

CASE REPORT

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Calciphylaxis - Case Report

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ABSTRACT

Introduction: Calciphylaxis is a rare, but serious, kidney complication. Calciphylaxia is a vasculopathy of small blood vessels characterized by the deposition of calcium deposits in intimal arterioles with the consequent proliferation of intima, fibrosis and thrombosis. **Aim:** The aim was to show the significance of recognition of calciphylaxis relies on heightened clinical awareness of the presence of atypical skin nodules or ulcers that occur in patients with hemodialysis dependence and to characterize features of calciphylaxis or components of treatment that may lead to improved outcome. **Case report:** We present the case of 84-year-old woman with chronic kidney disease and diabetes mellitus as well as severely painful, firm, indurated plaques on the lower extremities. The plaques progressed to involve larger areas with associated local ulceration and necrosis. Laboratory testing revealed hyperparathyroidism and incisional skin biopsy confirmed calciphylaxis. Wound microbiology confirmed *Staphylococcus aureus*. **Conclusion:** The diagnosis can be based on clinical grounds, supported by histological analysis if possible. The laboratory workout must cover all the possible implications of chronic kidney disease with special attention to Ca⁺ and P⁺ values and evidence of skin or systemic infection. Calciphylaxis must be known by dermatologist as early diagnosis and proper management can be decisive for better prognosis.

Keywords: Calciphylaxis, chronic kidney disease, hemodialysis.

1. INTRODUCTION

Calciphylaxis is a rare, but serious, kidney complication. Calciphylaxia is a vasculopathy of small blood vessels characterized by the deposition of calcium deposits in intimal arterioles with the consequent proliferation of intima, fibrosis and thrombosis (1).

It's most often seen in patients with advanced chronic kidney disease (end-stage renal disease), or patients with kidney failure who are on dialysis or have had a kidney transplant, diabetic patients and patients with rheumatoid arthritis. Though the described cases are related to obesity, Chron's disease, holangiocarcinoma, alcoholic liver cirrhosis, SLE, breast cancer treated with chemotherapy. This vasculopathy is most common by the females, but white race. Even in 60-80% , the mortality rate with sepsis is reported as a consequence of infected and necrotic skin lesions and multi-organ failure (2, 3).

Clinical, it is characterized by intense ischemic pain in lower extremitas. The classical clinical picture is that of a necrotic and progressive skin ulcer of reticular pattern, mostly in the lower legs and susceptible to local infection. It is a product of mural calcification and occlusion of cutaneous and sub-cutaneous arteries and arterioles. Then appears the efflorescence in level of the skin looks like as blue skin changes progressing into the brown efflorescence. Harder infiltrates are embedded in the subtle tissue. Later on these efflorescencas appear bubbles, which cause skin and subcutaneous tissue necrosis. The chronic wound is extremely painful (4). A patient with calciphylaxis may have higher than normal levels of calcium (hypercalcemia) and phosphate (hyperphosphatemia) in the blood. They may also have symptoms of hyperparathyroidism (5, 6).

Symptoms of calciphylaxis include:fatigue, weakness,cramps, depression, body aches. The diagnosis is based on the biopsy of the affected part of the skin (Figure 1). Also, before the treatment, it's necessary to do the inflammatory parameters, the wound microbiology, the X ray of the affected extremity necessary for looking of the presence irregular calcium deposits, skeletal scintigraphy and vascular estimate of the lower extremities, too. Treatment is focused on caring for the skin lesions, preventing infections, and correcting the calcium and phosphorous concentrations in the blood.

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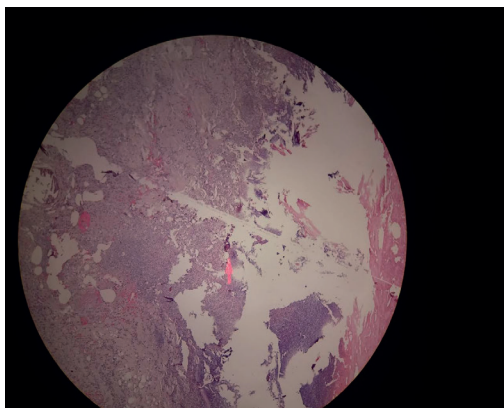


Figure 1. Calciphylaxis biopsy

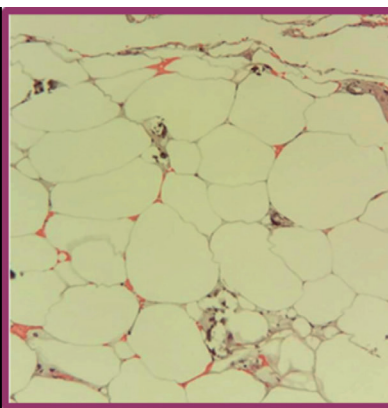


Figure 2. Morphology of calciphylaxis lesions

Treating the wounds and lesions might include: enzymatic debriding agents, hydrocolloid or hydrogel dressings, systemic antibiotics, hyperbaric oxygen therapy.

Medications may be prescribed to treat the wounds and to correct abnormal calcium and phosphorus concentration in the blood. These may include: intravenous sodium thiosulfate, a chelating agent for calcium and iron cinacalcet (Sensipar) (7).

2. AIM

The aim of this case report is to show the significance of recognition of calciphylaxis relies on heightened clinical awareness of the presence of atypical skin nodules or ulcers that occur in patients with hemodialysis dependence. Our aim was, also, to characterize features of calciphylaxis or components of treatment that may lead to improved outcome.

3. CASE REPORT

A 84-year-old-female patient, hemodialysis patient on the Clinic for Hemodialysis of the University Clinical Center Sarajevo (UCCS), was complained in December 2017. on following symptoms: a) Pain in leg; b) Dolor of leg; c) Rubor of leg; and d) Necrotic ulceration of the skin (Figure 2). Present illness has started in early spring of 2017. as allergic skin changes. At the beginning it was look like as red skin efflorescence with itching. Because patient is diabetic first consultation was angiologists (dg. Ulcera cruris bill. Diabetic mellitus type 2 cum complications; Th/Unknown Spray + Canestem cream). But there was no improvement on the therapy. Few months after she was found same skin changes but now on the other leg. Now, patient has pain in legs and she is dependent on someone else's help. Currently the skin changes are not red ones with itching, but necrotic with the inflammatory process of the surrounding tissue. First dermatologist consultation was on the 12th December 2017. (Dg. Vasculitis necroticans in obs with recommendation of looking for C3,C4,CIK complements Th/Vibramycin cps. 10 days and Hyper gel as a local therapy with rinsing skin changes with H₂O₂ and Argedin cream). But there was no improvement on the therapy because of the intolerance on local therapy.

Of course, we were consulted angiologists again too because of circular status of lower extremities. The angi-

ologists found stenosis-occlusive changes femoral right with necrotic ulcerations of skin on both legs. His recommendation was skin changes biopsy. On 5th January 2018. was admitted our patient to the Clinic for Skin diseases of the University Clinical Center Sarajevo (UCCS) because of skin changes biopsy (Figure 1 and 2).

1st day of hospitalization

On examination, she was afebrile. Her pulse rate was 80 beats per minute, blood pressure 120/80 mm Hg, respiratory rate 18 breaths per minute with oxygen saturation 94% on room air that improved to 100% on 2 liters of oxygen through a nasal cannula. She appeared comfortable. Cardiac examination revealed normal heart sounds and no jugular venous distention. There were bibasilar rales on auscultation of the lungs and no wheezing. The abdomen was non-distended, soft and non-tender; the liver was no palpable and bowel sounds were normal. She was alert and fully oriented, with motor strength and sensation normal in all extremities. On lower extremitas were necrotic skin changes with size as baby hand, irregular shape, filled with necrotic issue and erythematous edges. Similar changes were on inner side of the left thigh and left toe.

Her medical history included hypertension, diabetes mellitus and hyperlipidemia, chronic kidney disease and hepatitis C. Medications at the time of presentation included aspirin 100 mg on second day, Pantoprazol 20 mg daily, Pentoxiphyllin 200mg twice a day, Digoxin 0.05 mg on second day, Isosorbnitrate 10 mg twice a day, Amlodipin 10 mg daily, Folic acid 5 mg daily, Insulin with sheme and Letrox with sheme.

Laboratory findings

- Erythrocytes (RBC) 3.65x10⁹/L, hemoglobin 110 g/L (r.v. RBC 3.80-5.00x10⁹/L, Hgb 120-160g/L)
- White blood cell (WBC) count 9.31x10⁹/L(differential count: 5.38% neutrophils, 2.78% lymphocytes, 0.57% monocytes) (r.v. WBC 4.00-10.00x10⁹/l, Neu 1.80-7.80, Lym 0.800-4.60, Mono 0.800-1.50, Eos 0.00-2.00, Baso 0.00-0.200)
- Platelet count 209x10⁹/L (r.v. PLT 150-400x10⁹/L)
- C-reactive protein (CRP) 16.8 mg/L (r.v.0-5mg/l)
- Normal values of sodium, potassium, chloride (Na 140 mmol/l, K 4.5 mmol/l, Cl 101 mmol/l, serum calcium 2.02 mmol/l) and phosphate 1.65mmol/l.

(r.v. Na 136-145mmol/l, K3.6-5.2mmol/l, Ca 2.10-2.55mmol/l, Cl 98-108mmol/l, PO₄ 0.81-1.59mmol/l).

- PTH 15.6 pmol/L (r.v. 1,6 – 6,9 pmol/L), (PTH target values for dialysis patients and no needed therapy (8)).

- Urea nitrogen 23.4 mmol/L, serum creatinine 734 µmol/L (eGFR 4.92 mL/min/1.73m² V HBB) (r.v. urea 2.0-7.8mmol/l, kreatinine 45-115µmol/l).

- Acid-base status pH 7.48, pCO₂ 6.9 kPa, HCO₃ 24 mmol/L, base excess 0 mmol/L, pO₂ 6.8 kPa, sO₂ 96%.

2nd day of hospitalization

Consultation of plastic surgeon.

Indication – skin biopsy

4th day of hospitalization

Op. Excisio. Ph. Suturaa.

Th/ Toilete, Pain killers, Antibiotic, Swelling of the wound every second day.

13th day after hospitalization

Skin biopsy: Ph / Calciphylaxis.

15th day after hospitalization

Wound microbiology: Staphylococcus aureus (S. Gentamycin, Clinadamycin, Trimethoprim/sulphametaxazole, Fuscid acid, Chloramphenicol, Ciprophloxacin).

4. DISCUSSION

Calciphylaxis is a rare, but serious, kidney complication. Calciphylaxis was diagnosed based on clinical and histological data and antibiotics, diet regimen to reduce calcium and phosphate balance plus local hydrogel dressing were prescribed.

In our case laboratory investigations were consistent with chronic kidney injury as late complication of diabetic nephropathy. Complete blood count was significant for a hemoglobin level of 110 g/L (target values for dialysis patients) due to anemia of chronic disease with no evidence of leukocytosis or band cells. Platelet count was 209. Chemistry report was remarkable for normal anion gap metabolic acidosis, in addition to high level parathyroid hormone but as a target value for dialysis patients and no needed therapy. Phosphate level was 1.65 with calcium-phosphate product of 3.3 (Calcium level 2.02mmol/l). Calciphylaxis was suspected based on clinical grounds. Skin biopsy and histological evaluation revealed specific inflammation and necrosis with calcification involving small arteries and surrounding fibroadipose tissue. The cutaneous lesions are described as the sudden development of tender, violaceous skin lesion of livedo reticularis that progress to necrotic ulcerations, which frequently become superinfected. These ulcers heal poorly and are very painful. The diagnosis can be based on clinical grounds, supported by histological analysis if necessary. The laboratory workout must cover all the possible implications of chronic kidney disease with special attention to Ca⁺ and P⁺ values and evidence of skin or systemic infection. The treatment must focus on local wound care and metabolic control. It is essential to prevent local and systemic infection. Wound care involves the use of enzymatic debriding agents, hydrocolloid or hydrogel dressings, avoiding tissue trauma or

excessive manipulation and prescribing systemic antibiotics as needed. Surgical debridement is controversial due to increased risk of sepsis and worsening pain. As calciphylaxis is a very painful and debilitating disease nutritional and psychological support as well as specialized pain management must be provided. Sodium thiosulfate has been proposed as a novel and efficient therapy for calciphylaxis as marked improvements with reduction of pain, inflammation and healing of lesions have been demonstrated within a few days to months of use. In our case, goals of care and prognosis were discussed with the family, who continued to dialysis therapy and elected to proceed with palliative and comfort measures with no further invasive surgical or medical interventions. Although uncommon, calciphylaxis must be known by dermatologist and nephrologist as early diagnosis and proper management can be decisive for better prognosis.

5. CONCLUSION

The diagnosis can be based on clinical grounds, supported by histological analysis if possible. The laboratory workout must cover all the possible implications of chronic kidney disease with special attention to Ca⁺ and P⁺ values and evidence of skin or systemic infection. Calciphylaxis must be known by dermatologist as early diagnosis and proper management can be decisive for better prognosis. Calciphylaxis must be known by dermatologist as early diagnosis and proper management can be decisive for better prognosis.

- **Authors contribution:** All authors were included in all steps of preparation this case report. Final proof reading was made by the first author.
- **Conflict of interest:** None declared.
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