

Calcific Uremic Arteriopathy or Calciphylaxis in a Hemodialysis Patient: Case Study and Review of the Literature

Modou Ndongo^{1*}, Nestor Nankeu², Josephine Nkok², Helene Messet², Fabrice Tiako², Mamadou Mouctar Diallo², Misylia Bouaoud², Attia Houyem², Fatiha Lahouel², Djillali Ziane Berroudja², Tayeb Bensalem², Sid Ali Toufik Benyaghla², Catherine Albert², Sidy Mohamed Seck³, El Hadji Fary Ka¹

¹Department of Nephrology, Dialysis and Kidney Transplantation of Aristide Le Dantec Hospital, Dakar, Senegal

²Department of Nephrology, Dialysis of Louis Pasteur Hospital, Chartres, France

³Department of Nephrology, Dialysis of Ouakam Military Hospital, Dakar, Senegal

Email: *ndongomodou@gmail.com

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Abstract

Calcific uremic arteriopathy (CUA) is a rare pathology affecting 5% of dialysis patients but with a poor prognosis. It is characterized by calcification and thrombotic lesions of the microcirculation leading to hyperalgesic ischemic skin lesions. Several risk factors have been identified, mainly warfarin treatment, mineral and bone disorders (MBD), inflammation and malnutrition. In the evocative forms, the diagnosis is made based upon the physical examination finding of classic painful ulcerated lesions that are covered by a black eschar. Skin biopsy, due to the risk of aggravation and delayed healing, is only performed in case of doubt diagnosis. The therapeutic attitude due to the lack of solid randomized studies is based on expert consensus and requires a multidisciplinary approach. We report here the case of a patient with CUA revealed in the form of multiple ulcerative-necrotic skin lesions associated with pressure sores and arterial wounds.

Keywords

Calcific Uremic Arteriopathy, Calciphylaxis, Hemodialysis

1. Introduction

Calcific uremic arteriopathy (CUA) or calciphylaxis is a rare pathology with a poor prognosis. It is a pathology that is more common in patients with end-stage renal disease (ESRD) on dialysis. However, CUA can occur before end-stage as

well as in patients with normal renal function. Its prevalence is 5% in dialysis patients [1]. An analysis on the United States Renal Data System showed an increasing incidence [2]. CUA produces a thrombosing microangiopathy resulting from the reduction of blood flow in the dermo-hypodermic arterioles responsible for ischemic and necrotizing skin lesions. CUA is responsible of a high morbidity and mortality with a six-month survival estimated at 50% according to the series [3]. Therapeutic indications are based on expert consensus including wound care, pain management, mineral and bone disorders treatment and dialysis optimization.

We report the case of calciphylaxis diagnosed in a chronic hemodialysis patient in the context of superinfected limb ischemia on obliterating arteriopathy of the lower limbs.

2. Presentation of the Clinical Case

This was a 69-year-old diabetic, hypertensive, ESRD patient recently put on dialysis with a right radio-radial arteriovenous fistula, carrier of ischemic and rhythmic heart disease under coumadin. Also followed for an obliterating arteriopathy of the lower limbs and carrier of a right axilo-femoral bypass hospitalized for painful ulcerations of the two heels. On examination, blood pressure was 90/64 mmHg, heart rate 69 bpm and temperature 35°C. The physical examination showed ulcerated lesions of both heels (**Figure 1**) with a cold, painful and mottled left leg, necrosis of the left ring finger (**Figure 2**), painful ulcerations with a necrotic center and infiltrated bases sitting in the region under the left nipple, under the left umbilical and at the left scapular level (**Figure 3**) as well as stage 4 gluteal pressure sores (**Figure 4**). Biologically, there was a major inflammatory syndrome with CRP at 336 mg/l and hyperleukocytosis at 34.1 G/l. Albuminemia was 17.7 g/l, phosphoremia at 4.78 mmol/l, serum calcium at 1.55 mmol/l corrected to 2.2 mmol/l, PTH at 349 pg/ml (5.4N), blood culture negative. Doppler ultrasound of the lower limbs showed occlusion of the left femoral axes and patency of the right axilo-femoral bypass. The injected thoraco-abdomino-pelvic (TAP) CT scan showed diffuse atheroma of the entire arterial network of the main trunks and collaterals and obstruction of the common femoral and the left superficial femoral (**Figure 5**). The diagnosis of critical ischemia of the left lower limb with severe sepsis was retained and the patient was put on vancomycin-based antibiotic therapy and curative anticoagulation with sodium heparin 300 IU/kg at PSE. Amputation of the left thigh and left ring finger was performed six days later. A skin biopsy of the abdominal lesion looking for associated calciphylaxis showed hypodermic skin necrosis with large calcifications that seemed to develop at the expense of the vascular walls (**Figure 6**). The patient was put on a non-calcium phosphate binder, protein-caloric supplementation in dialysis, increase of the frequency of dialysis to 5 days out of 7, daily dressing of the skin lesions and thiosulphate 25 g three times a week. The evolution was favorable marked by a progressive disappearance of the sepsis, good healing of the thigh amputation stump (**Figure 7**), the finger stump (**Figure 8**) and the buttock pressure sores



Figure 1. Ulceronecrotic lesion of the left heel.



Figure 2. Left ring finger necrosis.

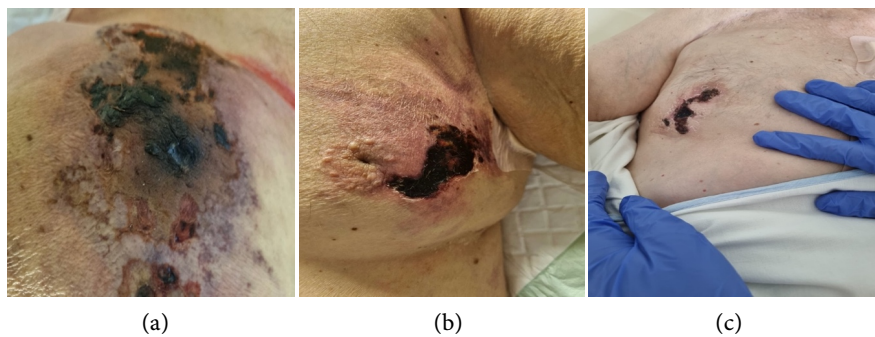


Figure 3. Ulceronecrotic skin lesions located at the left periumbilical (a), left latero-mammary (b) and left scapular (c) level.



Figure 4. Stage 4 right gluteal and inter-gluteal fold pressure ulcers.

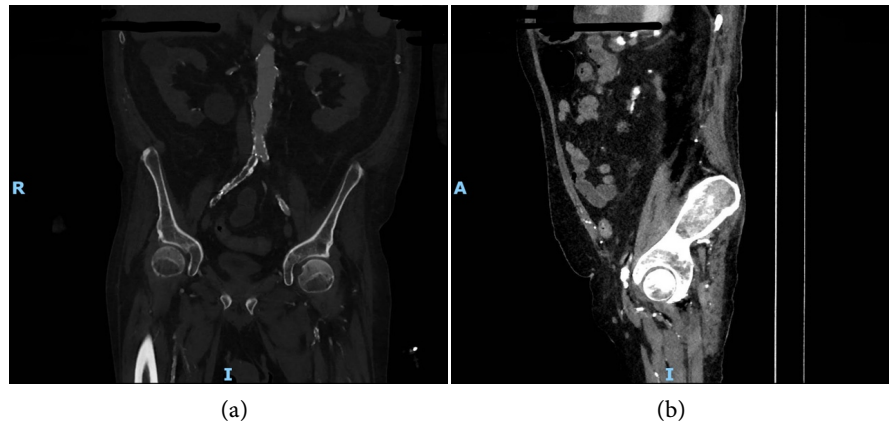


Figure 5. CT images showing diffuse vascular calcifications, at the aortic level (a), and at the abdominal subcutaneous level (b).

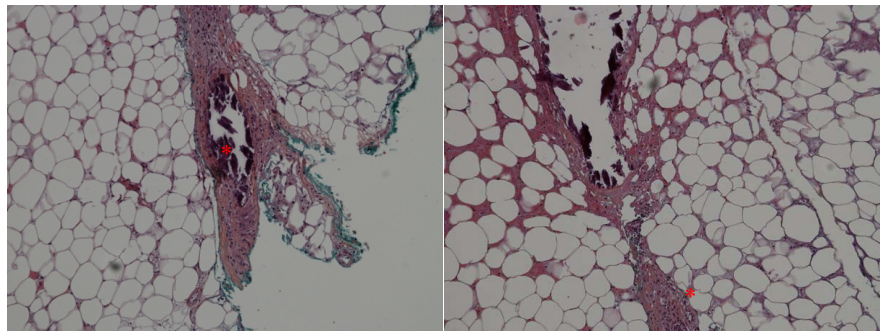


Figure 6. Skin biopsy hematoxylin-eosin-saffron (HES) staining, magnification 20× showing images of subcutaneous calcifications extending the vascular pathway (*).



Figure 7. Left lower limb amputation stump scar.



Figure 8. Evolution at the sixth month of the lesion of the left ring finger.

(**Figure 9**). The calciphylaxis lesions evolved favorably with regression then disappearance of the pain, and improvement of the wounds at 1 month authorizing the reduction of dialysis sessions to four times a week and continuation of thio-sulphate. At five months of treatment, there is complete healing of the calciphylaxis lesions (**Figure 10**). Biology at five months noted an albuminemia at 33.9 g/l, a calcemia at 2.41 mmol/l, phosphoremia at 1.73 mmol/l, PTH at 255 pg/ml (3.8N) a CRP at 58 mg/l. The patient was put back on three weekly dialysis sessions with continuation of 25 g thiosulfate twice a week.

3. Discussion

CUA lesions are secondary to a decrease in cutaneous blood flow mainly due to calcification, fibrosis and thrombus formation in the dermo-hypodermic arterioles [1]. It is a rare pathology with an estimated prevalence of 5%. This rarity is partly linked to a lack of knowledge of the disease by practitioners. Indeed, a Japanese study showed that only 40% of the doctors in the hemodialysis centers who participated in the study knew more about CUA than the name of the disease [4]. The first lesion is the calcification of the microcirculation involving factors involved in osteogenesis and bone remodeling [5]. Other factors are involved in the formation of these calcifications. Among which there are MBD and their treatments, the deficiency of calcification inhibitors as well as chronic inflammation. This fact was well noted in our patient with the TAP scan which revealed diffuse vascular calcification.



Figure 9. Evolution in the sixth month of gluteal pressure sores.

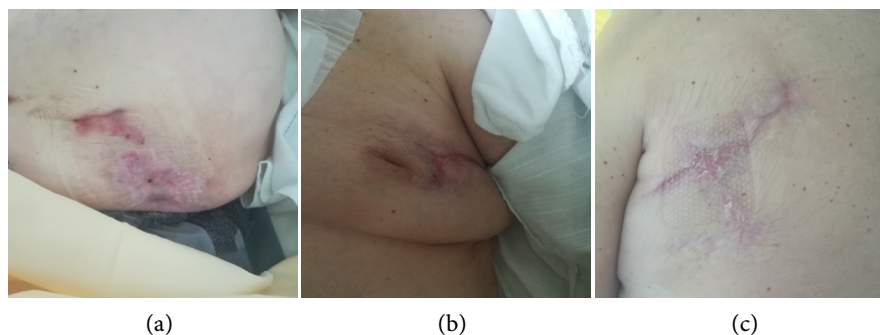


Figure 10. Evolution at the six month of ulcero-necrotic skin lesions located at the left periumbilical (a), left latero-mammary (b) and left scapular (c).

Several risk factors for calciphylaxis have been identified in patients with chronic renal failure, including female gender; hyperphosphatemia; obesity; certain medications such as warfarin, calcium chelators, vitamin D analogues, corticosteroids; hypoalbuminemia; diabetes; length of time on dialysis and inflammation [6]. The use of warfarin has been reported in several studies as an important factor in the occurrence of calciphylaxis lesions [7]. Several of these risk factors including diabetes, MBD, sepsis, severe malnutrition but especially the treatment with coumadin were noted in our patient.

The clinical picture associates at an early stage purplish, painful, plaque-shaped subcutaneous nodules, indurations or reticular livedo evolving into necrotic ulcerations once the vascular thrombosis is advanced. Axial involvement is the most frequent and concerns 70% to 80% of affected patients [8]. They develop especially in the fatty areas of the abdomen, pelvis, trunk and root of the limbs [6] [9]. These classic lesions in an ESRD patient are sufficient to establish the diagnosis. This topography was noted in our case with lesions located in the abdomen and trunk.

At the paraclinic, non-specific and inconstant abnormalities can be observed such as a disturbance of the mineral and bone balance with hyperparathyroidism, hyperphosphatemia, an increase in the phosphor-calcic product. Imaging may show tissue calcifications. Skin biopsy is only performed in case of diagnostic doubt because it carries a high risk of complications [10]. Indeed, it is likely to cause additional trauma, creating a new focus of necrosis and ulceration aggravating the skin lesions already present. The sample taken from the periphery of a lesion and avoiding the necrotic areas shows medial calcification of the arterioles, intimal proliferation, calcifications of the perivascular soft tissues, as well as necrosis of the epidermis. *Von Kossa* staining can identify microcalcifications [1]. In our case, the skin biopsy was performed to confirm the diagnosis of CUA in the presence of other associated skin lesions which could confuse the diagnosis.

The therapeutic indications available are based on expert consensus. They include effective analgesia with sometimes the need to resort to opioids, careful care of wounds to avoid extension and superinfection as well as the discontinuation of risky drugs such as the use of warfarin, iron, calcium products or vitamin D [1]. Correction of MBD is also essential. Hyperphosphatemia is treated with non-calcium phosphate binders and hyperparathyroidism preferentially with calcimimetics. Optimization of dialysis is necessary to reach the adequacy targets with an increase in the frequency of dialysis sessions and the use of a low calcium bath [1]. Sodium thiosulfate at a dosage of 25 g three times a week at the last hour of dialysis is recommended because of its vasodilating, antioxidant and calcium solubilizing properties [11] [12]. Other treatments such as bisphosphonates and hyperbaric oxygen therapy are reserved to resistant forms [11]. The evolution was favorable in our patient with good healing of his lesions.

4. Conclusion

CUA is a rare pathology with high morbidity and mortality. Several risk factors

have been identified, mainly warfarin treatment and MBD. It is more common in chronic kidney disease patients and the diagnosis should be considered in the presence of any painful skin lesion. Skin biopsy is reserved for doubtful cases as seen in polyvascular patients with multiple arterial wounds.

Patient Consent

The patient gave informed consent for the publication of this case.

Conflicts of Interest

The authors declare no conflict of interest for this article.

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