Folia Cardiologica 2020
tom 15, nr 2, strony 164–168
DOI: 10.5603/FC.2020.0022

ISSN 2353–7752

Calciphylaxis — a fatal complication not only in end-stage renal disease patients

Kalcyfilaksja — śmiertelne powikłanie nie tylko u pacjentów ze schyłkową niewydolnością nerek

Ada Bielejewska[1], Arkadiusz Bociek[1], Andrzej Jaroszyński[1, 2]

[1]Collegium Medicum, Jan Kochanowski University, Kielce, Poland
[2]Nephrology Clinic, Provincial Integrated Hospital in Kielce, Poland

Abstract

We present a fatal case of the end-stage renal disease complication that is calciphylaxis. Also known as calcific uremic arteriolopathy, it is characterised by vascular calcification, necrosis of the skin and adipose tissue, and constant severe pain of the affected areas.

Key words: calciphylaxis, calcific uremic arteriolopathy, end-stage renal disease, complications

Folia Cardiologica 2020; 15, 2: 164–168

Introduction

Calciphylaxis, also known as calcific uremic arteriolopathy (CUA), is a rare disease with an estimated annual incidence ranging from 1 to 35 in every 10,000 haemodialysed patients worldwide [1]. Its pathogenesis in unclear. Calciphylaxis affects small vessels of the skin and fatty tissue, as calcium deposits accumulate within their walls. This, together with thrombotic occlusion, leads to ischaemic necrosis of the skin that causes severe pain within the affected areas [1, 2]. Typical clinical manifestation of the disease includes extremely painful skin lesions, starting as tender red areas and often later transforming into eschars, ulcerations or gangrene, most commonly located on the patient's legs. The distal pattern involves extremities below the knee and elbow joints, and the proximal pattern involves the areas of the inner thighs, buttocks and abdomen [2]. Calciphylaxis is most commonly associated with end-stage renal disease (ESRD), although non-uremic calciphylaxis has been observed in patients with primary hyperparathyroidism, some cancers (treated with chemotherapy), liver cirrhosis, and autoimmune diseases. Risk factors of calciphylaxis include, among others, haemodialysis, female sex, obesity, diabetes mellitus, Caucasian ethnicity, hypercalcemia, hyperphosphatemia, hyperparathyroidism (both primary and secondary), adynamic bone disease, elevated alkaline phosphatase, autoimmune diseases, hypoalbuminemia, genetic polymorphisms, abnormalities within the coagulation system, recurring skin trauma (*e.g.* from subcutaneous injections) and medications (e.g. warfarin, calcium, vitamin D, iron, and recombinant PTH) [1, 3, 4]. Calciphylaxis is associated with high mortality: more than 50% of patients die within a year of diagnosis, with sepsis as the main cause of death [2, 4].

Case report

A 64-year-old obese woman, suffering from insulin-dependent diabetes, arterial hypertension, ischaemic heart disease, atherosclerosis and ESRD (on haemodialysis), was

Adres do korespondencji: lek. Arkadiusz Bociek, *Collegium Medicum*, Uniwersytet Jana Kochanowskiego, al. IX Wieków Kielc 19A, 25–317 Kielce, Poland, e-mail: arkadiusz33333@gmail.com

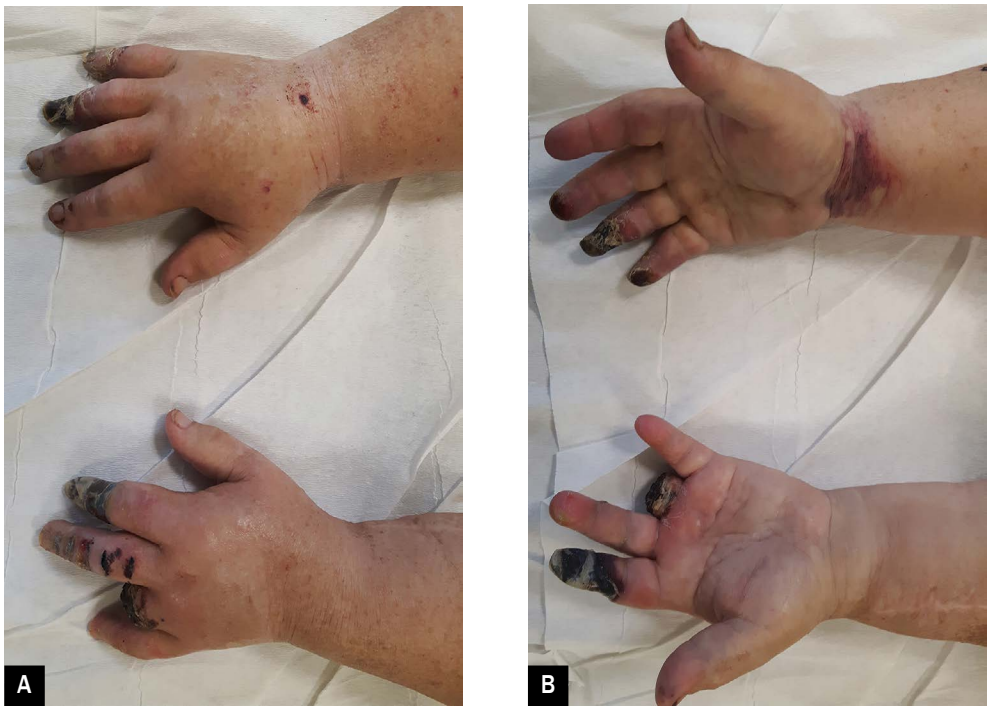

Figure 1. Patient's hands on admission — dorsal (**A**) and palmar (**B**) surface

referred to a vascular surgeon due to a suspicion of rapidly progressing atherosclerosis. After surgical consultation, she was admitted to hospital due to critical ischaemia of fingers and toes and suspected cutaneous necrotising vasculitis (Figures 1A, 1B and 2A–D). Physical examination revealed generalised oedema, bluish colouring of the skin proximally to ischaemic lesions on all extremities, an amputated left ring finger (up to the middle of proximal phalanx — Figures 1A and 1B), haematomas located on the skin of the abdomen and lumbosacral region, and restricted limb movement. The patient complained of constant severe pain in her hands and feet.

Laboratory tests revealed normocytic anaemia [red blood cells (RBC) 2.21 M/μL; hameoglobin (Hb) 6.8 g/dL; hematocrit (HCT) 21%], heightened inflammatory markers [white blood cells (WBC) 20.67 K/μL; C-reactive protein (CRP) 127.63 g/L], hyperparathyroidism [parathormone (PTH) 542 pg/mL, N: 15–65 pg/mL), hypoalbuminemia (2.74 g/dL, N: 3.50–5.50 g/dL), hypocalcemia (3.55 mEq/L, N: 4.50–5.50 mEq/L), and hyperphosphatemia (6.50 mg/dL, N: 2.50–4.80 mg/dL). A skin biopsy was performed, but no sign of calcification was found. Chest, abdomen and lower and upper limb X-rays were ordered. These showed extensive calcification in projections of visceral arteries and arteries of the limbs (Figures 3 and 4).

Due to an increased CRP, wounds were swabbed. Methicillin-susceptible *S. aureus* (MSSA), *A. baumannii* and *C. parapsilosis* were found. Therapy comprising ciprofloxacin, vancomycin and ceftriaxone was initiated. Haemodialysis was conducted daily, but due to oral mucosal bleeding, heparin was discontinued (coagulation parameters were within limits). A pain management consultation was made: morphine and paracetamol therapy was initiated, and later changed to buprenorphine. Due to anaemia, a total of 9 units of packed red blood cell were transfused. Cinacalcet was used to treat hyperparathyroidism. The patient's general state was slowly deteriorating: she was somnolent, limbs were oedematous, necrotic areas were enlarging, and liquefactive necrosis of the left hand appeared. A surgical consultation was made and the patient was preliminarily qualified for left upper limb amputation. Vascular disorder was treated with apixaban, and sodium thiosulfate was ordered, although the patient died due to multi-organ dysfunction before this could be received.

Discussion

Calciphylaxis, although uncommon even in high risk groups of patients [1], is an important, and potentially fatal, complication of ESRD. This is why doctors should be vigilant

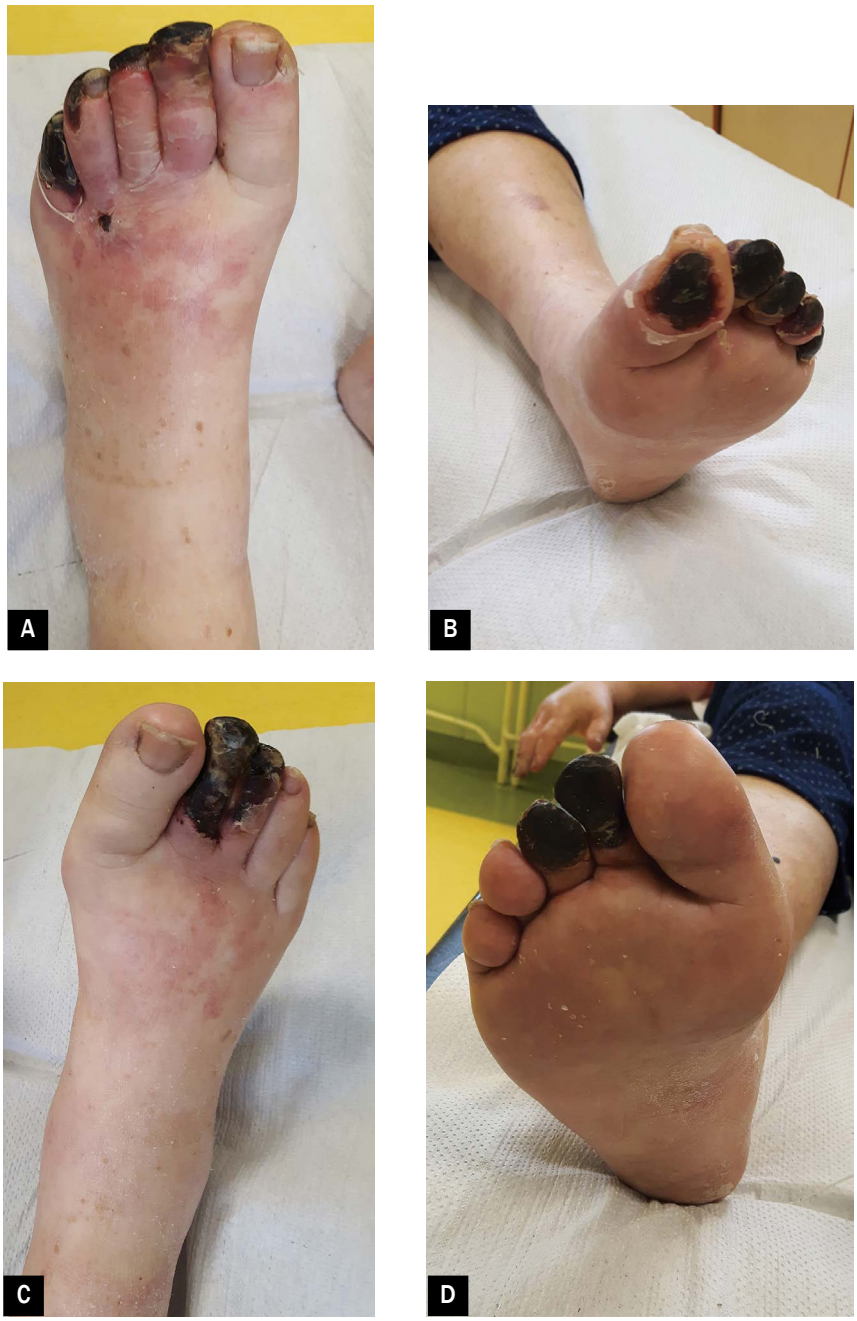

Figure 2. Patient's feet on admission — dorsal (**A**) and plantar (**B**) surface of left foot, dorsal (**C**) and plantar (**D**) surface of right foot

about it. If a patient presents risk factors for developing calciphylaxis, its typical signs, such as painful ischaemic skin lesions, should suggest the need for further diagnostics, which can be tricky.

In this particular case, the patient had multiple risk factors of developing calciphylaxis — she was a Caucasian obese woman suffering from diabetes and ESRD (undergoing haemodialysis), with hyperphosphatemia, hypoalbuminemia and hyperparathyroidism. She also presented with typical symptoms — necrosis of the skin and constant severe pain. She was consulted by a general practitioner, who believed that the lesions were a result of atherosclerosis, and then a vascular surgeon, who ruled out an atherosclerotic basis for the symptoms but did not make an alternative diagnosis. The diagnosis was not in fact made until after the patient had been admitted to the Nephrology Clinic. Even then, the results of additional tests were not consistent with the diagnosis. The skin biopsy, which is considered the gold standard in the diagnosis of calciphylaxis [4, 5], showed no signs of intravascular calcifications.

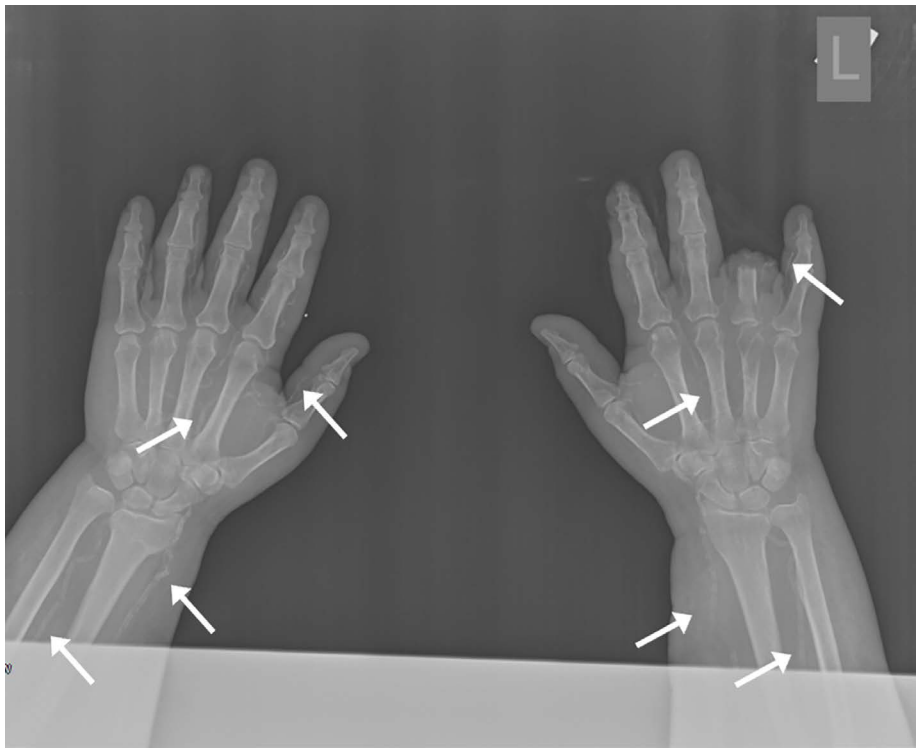

Figure 3. X-ray of both hands. Arrows point out massive calcifications in projections of arteries

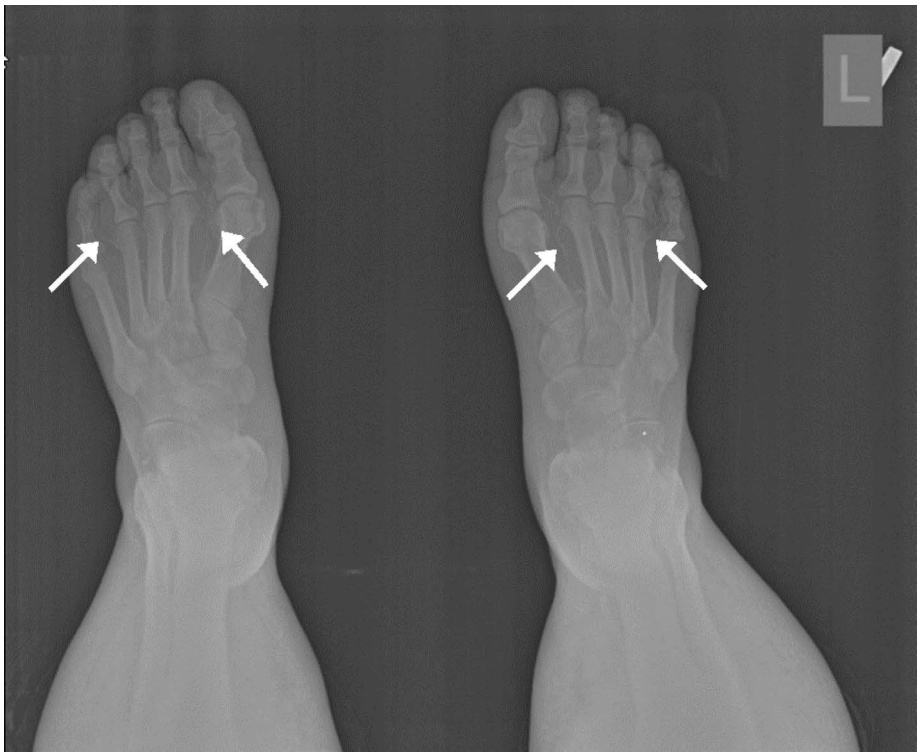

Figure 4. X-ray of both feet. Arrows point out massive calcifications in projections of arteries

Performed X-rays showed continuous calcifications in the projections of arteries, but these were misidentified as calcium deposits in atheromatous plaques.

When these symptoms occur, complex and multimodal treatment is necessary, including analgesics, wound debridement, use of a hyperbaric chamber, infection prevention, proper nutrition (to prevent malnutrition), and the elimination of risk factors. Pharmacological therapy involves the use of anticoagulants (the decision is made individually considering the risk of bleeding) or intravenous sodium thiosulfate [1, 4, 6]. Sodium thiosulfate is often used in treating calciphylaxis [1, 4], but it is not available in Poland and must be imported, which is time-consuming and reduces the chances of wound healing and overall survival.

Because of its high mortality and limited therapeutic options, prevention and early diagnosis are the key elements of treating calciphylaxis.

Conflict(s) of interest

The authors report no conflict of interest.

Streszczenie

Przedstawiono śmiertelny przypadek schyłkowej niewydolności nerek powikłanej wystąpieniem kalcyfilaksji — stanu, w którym dochodzi do kalcyfikacji w obrębie naczyń, martwicy skóry i tkanki podskórnej oraz stałego silnego bólu w obszarach dotkniętych procesem chorobowym.

Słowa kluczowe: kalcyfilaksja, wapniejąca arteriolopatia mocznicowa, schyłkowa niewydolność nerek, powikłania

Folia Cardiologica 2020; 15, 2: 164–168

References

1. Nigwekar SU, Thadhani R, Brandenburg VM. Calciphylaxis. N Engl J Med. 2018; 378(18): 1704–1714, doi: 10.1056/NEJMra1505292, indexed in Pubmed: 29719190.
2. Bhambri A, Del Rosso JQ. Calciphylaxis: a review. J Clin Aesthet Dermatol. 2008; 1(2): 38–41, indexed in Pubmed: 21103322.
3. Nigwekar SU, Kroshinsky D, Nazarian RM, et al. Calciphylaxis: risk factors, diagnosis, and treatment. Am J Kidney Dis. 2015; 66(1): 133–146, doi: 10.1053/j.ajkd.2015.01.034, indexed in Pubmed: 25960299.
4. Nigwekar SU. Calciphylaxis. Curr Opin Nephrol Hypertens. 2017; 26(4): 276–281, doi: 10.1007/springerreference_40538, indexed in Pubmed: 28375870.
5. Halasz CL, Munger DP, Frimmer H, et al. Calciphylaxis: comparison of radiologic imaging and histopathology. J Am Acad Dermatol. 2017; 77(2): 241–246.e3, doi: 10.1016/j.jaad.2017.01.040, indexed in Pubmed: 28285781.
6. Cucchiari D, Torregrosa JV. Calciphylaxis in patients with chronic kidney disease: a disease which is still bewildering and potentially fatal. Nefrología (English Edition). 2018; 38(6): 579–586, doi: 10.1016/j.nefroe.2018.09.001.