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Late Embolectomy of the Left Superficial Femoral Artery in a Patient with Arterial Embolism Caused by Carbamazepine: A Case Report

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Abstract

Acute ischemia of the inferior limbs is not frequent but is associated with high morbidity and mortality. The main etiologies are dominated by arterial emboli and thrombosis. We report the case of a 61-year-old male patient who presented with acute ischemia of the left lower limb caused by a cardiac arrythmia due to side effects of carbamazepine. He had a surgical treatment with a good result despite a long delay before management.

Keywords

Embolectomy, Acute Ischemia, Carbamazepine, Cardiac Arrythmia, Embolus

1. Introduction

Acute limb ischemia is caused by a sudden interruption of arterial blood flow in a limb, resulting in tissue ischemia. It is the most common vascular surgery emergency. The causes are usually arterial emboli caused by heart disease or thrombosis occurring on pre-existing atherosclerotic plaques. Despite therapeutic advances in vascular surgery, acute limb ischemia remains associated with a poor functional prognosis and high mortality. Treatment consists of Fogarty probe em-

bolectomy in cases of embolism or endarterectomy or even bypass surgery in cases of thrombosis. Surgical treatment has better results when performed within 4 to 6 hours of symptom onset. However, there is some controversy, as several studies describe cases of limb salvage even after delayed treatment. We report the case of a patient who presented with acute limb ischemia caused by an unusual etiology: the side effect of the anticonvulsant carbamazepine. We were able to save the limb despite late treatment.

2. Description of Case

This is a 61-year-old patient, a retired nurse, who came in for consultation for a necrotic wound on his left big toe associated with moderate pain in his left leg that had been developing for two weeks. The toe wound occurred two weeks before the consultation while the patient was cutting his nails. He then performed local cares with wound dressing, an antibiotic ointment and polyvidone iodine with no improvement and the evolution was marked by the appearance of a dark coloration with loss of sensitivity on the left great toe after four days. Meanwhile, two days after he wounded himself, he started experiencing a diffuse, burning pain in his left leg, which had been increasing in intensity during the two following weeks.

The patient had a history of epilepsy treated with carbamazepine 200 mg/day since 20 years, but no personal history of atrial fibrillation, valvular heart disease, atherosclerotic disease, diabetes, or high blood pressure. The clinical examination on admission revealed a blood pressure of 123/74 mmHg, a pulse rate of 74 beats/minute that was irregular, respiratory rate of 22 cycles/minute, a temperature of 36.4˚C, and dry gangrene of the pulp and nail bed of the left big toe, which was cyanotic and insensitive. Examination of the left leg revealed a limb that was darker in color than the contralateral limb, slight coldness, absence of popliteal, posterior tibial, pedal pulses, hypoesthesia and paresis of the other toes (motor strength of 3/5). A capillary refill time above 3 seconds. The rest of the examination was unremarkable.

Doppler ultrasound revealed obstruction of the left superficial femoral artery from its upper third to its distal end, with the presence of a few small collaterals on the artery axis. The CT angiogram showed a defect showed a lack of opacification of the entire left superficial femoral artery, as well as the popliteal artery, the posterior tibial artery, slight opacification of the proximal third of the anterior tibial artery and the fibular artery, and a lack of opacification of the dorsal artery of the foot. The arterial walls did not show any atherosclerotic plaques. The pre operative EKG of the patient showed PR interval > 200 ms and skipped beats suggesting an atrioventricular block.

We diagnosed an acute ischemia classified Rutherford IIA based on the moderately sensitive and motor deficits and absence of an arterial doppler signal, the absence of clinical signs of extensive gangrene on the limb. We indicated an emergency embolectomy, which was performed the day after admission due to a delay of several hours in performing the angiography scan because of financial constraints. The pre-

operative work-up showed no abnormality, creatinine level was 11 mg/l, Prothrombin time was 13 seconds, INR = 1. Assessment of the lactatemia and creatine kinase were not done because of lack of availability in the laboratory of our center. The patient underwent surgery under spinal anesthesia. We started with a popliteal approach, before arteriotomy, unfractionated heparin was given intraveinously at the dose of 50 IU/kg. During arteriotomy, we found an old, parietalized embolus (**Figure 1**). We tried to perform an embolectomy with a 4 Fr Fogarty catheter and an aspiration of this embolus, which was both unsuccessful. Then we removed half of the embolus with a Kelly forceps through the popliteal artery. The breakage of the embolus led us to completed the procedure with a second approach via the groin in order to extract the second half of the embolus (**Figure 2** and **Figure 3**).

We had a satisfactory back bleeding after the embolectomy and sutured the arteries with patches (**Figure 4**). At the end of the surgery the limb was warm, with no pulses on palpation and later in the ward we observed a significant improvement on motor and sensitive functions marked by the disappearance of the paresis and the hypoesthesia. The post-operative treatment was enoxaparin at 8000 UI every 12 hours, paracetamol 1 gram every 6 hours, tramadol 100 mg every 8 hours

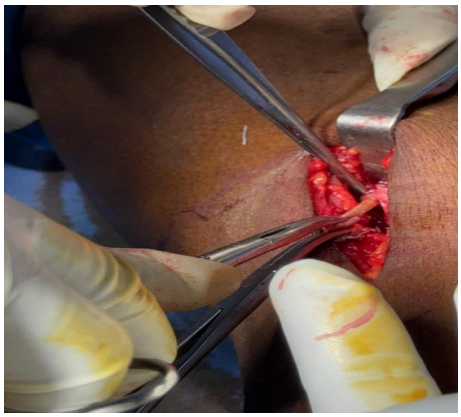

Figure 1. Surgical embolectomy of the inferior part of the clot at the left popliteal artery.

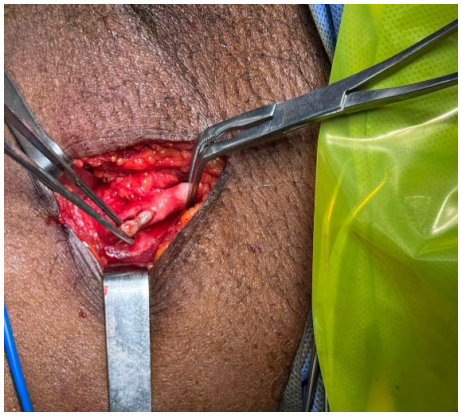

Figure 2. Surgical embolectomy of the superior part of the clot at the left common femoral artery.

Figure 3. A view of the embolus after its complete removal.

Figure 4. Suture of the common femoral artery with a bovine patch.

and saline 500 ml every 6 hours. The Doppler ultrasound done on the third day post-operative revealed a triphasic flux in the superficial femoral artery, the popliteal artery, the arteries of the leg and the Dorsalis pedis artery. We didn't found any abnormalities on cardiac ultrasound, EKG, however we found slight extrasystoles on holter EKG. There were no signs of thrombophilia on the biological workup. Thus, after we ruled out all the usual causes of embolism in this patient, we suspected that it could be associated with the carbamazepine since there are well described cardiac sides effects in some patients under this medication. We amputated the left hallux the 8th post-operative day, the patient was discharged under rivaroxaban 20 mg and clopidogrel 75 mg daily respectively either for prevention of a recurrence of embolism and a possible thrombosis secondary to the intimal trauma caused to the embolectomy. The patient was addressed to his neurologist for modification of his antiepileptic treatment. He is currently on phenobarbital 50 mg twice daily. He was seen in our service every two weeks during the first two months after the surgery, then once a month for six months. We stopped his anticoagulant therapy after monitoring his cardiac function for six months after the introduction of phenobarbital. His progress was straightforward, with no

episodes of recurrent embolism.

3. Discussion

Our study describes a case of late embolectomy in a patient having an arterial embolism due to arrythmia related to carbamazepine. To date, there have been no reports in the literature of limb ischemia caused by the cardiac side effects of carbamazepine.

Carbamazepine is an anti-epileptic drug widely used for the treatment of partial and generalized seizures, trigeminal neuralgia, neuropathic pain syndrome and bipolar disorders [1]. Carbamazepine has also been reported to be a part of the group of drugs-related bradycardia which includes beta blockers, calcium channel blockers, anti-arrythmic drugs, opioids, cocaine, lithium, antidepressants, sympatholytic antihypertensives, cimetidine, tedisamil [2] [3] and a recent study reported that it increases the risk of sudden cardiac arrest in humans [4]. Carbamazepine has antiarrythmic effects, normotimic and membrane-stabilizing effects however paradoxically its side effects include cardiotoxic effects such as atrioventricular effects, bradycardia and cardiac rhythm disorders [5]. Few studies have clearly demonstrated an association between epilepsy and arrythmia like the one of Wang *et al.* [6] which revealed not only a higher risk of atrial fibrillation and other cardiac arrhythmias in epileptic patients, but also a higher risk of cardiac arrythmia in patients under carbamazepine and valproic acid.

The most common reported side effect of carbamazepine is sinus tachycardia especially in case of overdose however, other effects are described, including sinus and nodal bradycardia, atrioventricular block, premature ventricular contraction, ventricular tachycardia, and junctional escape rhythm [7]. It has also been demonstrated that the second most frequent side effect associated with carbamazepine is bradyarrythmia or atrioventricular delay which occurs generally in elder women [5]. Our patient presented with skipped cardiac beats on admission and underwent several cardiac investigations, which formally ruled out the usual causes, namely arrhythmogenic heart disease and valvular heart disease. As his thrombophilia test results were also normal, the most obvious cause of the arrhythmia was the carbamazepine he had been taking for nearly 20 years.

Another distinctive feature of this case is the achievement of a good functional outcome after a long treatment delay of two weeks. Long delays in treatment are common in developing countries for cases of acute limb ischemia. They are generally due to the limited availability of vascular surgeons in these countries, patient ignorance, or sometimes even the inability of general practitioners to make a diagnosis and refer patients to specialists in a timely manner [8] [9]. In the case of our patient, this was a case of therapeutic wandering, as he was a former nurse and initially tried to treat himself before coming to our facility.

It is reported in the literature that revascularization performed between 6 and 12 hours is generally associated with good results, whereas beyond 12 hours, the risk of amputation and mortality increases significantly [10] [11]. The therapeutic

decision in patients presenting late is not always obvious and must be based on clinical signs and imaging results in order to improve patient prognosis. The treatment of this category of patients is controversial, as those who have developed critical ischemia after arterial occlusion have good outcomes provided they have no intimal lesions, intimal emboli, or secondary thrombi. While other patients with acute ischemia who undergo surgery after 8 hours are at high risk of reperfusion syndrome and gangrene, paradoxically, the risk of complications decreases for delays greater than 7 days [12]. The good outcome for our patient could perhaps be explained by the development of collateral circulation in the superficial femoral artery, as confirmed by CT angiography, although we found no atherosclerosis or cardiovascular risk factors in this patient.

We performed a surgical embolectomy due to the failure of the Fogarty catheter and thromboaspiration because of an old, parietalized embolus. This embolus extended from the superficial femoral artery to the posterior tibial artery, predicting uncertain revascularization by bypass surgery with a high probability of amputation. In situ thrombolysis is the first-line treatment in patients classified Rutherford IIA [13]-[15] but was not considered in that patient due to delay of management of the patient and for the fact that this procedure is not yet available in our surgery department. We were able to avoid amputation in this patient and included clopidogrel in his treatment to prevent secondary thrombosis related to microtrauma to the intima during clot extraction. Our results suggest that surgical embolectomy could be considered among the treatment options for patients treated after a long delay, but this would need to be verified in a study involving several patients.

4. Conclusion

Our case highlights the risk of the occurrence of acute limb ischemia during treatment with carbamazepine, which necessitates rigorous monitoring of the side effects of this drug in patients and even educating them about it. Etiological investigations during acute ischemia must be rigorous in order to prevent recurrence and improve the prognosis. Embolectomies should be considered even after a long delay in the absence of obvious signs of limb non-viability.

Disclosures

Informed consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Patient's confidentiality: All possible identifying information of the patient was kept secret.

Ethics: Ethical approval was not necessary since we did not perform any experiment on this patient; our case report focuses on the unusual aetiology of the disease found in this patient

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Author Contribution

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Concept and design: Biwole D, Ekani B, Mbele R, Kobe Z.

Drafting of the manuscript: Biwole D, Ekani B, Mbele R, Kobe Z, Arroye F, Ngo Yon L.

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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