

Metastatic Calcification and Calciphylaxis in a Hemodialysis Patient

Hemodiyaliz Hastasında Metastatik Kalsifikasyon ve Kalsiflaksi

ABSTRACT

While metastatic calcifications are frequently observed in patients treated with dialysis, calciphylaxis remains as a rare but a life-threatening complication. Calciphylaxis results in tissue ischemia and necrosis and is highly progressive. In this case, we report a rapidly progressing calciphylaxis case as well as pointing to the significance of early diagnosis and treatment and the need for a multidisciplinary approach.

KEY WORDS: Calciphylaxis, Chronic renal failure, Hemodialysis

ÖZ

Diyaliz tedavisi gören hastalarda metastatik kalsifikasyon sıklıkla gözlenmekle beraber, kalsiflaksi nadir ve hayatı tehdit eden bir komplikasyondur. Kalsiflaksi doku iskemi ve nekrozu sonucu oldukça hızlı ilerler. Bu yazıda, hızlı ilerleyen bir kalsiflaksi olgusunun erken tanı ve multidisipliner yaklaşımla tedavisini sunduk.

ANAHTAR SÖZCÜKLER: Kalsiflaksi, Kronik böbrek yetmezliği, Hemodiyaliz

Savaş SİPAHİ¹
Ayşenur UÇAR²
Selçuk YAYCI²
Reyhan ÇETİNKAYA³
Ali TAMER²

- 1 Sakarya University Education and Research Hospital, Division of Nephrology, Sakarya, Turkey
- 2 Sakarya University Education and Research Hospital, Department of Internal Medicine, Sakarya, Turkey
- 3 Sakarya University Education and Research Hospital, Department of Dermatology, Sakarya, Turkey

INTRODUCTION

Metastatic calcifications are frequent in patients treated with hemodialysis. Calciphylaxis, in other words calcific uremic arteriopathy (CUA), is a rare but life-threatening complication. The pathogenesis of calciphylaxis has not clearly been understood yet. Micro-vascular ischemia is observed on dermohypodermic arterioles as a result of mural calcification, intimal fibrosis and decreased arteriolar blood supply (1). Painful ischemic necrosis emerges on dermis and subcutaneous adipose tissue as a result. Painful and non-healing skin ulcers are clinically observed with progression and can result in evident morbidity and mortality. The lesions characteristically appear on the lower extremity, partially on the gluteal zone and rarely on the abdomen, upper extremity and penis (2). In hemodialysis patients, the incidence is around 1%, and the prevalence 4.1% (3).

CASE REPORT

A 54-year-old female patient, who had been on the hemodialysis program for 7 months due to chronic renal failure caused by type II Diabetes Mellitus, presented at our nephrology outpatient service with complaints of abdominal pain, feet pain and colour change on her skin. Physical examination revealed a blood pressure of 70/30 mmHg, pulse rate 96/mn, and body temperature of 38.2 C. The patient was morbidly obese and her BMI was 41 kg/m². The patient had ulcers of 22x8.5x1.5 cm from place to place on the necrosis ground in the suprapubic zone and lesions of 6x4.5x0.5 cm from place to place on the necrotized ground in the face area of the bilateral tibia (Figure 1A-F). Her biochemical findings were as follows: white blood cell count 12.400/mm³, haemoglobin 9.4 gr/dl, urea 205 mg/dl, creatinine 6.6 mg/dl, albumin 3.5 gr/dl, calcium 9.4mg/dl, phosphorus 8.4 mg/dl, calcium phosphorus factor 75.2 mg²/



Received : 18.01.2013

Accepted : 15.02.2013

Correspondence Address:

Savaş SİPAHİ
 Sakarya Üniversitesi Eğitim ve Araştırma Hastanesi, Nefroloji Bölümü,
 Sakarya, Turkey
 Phone : +90 264 275 10 10
 E-mail : savassipahi@yahoo.com



Figure 1: Pre-treatment and post-treatment skin lesion appearance of the case (pre-treatment A,B,C; post-treatment D,E,F)

dl², parathyroid hormone 209 pg/dl and C-reactive protein 124 mg/L. The patient was hospitalised with the pre-diagnoses of sepsis and CUA. Vancomycin was initiated at a dose of 1 gr/72 hours along with 100 mg/day amikacin according to Infectious Diseases and Dermatology consultations. An inotropic agent (Dopamine 10mcg/kg/min) was required within the first 24 hours of the patient's treatment. Additionally, surgical debridement was performed at the suprapubic zone. Result of the biopsy taken from lesions was reported as calciphylaxis and phlegmonous inflammation (Figure 2). During follow-up, hemodialysis sessions of the patient were increased to four times a week at five hours each (20 hours/week) from three times a

week at four hours each (12 hours/week). The protein content of the patient's diet was increased (1.5gr/kg/days). Abound solution® (beta-hydroxy-beta-methylbutyrate, arginine and glutamine) was added to the treatment in order to accelerate wound healing. The patient recovered one month later and was free of any skin lesions. She was discharged from the hospital and put on outpatient follow-up. At discharge, her laboratory findings were as follows: white blood cell count 5.500/mm³, haemoglobin 9.8 gr/dl, urea 146 mg/dl, creatinine 4.4 mg/dl, albumin 3.5 gr/dl, calcium 9.3 mg/dl, phosphorus 5.5 mg/dl, calcium phosphorus factor 51.15mg²/dl², parathyroid hormone 42.8 pg/dl and C-reactive protein 14mg/L.

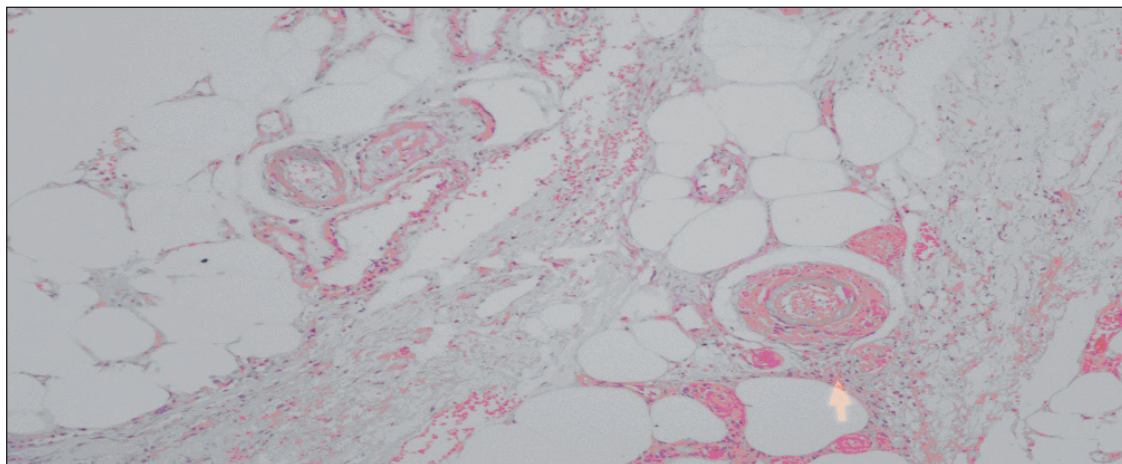


Figure 2: Calcification is observed on small and medium sized blood vessel walls in the zones that correspond to the skin dermis and subcutaneous adipose tissue.

DISCUSSION

In this article, we presented a successfully treated case with calcific uremic arteriopathy, which is rarely observed in hemodialysis patients.

While the pathogenesis of the calcific uremic arteriopathy is not clear, disorders in mineral metabolism are anticipated to play a role. Among them, the best known are hyperphosphatemia, hyperparathyroidism, increased calcium phosphorus factor and active use of vitamin D (4,5,6). Deficiencies of fetuin-A and matrix Gla protein, which are among the vascular calcification inhibitors, might also accompany these changes (7). While data on the treatment of CUA are limited in the literature, a prospective study showed an association between decreased use of calcium salts and decreased frequency of CUA (8). There is no consensus on treatment approach, due to the lack of a randomised-controlled studies. Multidisciplinary treatment approaches that involve the local wound, its care, a good metabolic control and correction of other underlying comorbid conditions are suggested (7).

Angelis et al. indicated that CUA would be more frequent compared to past due to the increase in the number of patients receiving HD treatment (9). CUA can generally result in tissue necrosis, gangrene and sepsis. While the prognosis is bad, the mortality rate is still high (7).

Even though CUA is a clinical condition that is frequently encountered in patients with chronic renal failure of generally 9 months and 2 years and a dialysis history, this case had been receiving the hemodialysis treatment for only 7 months (7). Her history revealed non-compliance with her treatment. Upon her application to the hospital, the primary approach was to struggle with sepsis since she suffered from worsening sepsis. Harler has suggested starting aggressive local wound care in order to prevent the local and systemic infections (10). Following the hospitalisation of the patient, we performed surgical debridement. Additionally, advanced nutritional support and more specifically increased diet protein intake have been suggested to be beneficial in accelerating the wound healing (10). In our case, Abound® was used in the treatment in addition to the diet in order to accelerate wound healing. The dialysis frequency and duration were extended to 20 hours a week in an attempt to prevent the negative metabolic control and enable faster recovery.

Secondary hyperparathyroidism is one of the factors accused in the pathogenesis of CUA (7). The parathyroid hormone level of our case was 209 pg/dl during the first hospital presentation. However, serum calcium level was 9.4 mg/dl, phosphorus 8.4 mg/dl and calcium phosphorus factor was 75.2mg²/dl², suggesting poorly controlled mineral metabolism. In order to control calcium phosphorus levels, we tried to keep the calcium phosphorus factor below 55 and the phosphorus level below 5 mg/dl. For that purpose, we added sevelamer HCl 3x2 tb regularly, increased the dialysis dose and switched to low-calcium dialysate (1.25 mmol).

Regarding the local wound care and debridement of CUA, which is rarely observed in final-stage renal failure patients and progresses with high mortality and morbidity, our case shows a successful approach with intensive dialysis treatment, for the struggle of the case with the sceptical condition and for a good metabolic control. The application of hyperbaric oxygen treatment would have contributed to faster treatment of the case but there is no hyperbaric oxygen treatment centre in our province. The available dynamic multidisciplinary approach enabled the patient to recover and get discharged from the hospital.

In conclusion, treating CUA at an early stage with a multidisciplinary intensive approach can prevent unfavourable outcomes.

ACKNOWLEDGEMENTS

The authors wish to warmly thank F Husniye Dilek, MD, from the Department of Pathology and Hakan Demir, MD, from the Department of General Surgery for their contributions.

REFERENCES

1. Weenig RH: Pathogenesis of calciphylaxis: Hans Selye to nuclear factor kappa-B. *J Am Acad Dermatol* 2008; 58(3): 458-471
2. Janigan DT, Hirsch DJ, Klassen GA, MacDonald AS: Calcified subcutaneous arterioles with infarcts of the subcutis and skin (Calciphylaxis) in chronic renal failure. *Am J Kidney Dis* 2000; 35(4): 588-597
3. Angelis M, Wong LL, Myers SA, Wong LM: Calciphylaxis in patients on hemodialysis: A prevalence study. *Surgery* 1997; 122(6): 1083-1089
4. Mazhar AR, Johnson RJ, Gillen D, Stivelman JC, Ryan MJ, Davis CL, Stehman-Breen CO: Risk factors and mortality associated with calciphylaxis in end-stage renal disease. *Kidney Int* 2001; 60(1): 324-332
5. Block GA: Hyperphosphatemia has been regarded as a risk factor for calciphylaxis. *Clin Nephrol* 2000; 54(4): 318-324
6. Wilmer WA, Magro CM: Calciphylaxis: Emerging concepts in prevention, diagnosis, and treatment. *Semin Dial* 2002; 15(3): 172-186
7. Goel SK, Bellovich K, McCullough PA: Treatment of severe metastatic calcification and calciphylaxis in dialysis patients. *Int J Nephrol* 2011; 2011: 701603
8. Fine A, Fontaine B: Calciphylaxis: the beginning of the end? *Perit Dial Int* 2008; 28(3): 268-270
9. Angelis M, Wong LL, Myers DPH, Wong LM: Calciphylaxis in patients on haemodialysis: A prevalence study. *Surgery* 1997; 122(6): 1083-1089
10. Hahler B: Calciphylaxis in the patient with chronic renal failure. *Dermatol Nurs* 2001; 13(6): 435-436, 449