A 36-year-old man with concomitant left ventricular apical thrombus and bilateral acute lower limb ischaemia: Is it only the heart to blame?

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Presentation of case

Dr. Isaac Ssinabulya: We share the story of a 36 year old black man who was previously healthy and worked for an electricity distribution company as a meter reader. This required him to ride long distances on a motor cycle which he did comfortably. In early October 2016, he developed 'abdominal pain' which required admission and was treated as peptic ulcer disease. There were no other associated symptoms. The pain resolved and he returned to work feeling a perfect health condition. 1 week later while carrying out his field work he felt very dizzy and decided to ride to the nearest health centre. On the way, he felt sudden severe burning pain in both his legs below the knees. He persisted riding his bike and reached the health centre approximately 30 minutes from the onset of this burning pain, from where he was referred to a regional referral hospital, where he arrived 4 hours later. At this hospital he was initially given pain killers as the medical team carried out investigations to find out the cause of his ‘burning legs’. On the 2nd day in this hospital, the patient noted that both legs were getting cold and turning dark, were losing sensation in the toes and the pain was still ongoing in the calves. An arterial doppler study was performed which suggested arterial occlusion in both legs. The patient was referred to a private hospital in Kampala, Uganda’s capital where he arrived in the early morning hours of the following day.

Tests done at this hospital in Kampala included blood tests (Table 1), an ECG and an echocardiogram. A CT angiogram of the abdomen and lower limbs was done at another hospital within Kampala and the images are shown in figures 1A and 1B. He was referred to vascular surgeons at our hospital for possible surgical embolectomy.

This 36 year old with a body mass index of 29.7 at admission and a current smoker with 9.6 pack years denied any history of chest pain or discomfort, difficulty in breathing or easy fatigability. He was reportedly completely healthy with no significant past medical history. He denied use of cocaine, cannabis, anabolic steroids or any other illicit substances. There was no prior history of skin rashes or arthritis to suggest a rheumatologic disorder. He did not have any history of leg claudication.

When he arrived at our hospital, he was a young man in a lot of pain. His temperature was 36.0°C, BP 105/62 mmHg, PR 98bpm and regular, and SPO2 95% while breathing room air. The lungs were clear to auscultation. The cardiac point of maximal impulse was displaced to the 6th inter-costal space in the mid-clavicular line, heart sounds 1 & 2 were heard and normal, there was a soft S3 gallop and a grade 2 murmur of mitral regurgitation. The abdomen was soft, non tender, moving with respiration and with no organ enlargement. Both lower

Table 1. Laboratory test results performed at the first hospital in Kampala.

| Test                      | 3rd November 2016 | NR          |
|---------------------------|-------------------|-------------|
| Fasting Blood sugar       | 6.2mmol/L         | (3.6-6.9)   |
| Total Cholesterol         | 320mg/dl          | (120-240)   |
| Triglycerides             | 135mg/dl          | (55-150)    |
| HDL                       | 91mg/dl           | (35-65)     |
| Creatinine                | 1.1mg/dl          | (0.7-1.3)   |
| Urea                      | 34.2mg/dl         | (18-55)     |
| Na⁺                       | 139.1mmol/L       | (135-155)   |
| K⁺                        | 4.63mmol/L        | (3.5-5.5)   |
| D-Dimers                  | <10,000ng/ml      | (0-500)     |

NR: Normal Range values; Na⁺: Sodium; K⁺: Potassium

Figure 1. A. CT-Angiogram of the abdomen and lower limbs, anteroposterior view. B. CT-Angiogram of the abdomen and lower limbs, lateral view.

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limbs appeared to have a dark discoloration, were cold below the knees, swollen with pitting oedema to mid shins and had an extremely delayed capillary refill. The calf muscles were excruciatingly tender. The dorsalis pedis and posterior tibialis pulses could not be appreciated by palpation on both sides. The popliteal pulses were difficult to examine due to the tenderness. There was loss of sensation in both feet to above the ankles. There was no hair loss, skin atrophy or thickened nails on both legs. An ECG (Figure 2) and ECHO (Figure 3) were performed and blood tests were taken (Table 2). The immediate working diagnoses were:

1. Bilateral acute lower limb ischemia of cardioembolic etiology

2. Recent myocardial infarction, dilated ischaemic cardiomyopathy with moderate left ventricular systolic dysfunction and a large left ventricular apical thrombus

The acute limb ischemia was graded as ‘threatened’ (Table 3) in both limbs. A heparin bolus was immediately administered and an infusion was started, targeting an activated partial thromboplastin time of 80-100 seconds. The patient was taken to the operating room (OR) for urgent revascularization by surgical thromboembolectomy. On the first post-operative day, the patient complained of mild pain in the left thigh. The right foot was warm with a strong, palpable dorsalis pedis artery, no sensation over dorsum but some sensation over the plantar and medial aspects. The left foot remained cool with no palpable pulses and no sensation. A firm decision was made on the 5th post operative day to perform an above knee amputation of the left leg as most of the anterior and lateral fascial compartments of the leg were necrotic and their debridement had exposed the tibia and fibula bones. He continued to have serial debridements and dressings of the right leg fasciotomy wounds. The extensor digitorum muscle became necrotic and was debrided, exposing the lateral sides of the lower 1/3 of tibia and

![Figure 2. ECG performed on arrival at our hospital, 4 days after onset of the leg pain.](image)

![Figure 3. 2-chamber trans-thoracic echocardiographic view showing the left atrium (LA), left ventricle (LV) and a large thrombus (yellow arrows) in the apex of the left ventricle.](image)

**Table 2. Some of the laboratory tests performed at our hospital.**

| Test (Normal Range) | 4/Nov | 7/Nov | 10/Nov | 14/Nov | 25/Nov | 28/Nov | 01/Dec | 05/Dec | 14/Dec |
|---------------------|-------|-------|--------|--------|--------|--------|--------|--------|--------|
| HBA1c (<5.7%)       |       |       |        | 5.2%   |        |        |        |        |        |
| Total Cholesterol  | 3.7-5.2 mmol/L | 5.0   |        |        |        |        |        |        |        |
| Triglycerides      | 0.1-2.3 mmol/L | 3.43  |        |        |        |        |        |        |        |
| HDL (0.9-1.45mmol/L) | 0.11  |        |        |        |        |        |        |        |        |
| LDL (0-2.59mmol/L)  | 1.29  |        |        |        |        |        |        |        |        |
| Creatinine         | (44-106 μmol/L) | 127.4 | 167.9  |        | 228.6  | 137.3  | 89.1   |        |        |
| BUN (8-21mg/dl)    | 24    | 37.5  |        | 23.4   | 8.7    | 8.4    |        |        |        |
| Na+ (135-145 mmol/L) | 141.4 |      |        | 135    | 136    | 138    |        |        |        |
| K+ (3.5-5.0 mmol/L) | 4.9   |        |        | 2.9    | 2.8    | 3.6    |        |        |        |
| Total WBC (4-10 x 10^9/L) | 12.8 | 11.92 | 17.61 | 16.15 | 10.7 | 7.52 | 6.46 | 6.7 |
| ANC (2.0-7.5 x 10^5/L) | 8.69 | 8.84 | 13.46 | 13.44 | 5.97 | 3.62 | 3.89 | 3.7 |
| Hb (13-17g/dl)     | 14.8  | 11.9  | 8.8    | 7.6    | 6.0   | 6.9   | 9.8   | 9.9   |
| Platelets (150-400 x 10^9/L) | 204 | 177 | 372 | 493 | 494 | 440 | 322 | 343 |
| CK-MB (0-25U/L)    | 694   |       |        |        | 13.3  |        |        |        |        |
| Troponin I (<0.4ng/ml) | 1.48 | <0.1 |        |        |        |        |        |        |
| INR (0.9-1.2)      |       | 1.08  | 2.68   |        |        |        |        |        |        |
| Anti-HIV & 2       | Neg.  |        |        |        |        |        |        |        |        |
| Blood Group        | O+    |        |        |        |        |        |        |        |        |

BUN: Blood Urea Nitrogen; Na+: Sodium; K+: Potassium; WBC: White Blood Cell Count; ANC: Absolute Neutrophil Count; Hb: Haemoglobin; INR: Internatioal Normalised Ratio; HIV: Human Immunodeficiency Virus
fibula bones, devoid of periosteum.

This patient’s complexity of cardiovascular pathology required a multimodality approach involving vascular surgeons, cardiologists, radiologists, hematologists and critical care specialists to provide the moment-to-moment care of a young patient with a fragile baseline medical state. We now get the attending clinicians to discuss this case.

Let us review the patient’s history

Dr. James Kayima: This 36 year old male had traditional risk factors for cardiovascular disease including smoking [1-3], very low HDL [4], male sex [5-7] and a family of cardiovascular disease [8]. It is not clear from the history when the heart attack happened, because our patient does not remember having chest pain or discomfort. We suspect that the abdominal pain that this patient experienced in the 2 weeks preceding the leg pains was related to myocardial ischaemia. Otherwise until the ECG, cardiac markers and ECHO were performed, there was not a strong history to suggest chronic cardiac ischemia or an acute coronary syndrome. The sudden onset of the lower limb pain points to an embolic occlusion of the arteries rather than in-situ thrombosis. We also have to note the family history of thrombotic events (Figure 4): an elder brother with unprovoked pulmonary embolism, a father who died of an acute coronary syndrome. The sudden onset of the lower limb pain points to an embolic occlusion of the arteries rather than in-situ thrombosis.

Table 3. Classification of acute limb ischaemia.

| Category of Limb Viability | Viable | Threatened | Non Viable |
|---------------------------|--------|------------|------------|
| Pain                      | Mild    | Severe     | Variable   |
| Capillary Refill          | Intact  | Delayed    | Absent     |
| Motor Deficit             | None    | Partial    | Complete   |
| Sensory Deficit           | None    | Partial    | Complete   |
| Arterial Doppler Signals  | Audible | Inaudible  | Inaudible  |
| Venous Doppler Signals    | Audible | Inaudible  | Inaudible  |
| Treatment                 | Urgent Work-Up | Emergency Surgery | Amputation |

The patient's family tree.

Dr. Emmy Okello: Although the history was not typical, the ECG, ECHO and cardiac marker results lead us to a diagnosis of a recent myocardial infarction. The unclear timing of the onset undermined decisions for primary reperfusion strategies. The patient had a soft S3 gallop but was not dyspnoeic, his lungs were clear to auscultation and he was maintaining a normal blood pressure, putting him in Killip Class 2 [13]. This was in the setting of bilateral acute limb ischaemia, which we considered a bigger threat to his life at this time. We therefore settled for conservative management of this patient’s ischaemic dilated cardiomyopathy. We initiated morphone, a heparin drip, a beta blocker, an angiotensin converting enzyme inhibitor and a statin. We did not initiate an antplatelet because of the planned surgery. At this time, we stipulated the mechanism for this patient’s myocardial infarction to be either underlying coronary atherosclerotic plaque in relation to the identified atherosclerosis risk factors or non atherosclerotic mechanisms of myocardial infarction, including coagulation disorders among others [14]. Left ventricular thrombosis is a recognized complication especially of anterior wall myocardial infarction due to the large area of poorly contracting ventricular muscle with subsequent sluggish adjacent intracavitary blood movement [10-12]. At a later date when the acute limb ischaemia issues were settling down and the patient was out of danger, we performed a diagnostic coronary angiogram which Dr. James Kayima will discuss.

Review of the coronary angiogram

Dr. James Kayima: This was performed on the 42nd day at our hospital. We used the radial approach for this diagnostic coronary angiogram. Figures 5A, 5B and 5C are some of the coronary angiographic views that we took. We found a codominant coronary system with a large caliber left main coronary artery (LMCA) that...
of disease. The distal RCA collateralized the LAD territory, suggesting that there had been chronic ischaemia in the LAD territory that allowed time for development of collaterals. This severe LAD disease was in keeping with the ECG findings of an extensive anterior wall myocardial infarction. We settled for medical management of this patient’s ischaemic heart disease. The identifiable risk factors for this aggressive coronary artery disease at 36 years of age are the smoking history, a very low HDL level, male sex and the family history of cardiovascular disease. We have not had opportunity to test for any of the newer and emerging cardiovascular risk factors.

And now to the lower limbs, a discussion of the history and physical examination

Mr. Michael Oketch: Although this patient’s 9.6 pack years history of smoking would put him at risk of atherosclerosis, he did not have history of intermittent claudication, thigh or gluteal pain on exertion to suggest a process of chronic limb ischemia. The sudden onset of the leg pain suggests an acute embolic cause of the arterial obstruction as opposed to in-situ vascular thrombosis. We received him at our hospital 4 days after the onset of the leg pain. Both limbs were graded as ‘threatened’ (Table 3) with rest pain and moderate sensory and motor dysfunction.

Review of the abdominal and peripheral angiogram

Mr. Tom Mwambu: A contrasted axial CT scan of the abdomen and lower limbs with coronal, sagittal and 3D reformats was performed (Figures 1A and 1B). There were no abnormalities in the abdomen and bones. The aorta, truncus coeliacus, superior and inferior mesenteric and renal arteries were normal. On the left side, there was occlusion of the external iliac artery distal to its origin and occlusion of the superficial femoral artery at its origin. On the right, there was occlusion of the internal iliac artery at its origin and occlusion of the superficial femoral artery at its origin. There was a small rim of contrast visible in the deep femoral arteries and in the popliteal arteries on both sides but complete occlusion of the bilateral calf vessels. These findings pointed to severe arterial occlusive disease involving nearly the entire lower extremities with normal upper abdominal arterial patency. There was no evidence of atherosclerosis or collateral circulation on this arteriogram.

Thromboembolectomy procedure

Mr. William Manyilarah: The classification of this patient’s acute limb ischaemia (ALI) as ‘threatened’ warranted emergent surgical revascularization. The extensive thrombosis, duration of symptoms and ALI classification did not favor thrombolytic therapy. We counseled the patient about the uncertain limb viability and the possibility of amputation, to which he consented. We performed bilateral surgical embolectomy with Fogarty catheter through the common femoral artery, to which he consented. We performed bilateral surgical embolectomy with Fogarty catheter through the common femoral artery, via a vertical incision over the mid-inguinal point. Figure 6 shows the thrombi that were evacuated from the right and left lower limbs. The thrombus extended from above the external iliac-common femoral junction to below the popliteal artery in the left limb and from the common femoral artery to below the popliteal artery in the right limb. There was excellent back-flow on both sides after embolectomy. We also performed performed bilateral fasciotomies to reduce the risk of compartment syndrome. There was noticeable improvement in the perfusion of most muscles of the fascial compartments of both legs, but a return of the right dorsalis pedis pulse only. Due to resource limitations, we did not perform a peri-operative angiogram or duplex ultrasound scan to confirm the success of embolectomy.
Macroskopically, the endothelial lining of the blood vessels appeared smooth with no gross evidence of atherosclerosis. Although we do not yet have histopathology reports of the thrombi and blood vessel biopsies, we are convinced that atherosclerosis did not have a key role to play in the pathogenesis of this acute limb ischaemia.

Other important discussion of this case
Dr. Joselyn Rwebemba: The sudden onset of this patient’s process of acute limb ischaemia gives credence to the mechanism of cardioembolism, although bilateral limb cardioembolism is quite unusual. There were a number of factors to facilitate rapid thrombus propagation in the lower limbs in this patient, including a low flow state secondary to low cardiac output from a recently infarcted and probably stunned left ventricle, and the highly likely - although not yet determined inherited thrombophilia.

We note the delay of over 72 hours from the onset of the pain in the lower limbs to the surgical thromboembolectomy. The diagnosis of arterial occlusion was actually made about 16 hours after the onset of the pain. The delay to revascularization can be explained by lack of specialized expertise at the regional referral hospital where the patient was first admitted, delays in transportation, and time wasted while the patient’s family organized resources to get imaging and laboratory tests done among other limitations. Thrombolytic therapy is not readily available in peripheral hospitals in Uganda. Had a revascularization strategy been affected at the first hospital where this patient was admitted, he would have most likely survived loss of a limb.

The post surgical course has been protracted due to the need for multiple extensive debridement sessions for the right leg fasciotomy wounds, amenia that has required blood transfusion, acute kidney injury secondary to aminyglycide antibiotics, depression, and a right foot drop among other issues. This patient has been initiated on warfarin [15], but we note his poor response to escalating doses with the international normalized ration (INR) failing to reach the targeted range of 2-3 on 10 mg of warfarin once daily. Although testing for genetic polymorphisms for determination of the starting dose of warfarin is not recommended in routine practice [16], this is a selected patient where such testing would be beneficial. Unfortunately, this test is not available locally. Patients with genetic factors that alter warfarin pharmacokinetics require doses that are fivefold to 20-fold higher than average to achieve an anticoagulant effect [17]. His elder brother whom we are treating for pulmonary embolism is on warfarin 12.5 mg once daily. Modifiable factors like vitamin K intake that can affect the warfarin dose requirement have received the necessary attention. Our patient continues to receive cloxane in this time when the INR is not yet therapeutic. He is also on a single antplatelet agent [18].

Despite the desirability of a complete work-up, the treatment of this patient’s ischemic limbs has taken priority over the complex and expensive investigations of thrombophilia screening.

Currently, the amputation stump has healed. The right leg fasciotosomy wounds are granulating and the foot is warm with good capillary refill although with a residual foot-drop which unfortunately is not expected to recover due to the extensive excision of the dorsiflexors.

The latest echocardiogram shows an unchanged left ventricular systolic function but a largely resolved apical thrombus. The kidneys have recovered to normal function.

Dr. Joselyn Rwebemba’s Diagnoses:
1. Large anterior wall myocardial infarction complicated by left ventricular thrombus formation
2. Cardioembolism with rapid thrombus propagation leading to bilateral acute limb ischemia
3. Likely underlying inherited thrombophilia

Clinical nuggets about acute limb ischaemia (ALI)
Acute limb ischaemia is defined as a sudden decrease in limb perfusion that causes a potential threat to limb viability in patients who present within two weeks of the acute event [19], which can be the result of an embolus dislodged from a distant source, acute thrombosis of a previously patent artery or graft, or direct trauma to an artery (Table 4). Thromboemboli are more likely to produce symptoms of acute limb ischaemia than atheroemboli because with underlying atherosclerosis, there is collateral circulation that has developed over time. ALI is associated with high rates of hospital morbidity, mortality and limb loss [20]. Early diagnosis and rapid initiation of therapy are essential in order to salvage the ischemic extremity.

From a thorough history and physical examination, an acutely ischaemic limb can be classified as viable, threatened or non-viable/irreversible (Table 3) [21]. The six “P”s of acute extremity ischemia include pain, pulselessness, pallor, paresthesias, paralysis and poikilo thermoia.

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Table 4. Causes of acute arterial occlusion.

| Embolus                     | Thrombosis | Trauma                        |
|-----------------------------|------------|-------------------------------|
| Cardiac source              | Vascular grafts | Blunt                         |
| Atrial fibrillation         | Atherosclerosis | Penetrating                   |
| Myocardial infarction       | Thrombosis of aneurysm | Iatrogenic                   |
| Endocarditis                | Entrapment syndrome | Hypercoagulable state |
| Valvular disease            | Hypermotile state | Low flow state               |
| Atrial Myxoma               |             |                               |
| Prosthetic Valves           |             |                               |
| Arterial source             |             |                               |
| Aneurysm                    |             |                               |
| Atherosclerotic plaque      |             |                               |
| Paradoxical embolus         |             |                               |

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