

Uraemic Gangrene Syndrome

LÁSZLÓ TÖRÖK¹ and LÁSZLÓ KÖZÉPESSY²

¹Department of Dermatology and ²Department of Nephrology and Dialysis, County Hospital, Kecskemét, Hungary

Cutaneous gangrene and vascular calcinosis are described in a patient with chronic kidney failure and hyperparathyroidism. A review of 67 earlier described cases suggests that the symptoms constitute a unique syndrome.

(Accepted March 4, 1991.)

Acta Derm Venereol (Stockh) 1991; 71: 455–457.

L. Török, Department of Dermatology, County Hospital, H-6000 Kecskemét, Nagykörösi u. 15, Hungary.

Simultaneous occurrence of cutaneous gangrene and vascular calcification following chronic renal failure was first described by Bryant & White in 1898 (1) as "gangrenous calcification". Later, as dialysis and kidney transplantation became increasingly common, this rare and bizarre group of symptoms has been observed several times casuistically (2–9). Thus up to 1990, case histories of 67 patients were related together with the 48 cases collected by Bourland et al. (10). It could be supposed that the above-mentioned symptoms form an independent clinical entity. The aim of this paper is to call attention to the syndrome as a new one, presenting a typical case with the help of related literature.

CASE REPORT

A 44-year-old female patient presented, who had undergone haemodialysis for 4 years. Painful livid erythema, having to some extent a web-like appearance, appeared with irregular shape on the curved surface of both calves. Subsequently the patient developed haemorrhagic necrosis, then extremely painful ulcers with a coated base (Fig. 1). Histologic examination of samples from the edge of the ulcers indicated pronounced vascular wall calcification (Fig. 2).

On the basis of these findings, metastatic calcinosis was suspected. The PTH level was markedly increased. Among various other laboratory results we can mention slight anaemia, an increased alkaline phosphatase value (179 μ l), a normal value of calcium and increased phosphorus value (2.7 μ mol/l). Calcium and phosphorus product was 5.9.

X-ray examination revealed subperiosteal cystic zones in area of the handbones, while slight calcification of the walls of blood vessels could be detected in the region of lower arms. Ultrasonic examinations revealed calcification in the aorta, in one aorta-valve and in the right kidney.

On the basis of our findings, secondary hyperparathyroidism developing as a result of chronic uraemia was diagnosed. Metastatic calcinosis in the heart and in blood vessels was assumed to have been caused by it. Since the syndrome did not respond to conservative treatment, subtotal parathyroidectomy was performed.

No hyperplasia could be observed in the removed parathyroids. Following operation, ulcers soon became less and less painful and healed with local treatment. No dermatologic symptoms were observed during an observation period of 2 years.

DISCUSSION

The question of grouping these characteristic symptoms into the syndrome was first raised by Gipstein et al. in 1976 (11): They called it "a syndrome of tissue necrosis and vascular calcification in patients with chronic renal failure". We would prefer to suggest the name 'Uraemic gangrene syndrome' since the dominant symptoms of the syndrome are cutaneous necroses and ulcers reluctant to heal. The ischaemic gangrene mainly affects the acral parts of the limbs and the trunk (10). Ulcers frequently develop with painful sooty or web-like livido erythema



Fig. 1. Ulcer with haemorrhagic base.

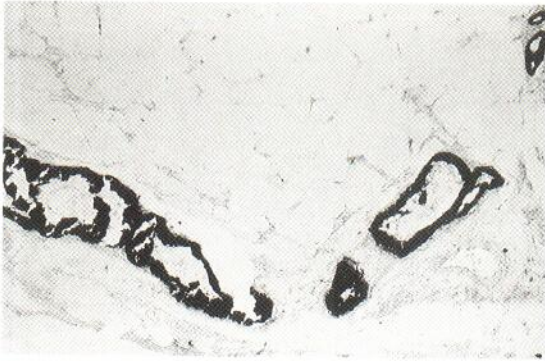


Fig. 2. Venula size vessel with subendothelial calcification. Kossa dye, $\times 100$.

(12, 17). More rarely, subcutaneous lupus, palpable and reticular necrotic purpurae are observed. The ischaemic process can also in some cases affect muscles and bowel (3, 4, 19, 20).

This group of symptom occur among patients with long-term chronic uraemia, requiring dialysis and kidney transplantation (2, 4, 12, 16). The cause of the renal failure does not seem to play an essential role in development of the complication. Nor was any characteristic age of predilection found, although it seems to be more frequent in women (10).

Various blood vessel changes have been described in the dermis and subcutis through histological examinations: media calcification with thrombosis and with intima-proliferation occur more frequently, while intima-calcification or that of media and even lack of vessel-wall calcification are relatively rare (9, 10, 18).

Secondary hyperparathyroidism was found in nearly every case (1). In making the diagnosis of azotaemic hyperparathyroidism, normal or increased calcium and phosphorus products, elevated PTH level, osteitis fibrosa, ectopic calcifications and, following operation, histologic examination of the parathyroids displaying diffuse hyperplasia can be of some help. Vascular calcification develops with uraemic necroses in almost every patient (9). On the other hand, in patients with uraemia but without gangrene, calcification was seen in only 20% of the patients. If hyperparathyroidism also developed it was found in 50–70% of the patients (4, 10, 14, 15). Radiologic examinations revealed changes mainly in small and medium arteries, but they can also be traced in 0.5–0.1 mm subcutaneous blood vessels, with the help of xeroradiography (21).

The pathomechanism of uraemic necroses has not

been clarified yet. It is very probably of multifactorial origin, in the development of which renal failure, elevated calcium and phosphorus products, secondary hyperparathyroidism, calciphylaxis as predisposing factor, and other known or unknown precipitating factors (tissue damage, medications, etc) may play a role (7, 10–12, 18, 22). Among the above-mentioned factors, secondary hyperparathyroidism or PTH seem to be the most interesting (7, 10–12, 14). A high PTH level in renal failure can damage the vessel-wall *per se* (9). Recently the role of coagulation factors such as protein C was described (9, 23).

In the treatment of developed torpid gangrene, it is always worth carrying out a subtotal or total parathyroidectomy (10, 11). Following the operation, in two-thirds of all cases, pain abates quickly, progression stops and therapy-resistant ulcers do heal. An operation is also worth considering in cases where the skin symptoms are livido racemosa and palpable haemorrhagic infiltration. Some authors recommend an operation prophylactically, when there is vascular calcification detected by xeroradiography at an early stage (24).

REFERENCES

1. Bryant JH, White WH. A case of calcification of the arteries and obliterative endarteritis associated with hydronephrosis in a child aged six months. *Guys Hosp Rep* 1899; 55: 17–28.
2. Friedman S, Novack S, Thomson G. Arterial calcification and gangrene in uremia. *N Engl J Med* 1969; 220: 1392–1394.
3. Goodhue WW, Davis JN, Porro R. Ischemic myopathy in uremic hyperparathyroidism. *JAMA* 1972; 221: 911–912.
4. Rosen H, Fiedman SA, Raizner AE. Azotemic arteriopathy. *Am Heart J* 1972; 84: 250–255.
5. Coburn JW, Gipstein RM, Mirahmadi KS, et al. Calciphylaxis in patients with renal disease: A unique syndrome manifested by soft tissue calcification and necrosis and linked to secondary hyperparathyroidism. *Clin Res* 1973; 21: 281.
6. Koranda FC, Dehmel EM, Kahn G. Cutaneous complications in immunosuppressed renal homograft recipients. *JAMA*; 229: 419–423.
7. Huertas VE, Maletz RM, Weller JM. Dermal necrosis due to thrombosis in severe secondary hyperparathyroidism. *Arch Intern Med* 1976; 136: 712–716.
8. Weidmann P. Successful treatment of ischaemic ulceration of the skin in azotaemic hyperparathyroidism with parathyroidectomy. *Br Med J* 1977; i: 552–553.
9. Miller JA, Machin SJ, Dowd PM. Cutaneous gangrene with hyperparathyroidism. *Clin Exp Dermatol* 1988; 13: 204–206.

10. Bourland A, Eggers S, Willcox D, et al. Calciphylaxie? *Dermatologica* 1989; 179: 165-169.
11. Gipstein RM, Coburn JW, Adams DA, et al. Calciphylaxis in Man. *Arch Intern Med* 1976; 136: 1273-1280.
12. Landerer CI, Dambacher MA, Staub JJ. Urämische Arteriopathie und ischämische Hautveränderungen. *Schweiz Med Wschr* 1983; 113: 162-170.
13. Gupta AK, Gupta MA, Cardella CJ, et al. Cutaneous associations of chronic renal failure and dialysis. *Int J Dermatol* 1986; 25: 498-503.
14. Hällgren R, Wibell L, Ejerblad S. Arterial calcification and progressive peripheral gangrene after renal transplantation. *Acta Med Scand* 1975; 198: 331-335.
15. Massry SG, Gordon A, Coburn JW, et al. Vascular calcification and peripheral necrosis in a renal transplant recipient. *Am J Med* 1970; 49: 416-422.
16. Cohen EB, Komorowski RA, Clowry LJ. Cutaneous complications in renal transplant recipients. *Am J Clin Pathol* 1987; 88: 32-37.
17. Winkelmann RK, Keating FR. Cutaneous vascular calcification, gangrene and hyperparathyroidism. *Br J Dermatol* 1970; 83: 263-268.
18. Leroy D, Barrellier M-T, Zanella D, et al. Purpura réticulé et nécrotique (A type d'angiodermite nécrotique) du a des calcifications artérielles au cours d'une insuffisance rénale chronique. *Ann Dermatol Veneréol* 1984; 111: 461-466.
19. Richardson JA, Herron G, Reitz R, et al. Ischemic ulcerations of skin and necrosis of muscle in azotemic hyperparathyroidism. *Ann Int Med* 1969; 71: 129-138.
20. Clark JG, Sumerling MD. Muscle necrosis and calcification in acute renal failure due to barbiturate intoxication. *Br Med J* 1966; ii: 215-216.
21. Lazarik FC, Friedman AK, Leyden JJ. Xeroradiographic observations in four patients with chronic renal disease and cutaneous gangrene. *Arch Dermatol* 1981; 117: 325-328.
22. Conn J, Krumlowsky FA, et al. Calciphylaxis: Etiology of progressive vascular calcification and gangrene? *Ann Surg* 1973; 177: 206-210.
23. Mehta RL, Scott G, Sloand JA, et al. Skin necrosis associated with acquired protein C deficiency in patients with renal failure and calciphylaxis. *Am J Med* 1990; 88: 252-257.