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Synergy of sodium thiosulphate treatment and expanded hemodialysis in the management of calciphylaxis? A case report

¿Sinergia del tratamiento con tiosulfato sódico y hemodiálisis extendida en el manejo de la calcifilaxis? A propósito de un caso

Dear Editor,

Calciphylaxis, also known as calcific uraemic arteriolopathy (CUA), is a serious and uncommon complication in patients on chronic haemodialysis.[1] In its pathogenesis, in addition to the involvement of bone-mineral metabolism, the possible deleterious role that certain medium-sized molecules could play has been hypothesised.[2] Expanded haemodialysis (HDx) facilitates the effective removal of this type of molecules, so we believe that they could play a role in the management of this condition.

We present the case of a 47-year-old woman with a history of long-standing and poorly-controlled type 1 diabetes mellitus, arterial hypertension, chronic ischaemic heart disease, and severe aortic stenosis, who required aortic valve replacement with initiation of anticoagulation with acenocoumarol two months before admission. The patient also had secondary hyperparathyroidism and chronic kidney disease category G5 according to KDIGO 2012 of probable diabetic aetiology, receiving chronic haemodialysis through a radiocephalic arteriovenous fistula placed in the left upper limb.

She reported a two-week history characterised by the presence of initially small and erythematous lesions that progressed to being ulcerative, some of them were circular with a blackish centre, very painful, and with exudate that was positive for *Pseudomonas aeruginosa*. A skin biopsy of one of the lesions was consistent with calciphylaxis, so the patient was admitted to nephrology ward. The following blood test results were obtained: procalcitonin 1.49 ng/m; C-reactive protein 26.6 mg; neutrophil-to-lymphocyte ratio (NLR) 5.75; platelet-to-lymphocyte ratio (PLR) 413.70 and systemic immune-inflammation index (SII) 1,737; calcium 10.30 mg/dl; phosphate 5.05 mg/dl; biointact parathyroid hormone (PTH) (1–84) 490 pg/m and 25-OH-vitamin D 10.8 ng/m. Cervical ultrasound showed a hypoechoic nodule 1.38 cm in diameter suggesting parathyroid gland hyperplasia vs hypertrophy.

Joint management with dermatology was decided upon with treatment every 48 hours with topical sodium thiosulfate, in addition to intravenous sodium thiosulfate at a dose of 12.5 g post-haemodialysis (three times a week). The dialysis dose was intensified with daily 210-minute sessions and changed to expanded haemodialysis with Theranova 500® 2 m^2 filter (Baxter International Inc., Deerfield, IL, USA) with a mean Qb of 313 ml/min, a mean Qd of 500 ml/min and a mean Kt of 41 L. Among other measures, the patient was changed to anticoagulation with enoxaparin and her treatment with paricalcitol, vitamin D and iron was suspended. Management of the patient's secondary hyperparathyroidism was optimised with cinacalcet, non-calcium-based phosphate binders and a low-calcium dialysis bath (1.25 mEq/L). Combination antibiotic therapy with ceftazidime and vancomycin was administered.

At discharge, there was evidence of improved inflammatory parameters along with favourable skin lesion progression until their complete resolution five months after the start of treatment (Table 1 and Fig. 1). However, we observed a worsening of PTH despite progressively increasing the calcimimetic dose. It was decided to start intradialysis etelcalcetide, pending progression at the present time.

Despite correct treatment, a large percentage of patients die (35% in one year, despite treatment and 55% if not treated).[3] It has been reported that the alteration of bone-mineral metabolism is the main predisposing factor for this disease.[1] However, this case highlights the possible role other non-traditional factors might play given the persis-

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Table 1 – Evolution of the patient's inflammatory parameters and bone-mineral metabolism.

	2 days before admission	Day 1	Day 2	Day 5	Day 10	Day 25	Day 27	Day 62	Day 64	Day 97	Day 125	Day 153
C-reactive protein (mg/L)	31.26	35.58	26.6		25.57	8.46		3.21		0.98		1.03
Procalcitonin (ng/mL)	0.83	1.35	1.49		1.04	0.74		0.99				
NLR	7.85	5.75	6.55	5.73	10.44	2.67	3.69	8.63	3.61	3.25	3.45	3.53
PLR	564.58	413.70	378.95	362.86	425.42	237.84	205.69	261.45	253.52	248.24	215.31	205.49
SII	2,128.48	1,737.53	1,887.16	1,455.06	2,620.61	704.00	933.84	1,871.95	649.01	685.13	727.73	659.64
Ferritin (ng/mL)										458.00		
Total protein (g/dL)	6.66		6.68	6.95	7.57			6.87		6.94		6.67
Leukocytes ($10^3/\mu l$)	5.00	5.93	6.59	5.74	7.81	5.05	6.76	8.97	3.90	4.06	4.95	4.80
Neutrophils ($10^3/\mu l$)	3.77	4.20	4.98	4.01	6.16	2.96	4.54	7.16	2.56	2.76	3.38	3.21
Lymphocytes ($10^3/\mu l$)	0.48	0.73	0.76	0.70	0.59	1.11	1.23	0.83	0.71	0.85	0.98	0.91
Haemoglobin (g/dL)	7.80	8.50	10.70	10.00	10.80	10.90	11.20	10.90	11.00	10.10	10.20	10.80
Platelets ($10^3/\mu l$)	271.00	302.00	288.00	254.00	251.00	264.00	253.00	217.00	180.00	211.00	211.00	187.00
Calcium (mg/dl)	10.19		10.30	9.64	9.77	9.79		10.18		10.06		9.92
Phosphates (mg/dl)	6.78		5.05		2.72					4.90		4.45
Biointact PTH (1-84) (pg/mL)			490.00		315.00					824.00		1,046.00

NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio: SII: systemic immune-inflammation index.

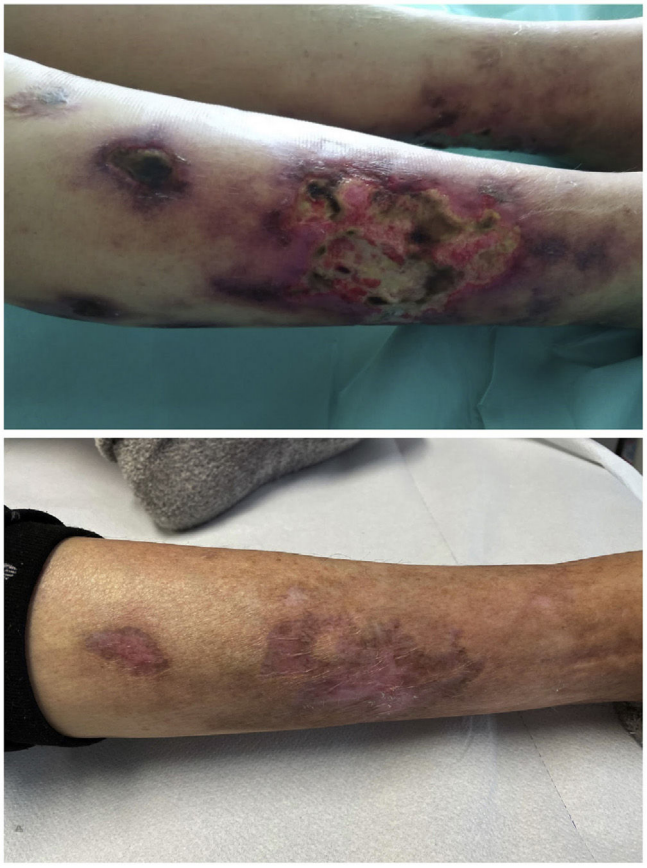

Fig. 1 – Lesions on the right lower limb during hospital admission (top) and five months after treatment with thiosulfate and expanded daily haemodialysis (bottom).

tence of hyperparathyroidism over time, despite there being substantial and sustained improvement in both lesions and inflammatory parameters.

Intravenous and topical thiosulfate could play a very important role in this regard. However, this may not be enough to explain the patient's rapid inflammatory and cutaneous improvement. In this sense, it should be noted that within the pathophysiology of the disease, the involvement of both an excess of cytokines and coagulation alteration has been postulated.[4] The possible role of adipokines deserves special mention, including Vascular Endothelial Growth Factor A (VEGF-A), which induces calcification and could explain the higher frequency of calciphylaxis in POEMS syndrome.[5] Similarly, leptin, another adipokine, has been linked to osteoblast promotion and smooth muscle cell mineralisation.[2] These two proteins weigh 46 kDa and 16 kDa, respectively, and this places them within the group of medium-sized molecules[6], which are the main target of expanded haemodialysis through the new medium cut-off membranes.

Therefore, in the absence of larger studies, we conclude that expanded haemodialysis could be a good complement to thiosulfate treatment in the management of calciphylaxis in patients on chronic haemodialysis.

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Acute kidney injury following naphthalene poisoning in children

Lesión renal aguda después de la intoxicación por naftalina en niños

Dear Editor:

Acute poisoning in children is a frequent cause of admission to emergency units and can lead to death and acute kidney injury (AKI). The incidence of poisoning in children varies from 0.33% to 7.6%.[1] Naphthalene poisoning can lead to a severe clinical Picture.[2] AKI due to naphthalene poisoning is very uncommonly reported in the literature, especially if it requires renal replacement therapy. Acute intravascular hemolysis may be the major mechanism of AKI in naphthalene poisoning.[3,4] In this study, we described a rare case of AKI following naphthalene poisoning in a pediatric patient successfully treated.

Table 1 – Laboratory findings on admission and during the follow-up of the patient.

Parameters	Admission	9 h	24 h	3rd Day	5th Day	10th Day	12th Day	13th Day	Discharge
Potassium	4.09	4.04	4.53	4.23	3.33	5.39	6.93	5.63	3.83
Sodium	135	136	130	137	139	137	135	136	134
Urea	45	62	55	80	51	67	79	65	69
Creatinine	0.7	1.4	1.4	2.1	1.9	2.2	2.6	1.7	1.2
eGFR	51	25.5	0	0	0	16.2	21	32.4	30
AST	75	1281	738	64	**	**	**	**	23
ALT	22	687	569	139	**	**	**	**	10
DB	0.23	**	2.87	1.31	0.33	**	**	**	**
IB	0.34	**	3.14	1.23	1.02	**	**	**	**
PT	12.1	12.2	13.8	11.6	11.2	12	**	12.5	**
aPTT	26.7	25.9	32	27.5	23.8	31.3	**	31.7	**
D-LDH	**	3205	**	972	**	**	**	**	**
Hemoglobin	13	11.1	10.1	8.5	7.8	7.4	8.1	9.5	10.1
Leukocytes	12,420	7940	8020	15,820	11,170	10,230	**	11,000	7530
Platelets	479,000	281,000	209,000	188,000	139,000	323,000	**	403,000	367,000
PH***	**	7.38	**	**	**	**	**	**	**
pCO2***	**	30.5	**	**	**	**	**	**	**
HCO3***	**	19.5	**	**	**	**	**	**	**

AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; D-LDH: D-lactate dehydrogenase; CK: Creatine phosphokinase; PT: Prothrombin time; aPTT: partial time of thromboplastin; DB: direct bilirubin; IB: Indirect bilirubin; eGFR: estimated Glomerular Filtration Rate. ** Not available. ***Arterial Gasometry.
Reference values: Potassium (3.5–5.5 mmol/L); Sodium (135–145 mmol/L); Chloride (96–109 mmol/L); Glucose (74–106 mg/dL); Urea (13–43 mmol/L); Creatinine (0.6–1.1 mmol/L); AST (<32 mg/dL); ALT (< 31 mg/dL); DB (< 1 UI/L); DI (< 1 UI/L); PT (10–14 s); aPTT (22–28 s); D-LDH (230–460 UI/L); Albumin (>3.5 UI/L); Hemoglobin 11.3/15.2 g/dL); leukocytes (3600–10,000/mm^3); platelets (150,000–450,000/mm^3); PH (7.35–7.45); pCO2 (35/45 mmHg); pO2 (85–100 mmHg); HCO3 (22/26 mmol/L); BE (−4/+4).

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