reducing the burden of walking with a prosthesis and to achieve rehabilitation success (Micthell et al 2008, Kasirajan & Ouriel 2002).

In the 1960s, balloon catheter thrombectomy was first introduced by Fogarty and his friends, became the first stone therapy for ALI. Interestingly, this marks the beginning of endovascular therapy which introduces the concept of less than open surgery for the treatment of arterial occlusive disease. Open surgical techniques to save the limb ischemia include: (1) balloon catheter thrombectomy; (2) shortcut procedure directly below the occlusion of blood vessels; (3) endarterectomy with or without angioplasty and (4) thrombolytic intra-operative (Clagett et al 2004).

Although the development of open surgical techniques have reduced the rate of loss of limb, but the mortality rate remains high. Patient survival rate has not changed dramatically since the report by Bleisdell and friends 20 years ago. High mortality rate is due to comorbid diseases that accompany ALI while the rate of extremity loss is due to unsuccessful revascularization procedures (Micthell et al 2008, Kasirajan & Ouriel 2002).

The search for a less invasive revascularization procedures continues to run with the goal of reducing morbidity without reducing limb safety figures that has been achieved with earlier procedures. Eliminating mechanical thrombus is the dream of the vascular interventionist. In addition to thrombolytic therapy, percutaneous mechanical thrombectomy (PMT) is a treatment option at this time. Both of these techniques can clean from peripheral arterial thrombus with less invasive procedures and facilitate blood flow to the extremities. The next procedure can be performed electively PTA or stenting. There are 4 PMT working principles, (1) clot aspiration; (2) hidrodynamic catheters; (3) mechanical clot destruction and (4) ultrasound (Kasirajan & Ouriel 2002, Vorwerk 2003).

Clot aspiration is a technique often used in everyday life. The advantage is easy to learn, cheap, fast and effective. This technique was introduced by Stark and his colleagues in 1980s and can be applied to embolism or thrombus. Clot aspiration is to remove artery occlusion in the aspiration by using a catheter directly into the proximal occlusion site, then performed manually aspiration with 50 cc syringe. This action is repeated until the occlusion is lost. Hydrodynamic catheter uses the ventury principle to remove thrombus. Saline is injected through the catheter opening at high speed and then at the end of the catheter will arise vortex. At the time vortex flow generated clot removes material through the lumen disposal. This system has been used by Angiojet® (Possis Medical, Minneapolis, MN), Hydrolyser® (Cordis Corporation, Miami, FL) and Oasis® (Boston Scientific, Natick, MA). Mechanical clot destruction uses two instruments, one to break the thrombus into small parts and one to remove the thrombus. This tool has been adapted by a Amplatz clot buster catheter and Rotarex catheter. High frequency ultrasound can remove thrombus to spur the process of thrombolysis splitting fibrin bonds. This tool has been adapted by Resolution® Ultrasonic Endovascular Ablation System (OmniSonic Medical Technology, Inc., Wilmington, MA) and Acolysis® (Vascular Solutions, Inc., Minneapolis, MN) (Kasirajan & Ouriel 2002, Vorwerk 2003).

Angioplasty is derived from the word *angio* meaning blood vessels and *plasticos* means printing. Angioplasty means changes mechanically the narrowed or clogged blood vessels lumen. PTA is used to describe blood vessels other than angioplasty in the coronary arteries. An expert on Vascular Radiology, Charles Dotter introduced transluminal angioplasty in 1964. Then Andreas Gruenzig perform PTA in human peripheral arteries for the first time in 1974. After that there is a change in surgical approach to patients with limb ischemia, because the PTA considered successful as well as the surgical complication rate, morbidity and shorter hospitalization time (Jeans et al 1990, Collins & McMullan 2008).

PTA is a procedure by inserting a catheter into the artery through the groin, arm or hand. Mechanism of action of PTA in the lumen of the blood vessel is by using centrifugal pressure. The strength of this pressure comes from a balloon inserted percutaneously and pumped in the target area. Strength move radially to outward direction, referred to as hoop stress, will stretch or separate lumen of blood vessel walls. Hoop stress can be described by the Laplace law as follows: (Collins & McMullan 2008).

Hoop stress = Pressure x Diameter

PTA angiography performed in the laboratory using fluoroscopic visualization and cine-angiographic. With the Seldinger technique venous or arterial access is done followed by the installation of a sheath. Access the superficial femoral artery (SFA) and popliteal arteries can be achieved through the contralateral femoral artery. Through this sheath, a catheter with a specific shape and size can be entered with a guide wire. Then the catheter is inserted into the artery through the experience occlusion, contrast injection into the blood vessels proficiency level while do some photo X ray to determine visually artery occlusion (Collins & McMullan 2008).

Lesions that are simple to use balloon insertion – was straight floppy-tipped stiff wire. More complex lesions or total occlusions as a preliminary step used suport 4 French catheter (JR4, MP, IMA), then use the angled hydrophilic wire 0.035 inch in size. Sometimes wire with a smaller size 0.014 to 0.018 inch is used to pass the lesion. Furthermore, the balloon is inserted through a catheter to place the occlusion, the balloon further developed and flattened several times until the pressure arterial plaque and artery back width and flow improved. Balloon with 4-6 mm size are often used for femoropopliteal lesions. If the residual stenosis after PTA obtained, then the indication is done stenting. Once the balloon was withdrawn to be replaced stent is inserted through a catheter into the blood vessel has been opened, the balloon stent developed, the balloon was then pulled back so that the stent stays in the artery as a buffer and arteries around the stent will improve (Collins & McMullan 2008).

Thrombectomy revascularization performed by Fogarty obtained thrombus length of 15 cm. Arteriography evaluation obtained the same results as high as one third that total occlusion distal superficial femoral artery left. Performed PTA decided to lower the level of

amputation with Poba with balloons Powerline 2.5x20 mm, followed by a 4.5x8 mm Maverick balloon began to 1/3 distal superficial femoral artery to the left anterior tibial artery with distal run off to the anterior tibial artery.

REFERENCES

Belizna C, Pistorius MA, Planchon B (2009). Lethal limb ischaemia in leukaemia. Case report and review of the literature. J Thromb Thrombolysis 28, 354-357

Bick RL (2003). Cancer-associated thrombosis. N Engl J Med 349, 109-111

Callum K and Bradbury A (2000). Acute limb ischaemia. BMJ 320, 764–767

Chang VT, Aviv H, Howard LM, Padberg F (2003). Acute myelogenous leukemia associated with extreme symptomatic thrombocytosis and chromosome 3q translocation: case report and review of literature. Am J Hematol 72, 20-26

Clagett GP, Sobel M, Jackson MR, Lip GY, Tangelder M, Verhaeghe R (2004). Antithrombotic therapy in peripheral arterial occlusive disease: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 126, 609S-626S

Collins T and McMullan PW (2008). Percutaneous transluminal angioplasty. In: Heuser RR and Henry M (eds). Textbook of Peripheral Vascular Intervention, 2nd ed. Boca Raton, CRC Press, p 39-44

Gray BH, Conte MS, Dake MD, Jaff MR, Kandarpa K, Ramee SR, Rundback J, Waksman R (2008). Atherosclerotic Peripheral Vascular Disease Symposium II: lower-extremity revascularization: state of the art. Circulation 118, 2864-2872

Handa A, Turner K, Jones A (2000). Surgical emergency: acute limb ischaemia. BMJ 8, 217-258

Heit JA (2005). Cancer and venous thromboembolism: scope of the problem. Cancer Control 12, 5-10

Hirsch AT, Haskal ZJ, Hertzer NR, Bakal CW, Creager MA, Halperin JL, Hiratzka LF, Murphy WRC, Olin JW, Puschett JB, Rosenfield KA, Sacks D, Stanley JC, Taylor LM, White CJ, White J, White RA (2006). ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic). Circulation 113, e463-e654

Jeans WD, Armstrong S, Cole SE, Horrocks M, Baird RN (1990). Fate of patients undergoing transluminal angioplasty for lower-limb ischemia. Radiology 177, 559-564

Kalk E, Goede A, Rose P (2003). Acute arterial thrombosis in acute promyelocytic leukaemia. Clin Lab Haematol 25, 267-270

Kasirajan K and Ouriel K (2002). Current options in the diagnosis and management of acute limb ischemia. Prog Cardiovasc Nurs 17, 26-34

Libby P, Bonow RO, Mann DL, Zipes DP (2008). Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 8th ed, Philadelphia, Saunders, p 1491-1511

Micthell ME, Mohler ER, Carpenter JP (2008). Overview of Acute Arterial Occlusion of the Extremities (Acute Limb Ischemia). Available from http://www.uptodate.com/contents/overview-of-acute-arterial-occlusion-of-the-extremities-acute-limb-ischemia. Accessed September 13, 2010

Rajan DK, Patel NH, Valji K, Cardella JF, Bakal C, Brown D, Brountzos E, Clark TW, Grassi C, Meranze S, Miller D, Neithamer C, Rholl K, Roberts A, Schwartzberg M, Swan T, Thorpe P, Towbin R, Sacks D (2005). Quality improvement guidelines for percutaneous management of acute limb ischemia. J Vasc Interv Radiol 16, 585-595

Singh D (2006). Management of peripheral arterial disease: an overview. The Internet Journal of Surgery 8

Vorwerk D (2003). Mechanical thrombectomy in acute and subacute limb ischemia. Acta Chir Belg 103, 548-554

Working Party on Thrombolysis in the Management of Limb Ischemia (2003). Thrombolysis in the management of lower limb peripheral arterial occlusion--a consensus document. J Vasc Interv Radiol 14, S337-S349