

Bilateral Acute Limb Ischemia due to Severe Rheumatic Mitral Stenosis and Atrial Fibrillation with Neglected International Normalized Ratio Control

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SOUHRN

Akutní končetinová ischemie (acute limb ischemia, ALI) představuje zásadní hrozbu pro životaschopnost končetin vyžadující urgentní revaskularizační intervence. V této kazuistice popisujeme případ 47leté Asiatky s bilaterální ALI v důsledku těžké mitrální stenózy (MS) revmatické etiologie a fibrilace síní (FS) se zanedbanou úpravou mezinárodního normalizačního poměru (INR). Pacientka byla přivezena do nemocnice s náhlou klidovou bolestí obou dolních končetin, již namodralých a naprosto bez citu. Echokardiografické vyšetření prokázalo těžkou MS revmatické etiologie spolu s trombem v oušku levé síně. CT angiogram odhalil téměř úplně obturující trombus v místě odstupu horní břišní aorty. Okamžitě byla provedena bilaterální tromboembolektomie, po níž došlo ke zlepšení stavu, a pacientka byla nakonec propuštěna z nemocnice ve stabilizovaném stavu. Pro optimální výsledek v případech ALI zahrnujících současně MS a FS jsou absolutně nezbytné vhodná antikoagulační terapie, důsledné monitorování INR a použití vhodné strategie k náhradě chlopně.

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ABSTRACT

Acute limb ischemia (ALI) poses a critical threat to limb viability, necessitating urgent revascularization interventions. This case report discusses a 47-year-old Asian woman with bilateral ALI due to severe rheumatic mitral stenosis (MS) and atrial fibrillation (AF), with neglected international normalized ratio (INR) control. The patient presented with sudden bilateral leg pain at rest, accompanied by bluish discoloration and sensory loss. Echocardiographic findings indicated severe rheumatic MS along with a thrombus in the left atrial appendage. The computed tomography angiogram revealed a near-total thrombus originating from the upper abdominal aorta. Immediate bilateral thromboembolectomy was performed. Subsequent improvements were observed, and the patient was eventually discharged in stable condition. Proper anticoagulant therapy, vigilant INR monitoring, and a strategic approach to valve replacement are crucial for optimizing outcomes in cases of ALI involving concurrent MS and AF.

Keywords:

Acute limb ischemia

Atrial fibrillation

International normalized ratio

Rheumatic mitral stenosis

Introduction

Acute limb ischemia (ALI) is an emergency vascular condition capable of threatening limb viability.¹postrandomization ALI hospitalization. Baseline factors associated with ALI were identified using Cox proportional hazards modeling. Models with ALI hospitalization as a time-dependent covariate were developed for secondary outcomes of major adverse cardiovascular events (myocardial infarction, cardiovascular death, ischemic stroke This phenomenon arises due to the insufficient timeframe for the establishment of compensatory neovascularization sub-

sequent to the abrupt cessation of blood supply.² Urgent revascularization interventions are crucial to maintain the viability of the limb.

The etiology of ALI is predominantly attributed to arterial occlusion resulting from thrombosis of an existing diseased artery (40%) and arterial embolism (30%).² The coexistence of mitral stenosis (MS) with atrial fibrillation (AF) increases the risk of cardiac embolization.³ Inadequate achievement of the recommended international normalized ratio (INR) through the utilization of oral anticoagulant (OAC) potentially predisposes to thromboembolic events, such as acute limb ischemia. In this report,

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we present a case of bilateral acute limb ischemia secondary to severe rheumatic mitral stenosis and atrial fibrillation due to neglected INR control. Written consent was obtained from the patient before collecting her medical information.

Case description

A 47-year-old Asian woman was referred from a rural hospital due to the sudden onset of bilateral leg pain at rest that had been experienced for 3 days prior to admission. The complaint was accompanied by tingling sensations and sensory loss extending up to the ankles. No motor disturbances were observed. Bluish discoloration extended up to the ankles on both legs, with no evidence of tissue loss (Fig. 1). As initial therapy, the referring hospital administered a bolus of 5,000 units of unfractionated heparin (UFH), followed by a continuous infusion of 1,000 units per hour, and 30 mg of ketorolac injection every 8 hours.

The patient has a history of severe mitral stenosis accompanied by atrial fibrillation, which was only diagnosed in the last 3 months. Since then, the patient has been regularly taking 2 mg of warfarin once a day, 2.5 mg of bisoprolol once a day, and 40 mg of furosemide *pro re nata*. There is no record of INR measurements during warfarin treatment, and dose titration of warfarin has never been performed.

The patient is fully conscious with a blood pressure of 124/84 mmHg, a heart rate of 94 beats per minute irregularly, a respiratory rate of 18 breaths per minute, and a body temperature of 36.7 °C. A Grade II/IV diastolic murmur was audible at the cardiac apex. Pulse in the femoral artery extending to the dorsalis pedis artery of both lower limbs was not palpable. Both legs from the ankles downward felt cold. The pulse oximetry device was unable to detect oxygen saturation in the digits of both feet.

The electrocardiogram exhibited atrial fibrillation. The chest X-ray disclosed cardiomegaly with a dual atrial contour. The laboratory assessment revealed an out-of-range



Fig. 1 – Bluish discoloration extended up to the ankles on both legs, with no evidence of tissue loss.

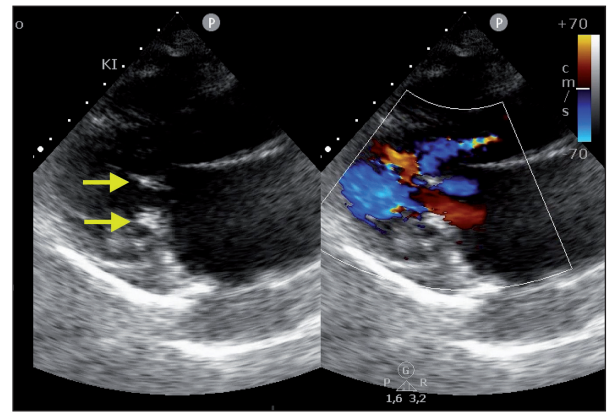


Fig. 2A – Transthoracic echocardiography in the parasternal long-axis view showed calcified anterior and posterior mitral leaflets (arrow).

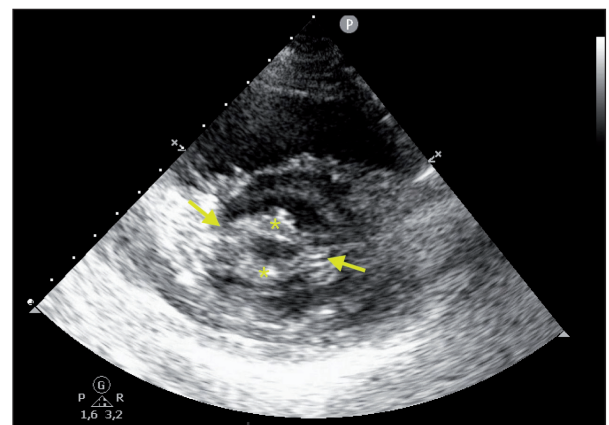


Fig. 2B – Transthoracic echocardiography in the parasternal short-axis view showed calcified and thickened anterior and posterior mitral leaflets (asterisk) with commissural fusion (arrow).

INR of 1.7. Transthoracic echocardiography displayed thickened mitral leaflets with commissural fusion, indicative of severe rheumatic mitral stenosis (mitral valve area planimetry 1.15 cm) (Figs 2A and 2B). There was a mild mitral regurgitation, as well as aortic and tricuspid regurgitation, coupled with left atrial (LA) dilation. Both normal left ventricle systolic function (ejection fraction of 68%) and normal right ventricle systolic function were observed. Doppler ultrasound was conducted, detecting a thrombus without flow in the right common femoral artery (Figs 3A and 3B). Meanwhile, the left common femoral artery exhibited slow flow. Subsequent to these findings and due to suspicions of a thrombus extending to the abdominal aorta, an immediate computed tomography angiogram (CTA) was performed. The CTA revealed a near-total thrombus originating from the upper abdominal aorta at the level of the 3rd lumbar vertebrae, with a distance of 2.6 cm from the bifurcation (Fig. 4). Furthermore, near-total thrombi were observed in the right common iliac artery (approximately 5.0 cm in length), the right external iliac artery (approximately 13.8 cm in length), the right internal iliac artery (approximately 4.2 cm in length), and the left common iliac artery (approximately 2.6 cm in length).

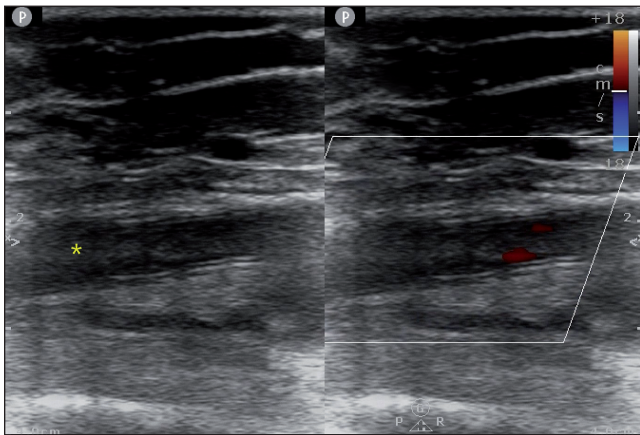


Fig. 3A – Doppler ultrasound of the right common femoral artery showed thrombus (asterisk) without flow.

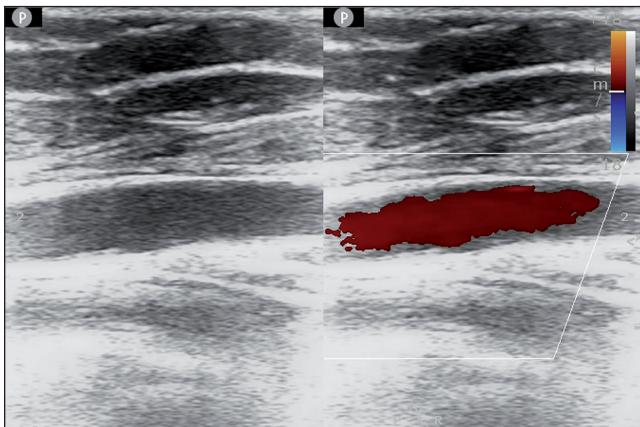


Fig. 3B – Doppler ultrasound of the left common femoral artery showed slow flow.

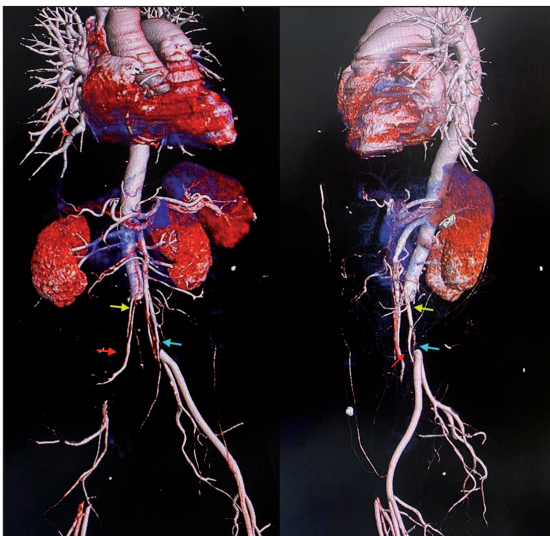


Fig. 4 – The computed tomography in the front view (left panel) and lateral view (right panel) revealed a near-total thrombus originating from the upper abdominal aorta at the level of the 3rd lumbar vertebrae with a distance of 2.6 cm from the bifurcation (yellow arrow), while nearly complete thrombi were observed in the right common iliac artery (red arrow), encompassing the right external iliac artery and the right internal iliac artery, as well as in the left common iliac artery (blue arrow).

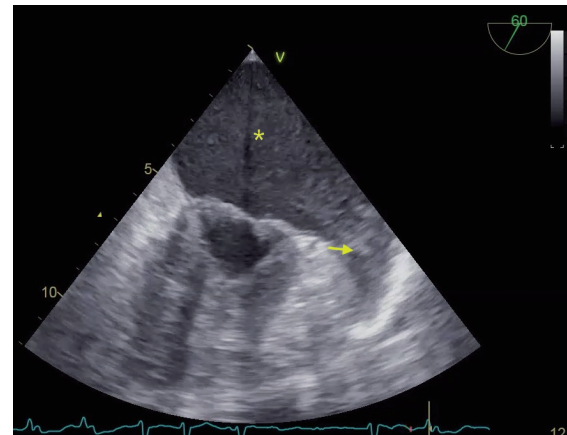


Fig. 5 – Transesophageal echocardiography revealed the presence of a thrombus within the left atrial appendage (arrow) along with spontaneous echocontrast in the left atrium (asterisk).

The patient was diagnosed with Rutherford grade IIb ALI. Subsequently, urgent bilateral thromboembolectomy was performed, followed by the initiation of warfarin bridged with heparin. After the surgery, the patient underwent a 5-day rehabilitation period and demonstrated improvements in both legs. The patient could ambulate without pain or tingling sensations. Both legs were warm to touch with no sensory loss. Peripheral pulse oximetry readings showed 98% in both extremities.

A day prior to discharge, transesophageal echocardiography was conducted, revealing calcification and thickening of the anterior and posterior mitral leaflets with severe mitral stenosis, accompanied by mild mitral regurgitation, mild aortic regurgitation, and mild tricuspid regurgitation. A 3.1×1.9 cm thrombus was detected in the left atrial appendage, accompanied by LA spontaneous echocontrast (Fig. 5). On the 8th day of treatment, the patient was discharged in good condition, without complaints, with an INR of 2.4 on warfarin. Subsequently, the patient received regular follow-up care at our hospital's outpatient clinic. The next step in the management plan is mitral valve replacement; however, the patient is still unwilling to undergo the valve replacement surgery.

Discussion

Acute limb ischemia is characterized by a sudden decrease in perfusion to the limb.⁴ This condition can lead to nerve, muscle, and skin damage, with amputation rates ranging from 10–15%.² Immediate revascularization is necessary to preserve limb viability.

In the observed case, there was extensive thrombosis affecting the abdominal aorta, right common iliac, right internal and external iliac arteries, as well as the left common iliac artery. The occurrence was suspected to be a result of embolism inducing vascular stasis (Virchow's triad) and inflammatory reactions, consequently initiating subsequent thrombotic processes.^{5,6} Evaluation of hypercoagulable conditions, such as thrombophilia screening, may be considered.^{6,7}

The initial management that can be undertaken includes providing adequate analgesia and the intravenous

administration of UFH.^{4,8} The UFH is administered as an intravenous bolus of 70–100 international units per kilogram of body weight, followed by an infusion with a dosage adjusted according to the patient's response.⁸ Activated partial thromboplastin time should be monitored during the administration of UFH. ALI patients in non-vascular centers should be promptly transferred to a vascular center to facilitate revascularization procedures.

Revascularization strategies can take the form of either endovascular or surgical approaches.^{2,8} Endovascular techniques that can be performed include catheter-directed thrombolysis (for Rutherford grade IIa ALI), percutaneous thromboaspiration (with or without thrombolysis), and percutaneous mechanical thrombectomy.^{2,4,8} Thrombolysis typically requires time, and the ischemic process continues during thrombolysis, making it not indicated for Rutherford grade IIb ALI.⁸ Percutaneous mechanical thrombectomy is indicated for Rutherford grade IIb due to its shorter reperfusion time compared to catheter-directed thrombolysis.² Surgery is recommended for patients with thromboembolism, Rutherford IIb, non-viable limbs, or those who are not candidates for thrombolysis.^{2,8} Surgical interventions may involve thrombectomy using a balloon catheter (Fogarty) or bypass surgery.

The coexistence of mitral stenosis (MS) and atrial fibrillation (AF) increases the risk of thromboembolic events.^{3,9} Transesophageal echocardiography should be performed after an embolic episode.¹⁰ Oral anticoagulant (OAC) is necessary to prevent thromboembolism. Monotherapy with oral anticoagulant is recommended for post-surgery ALI patients requiring long-term oral anticoagulation.⁴ In patients with rheumatic mitral stenosis and atrial fibrillation / a history of previous emboli / thrombus in the left atrium, anticoagulation with vitamin K antagonists (VKAs) is recommended.³ The use of non-vitamin K antagonist oral anticoagulants is not recommended in patients with AF and moderate to severe mitral stenosis.¹⁰

Warfarin (VKA) is a commonly used oral anticoagulant. The use of VKA requires monitoring through the measurement of INR. The target INR that should be achieved with VKA usage is between 2 and 3 to prevent both thromboembolic events and bleeding incidents.¹⁰ INR values below the target range place the patient at risk of thromboembolism, while excessively high INR values can elevate the risk of bleeding. INR values exceeding 4.5 pose a significant risk of bleeding.¹¹ The 2012 guidelines of the American College of Chest Physicians discourage administration of vitamin K. At the study hospital, it was observed that vitamin K was frequently prescribed for patients with INR of 4.5 or higher and no bleeding. Objectives: To compare efficacy and safety outcomes between holding warfarin alone and holding warfarin with administration of vitamin K and to compare these outcomes among various doses and routes of vitamin K administration in non-critical care inpatients experiencing supratherapeutic INR without evidence of bleeding. Methods: This single-centre retrospective chart review involved non-critical care inpatients with supratherapeutic INR (4.5–8.9

Mitral valve replacement surgery is the established management for patients with severe rheumatic mitral stenosis who are not suitable candidates for percutaneous mitral commissurotomy.¹⁰ The presence of severe

valvular thickening and subvalvular fibrosis with leaflet tethering necessitates mitral valve replacement as the preferred therapeutic option.³ Bioprosthetic valves can be considered for patients with limited access for INR monitoring or an inability to regulate VKA.³ In our case, the patient was not willing to undergo valve replacement surgery. Patients in such a condition are at a high risk of recurrent thromboembolic events. Hence, it is crucial to consistently motivate the patient to undergo mitral valve replacement during each outpatient visit.

Conclusions

Acute limb ischemia can occur as a secondary result of coexisting rheumatic mitral stenosis and atrial fibrillation with poorly controlled INR. Proper anticoagulant therapy, INR monitoring, and valve replacement strategy are crucial for optimizing outcomes in ALI cases involving MS and AF.

Conflict of interest

No conflicts of interest were disclosed.

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