

Calciphylaxis in renal substitution therapy

Calcifilaxis en terapia de sustitución renal

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Abstract

Calciphylaxis is one of the less common complications of Chronic Advanced Kidney Disease, especially in renal replacement therapy, the exact pathophysiology of its appearance is unknown, but it is believed that it is due to an alteration in bone-mineral metabolism.

We describe a clinical case of a patient with chronic kidney disease, who presented as a serious complication calciphylaxis, reaching this diagnosis thanks to the characteristic images of this pathology taken from the bank of the Hospital's imaging service.

In conclusion, calciphylaxis, despite being a pathology difficult to find nowadays due to better control of bone-mineral metabolism, should be considered especially in those patients with rapid progression of renal disease and presence of suppurative calcified lesions in extremities.

Key words: chronic kidney disease, calciphylaxis, bone-mineral metabolism, renal replacement therapy.

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Resumen

La calcifilaxis es una de las complicaciones menos comunes de la enfermedad renal crónica avanzada, sobre todo en terapia de sustitución renal, se desconoce la fisiopatología exacta de aparición, pero se cree, que es por una alteración en el metabolismo óseo-mineral.

Se describe un caso clínico, de un paciente con enfermedad renal crónica, que presentó como complicación grave calcifilaxis, llegando a dicho diagnóstico gracias a las imágenes características de dicha patología tomadas del banco del servicio de imagenología del hospital.

En conclusión, la calcifilaxis, a pesar de ser una patología difícil de encontrar en la actualidad, debido al mejor control del metabolismo óseo-mineral, se debe considerar en aquellos pacientes con progresión rápida de la enfermedad renal y con presencia de lesiones calcificadas supurativas en extremidades.

Palabras clave: enfermedad renal crónica, calcifilaxis, metabolismo óseo-mineral, terapia de sustitución renal.

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Introduction

Calciphylaxis, also called calcific uremic arteriopathy (CUA), is a clinical syndrome characterized by necrotic ulceration of the skin due to calcification of the arteriolar media layer plus fibrosis of the intima and subsequent cutaneous ischemia due to thrombosis¹.

It usually manifests in patients on renal replacement therapy or with low glomerular filtration rate, whose alteration of the phosphocalcium metabolism seems to represent the main cause of this pathology².

Clinical case presentation

A 54-year-old male patient, with advanced chronic kidney disease of 5 years of evolution, on renal replacement therapy for approximately 2 years, (method of conventional hemodialysis three times a week in an agreement house), in whom renal transplantation was initially proposed, due to the lack of adherence to treatment, the patient requested a change of location of the hemodialysis center to one close to his house.

The patient was admitted because he presented effusion of serous liquid material in the hands and the left thigh, reason for which a culture of this secretion was performed, evidencing calcium oxalate crystals; associated with this, paraclinical tests were carried out, observing elevated procalcitonin, leukocytosis and neutrophilia on admission, it was catalogued as a soft tissue infectious process; in the control exam performed subsequently it was evidenced the low level of parathormone, without electrolytic alteration or criteria for urgent dialysis. (Table 1).

In addition, it was performed a simple thigh CT scan, observing the presence of calcic material in this area, draws attention even the calcification of the femoral and spermatic arteries that make even more serious the pathology of the patient. (Figure 1).

Not having other treatment than the one offered (renal replacement therapy), because the only

Table 1. Paraclinical tests of the patient.

Parameters	Results	
	Admission	2 days of hospitalization
Leukocytes	17.88	
Neutrophils	15.91	
Lymphocytes	730	
Monocytes	1.1	
Eosinophils	40	
Basophils	100	
Red blood cells	3,750,000	
Hemoglobin	11.5 g/dl	
Hematocrit	34.10 %	
Mean corpuscular volume	91 fl	
Mean hemoglobin concentration	30.7 pg	
Platelets	310	
Glucose	158	111
Urea	81	81
Creatinine	4.76	4.58
Sodium	133	133
Potassium	3.9	3.8
Chloride	97	95
Procalcitonin	6.63	
Uric acid		4.5
Alkaline phosphatase		171
Lactic dehydrogenase		174
Total serum proteins		6.5
Serum albumin		2.3
Ionized calcium		7.05
Total calcium		10.6
Phosphorus		4.4
Magnesium		2.4
Testosterone		35.7
Parathormone		< 3
Carcinoembryonic antigen		1.95
Alpha-fetoprotein		0.6
CA 125		87.6
CA 19-9		9.3
TSH		5.94
FT4		0.9 L

therapeutic option is the hip disarticulation, and taking into account that it is most probable that this effusion of material would be observed in other areas of the body and since it was not the first event of this secretion, the fifth in the year, with poor adherence of the patient to treatment, it was decided to maintain the replacement therapy. The patient was discharged

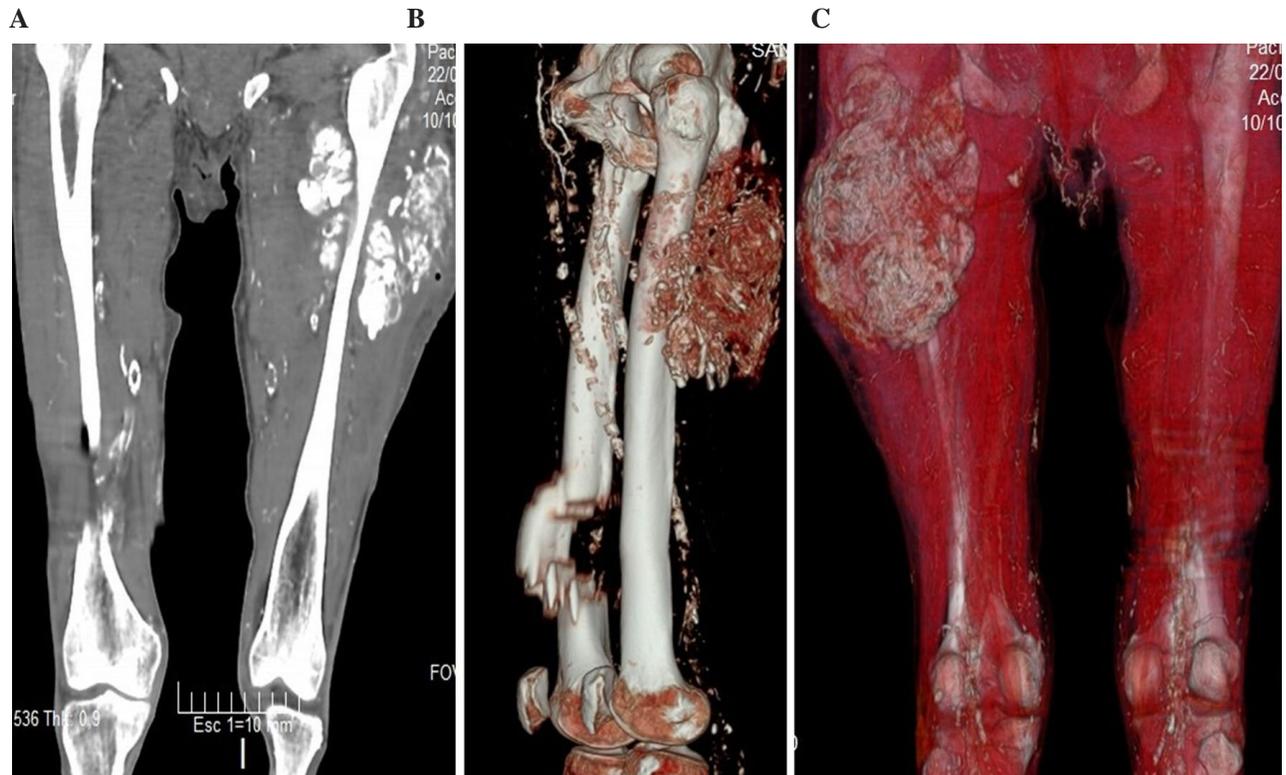


Figure 1. Simple thigh CT-scan. **A.** An image compatible with calcium density is observed in the left thigh. **B.** Lateral image with reconstruction of the bone, where calcification of femoral arteries is observed. **C.** Reconstruction of tissues where the calcium mass is observed in the thigh, as well as calcification of spermatic arteries.

home, after 7 days of hospitalization, continuing so far on hemodialysis three times per week in a place of agreement with slow but progressive decrease of the effusion of serous material.

Discussion

Calciphylaxis has a prevalence that ranges between 1 and 4 % of patients with chronic kidney disease³. Recently, a study of the dialysis units of the Fresenius Medical Care North America reported an annual incidence of 0.34%⁴. The incidence in patients on peritoneal dialysis is less known, although a study focused on this group shows an annual incidence of 0.9%. It affects with higher frequency advanced-middle aged women, white and diabetic patients⁵. The pathogenesis of this disease has not yet been clear, but several risk factors have been involved, including secondary hyperparathyroidism, elevation of the calcium-phosphorus product (CaxP)

greater than 55 mg/dl, normal or high levels of calcium in blood, high doses of active metabolites of 25-hydroxyvitamin D⁶. On the other hand, we still have little information of patients with advanced chronic kidney disease who are not yet in renal replacement therapy⁷.

In general, it is more prevalent in obese women, which contrasts with our case, the alteration of the bone-mineral metabolism is common; however, other risk factors (hypertension, diabetes mellitus, obesity) are gaining prominence, as well as the use of steroids, this finding is of utmost importance and of great clinical interest to reconsider the indication of these treatments in high-risk patients⁸. With all these appreciations, we can draw a new phenotype of patient with calciphylaxis to which we should pay special attention: a subject with chronic kidney disease (patient on dialysis or kidney transplant) with a significant comorbidity, among which a marked

cardiovascular profile stands out, in treatment (in some cases) with oral anticoagulants and with hypoalbuminemia due to chronic inflammation or malnutrition⁹.

Regarding the treatment, a fundamental aspect that has gained extraordinary importance in the world of calciphylaxis is the use of a combined or multitarget treatment¹⁰. There is strong evidence that confirms the improvement of the lesions and the increase in survival when this treatment is used. Although there is no standardized therapy, it is recommended to suspend calcium chelators, oral anticoagulants (changing to a low molecular weight heparin) and 25- hydroxyvitamin D, as well as to increase the frequency of dialysis (where necessary) to 5-6 weekly sessions with low calcium bath; other options that could be considered are the use of drugs such as non-calcium chelators (for example, sevelamer, which inhibits ectopic calcifications and reduces cholesterol, in our case, the patient was already taking this medication), cinacalcet (reduces PTH, calcium and phosphorus in patients on dialysis with secondary hyperparathyroidism) the latter is not for sale in our country, sodium thiosulfate (antioxidant and anti-inflammatory that mobilizes the calcium deposits of the vessels) and bisphosphonates (inhibitors of the formation of ectopic calcifications with anti-inflammatory effect). We should consider the administration of vitamin K in cases of deficiency. There is controversy regarding the use of hyperbaric chamber (it could be beneficial in distal lesions) and parathyroidectomy in cases of severe hyperparathyroidism, since they do not seem to improve the general condition of these patients. The prognosis of this disease is ominous, reaching a mortality of up to 60-80%, being the sepsis related with calciphylaxis the most frequent cause. Proximal lesions have a higher mortality than distal.

In conclusion, although calciphylaxis is an infrequent entity, it has a high mortality rate. The profile of the patient has changed: it is not exclusive of uremic situations, it also occurs in patients with normal functioning renal transplant or in subjects without kidney disease. The cardiovascular risk factors displace the classic factors of the bone-mineral metabolism. A “risk score” should be established

for early diagnosis, as well as a standard treatment, it is recommended to conduct multicenter studies that allow the protocolization of a treatment that improves the quality of life of these patients¹¹.

Conflict of interest

The authors declare they do not have any conflict of interest.

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Ethical responsibilities

Protection of people and animals

The authors declare that no experiments were performed on human beings or animals for this research.

Data confidentiality

The authors declare that they have followed the protocols of their workplace on the publication of patient data.

Right to privacy and informed consent

The authors declare that patient data do not appear in this article.

Contribution of the authors

Diego Alexander Mendoza Panta: came up with the idea of presenting the case and was responsible for collecting all the information regarding the patient.

Jorge Washington Huertas Garzón: responsible for retouching and approving the final product, also contributed to the structure of the entire document.

Washington Xavier Osorio Chuquitarco: responsible for providing information for the development of the Discussion of the document, was crucial in the search of scientific evidence for structuring it.

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