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Reflex sympathetic dystrophy of the lower limbs after kidney transplantation

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Abstract Reflex sympathetic dystrophy syndrome (RSDS) is a rarely described complication after different types of organ transplants. Three out of 147 kidney recipients treated at our center during the last 6 years developed severe bilateral symmetrical pain in the ankles and knees, with great difficulties in walking 2–3 months after kidney transplantation. Clinical examination revealed periarticular soft tissue swelling and vasomotor changes with no effusion. Patchy osteoporotic patterns were seen radiographically in clinically affected areas. Scintigraphy showed increased epiphyseal uptake of ^{99m}Tc with a periarticular distribution. Clinical symptoms, radiographic, and scintigraphic signs were compatible with so-called RSDS. The exact cause of the syndrome remained obscure. All patients received standard immunosuppression with cyclosporine A (CyA), azathioprine, and prednisone. Symptoms of RSDS improved when doses of CyA were reduced and blood levels declined; patients were treated with calcitonin and calcium channel blockers simultaneously. Non-steroidal antiinflammatory drugs were not effective in symptom relief. In all three cases, most probably spontaneous complete recovery was achieved over the course of 2–8 months; no one patient progressed to aseptic osteonecrosis.

Key words Reflex sympathetic dystrophy · Kidney transplantation

Introduction

Reflex sympathetic dystrophy syndrome (RSDS) consists of five fundamental features: a pseudo inflammatory syndrome of burning pain, hyperesthesia, edema, and hyperhidrosis of the affected extremity. RSDS is defined by a biochemical syndrome characterized by the absence of inflammatory signs, a radiological syndrome with a regional demineralization, a scintigraphic syndrome with an increased uptake of bone agent, and a more or less rapid regression of the condition with or without sequelae [2, 6].

We add three new cases to this interesting and rarely described osteoarticular complication following kidney transplantation.

Patients

One hundred and forty seven patients received a kidney graft at our center during the last 6 years. Three of them fulfilled the diagnostic criteria of RSDS. Their data are summarized in Table 1.

Results

Clinical symptomatology and physical examination

Between 1.5 and 3 months after transplantation, three patients started to complain of progressive bilateral symmetrical joint pain affecting the lower extremities, especially the knees, ankles, tarsi, and metatarsi, to dif-

Table 1 Characteristics of patients; normal values in parenthesis (*M* male, *F* female, *LRD* living, related donor, *CAD* cadaveric donor, *GN* glomerulonephritis, *ATN* acute tubular necrosis, *CyA* cyclosporine A)

Parameter	Patient number		
	1	2	3
Age (years)/sex	33/M	20/M	55/F
Graft number	2	1	1
Type of transplant	LRD	LRD	CAD
Nephropathy	GN	Reflex nephropathy	GN
Dialysis duration (years)	6.5	2.0	3.0
Transplantation complications	Second graft: ATN, ureteral fistula	Steroid-resistant rejection	None
S-creatinine (M 115, F 97 μmol/l)	173	135	67
S-calcium (2.25–2.65 mmol/l)	2.5	2.47	2.93
S-phosphorus (0.65–1.62 mmol/l)	0.91	0.89	0.72
S-magnesium (0.75–0.95 mmol/l)	0.78	0.71	0.60
Uric acid (167–416 μmol/l)	465	556	374
Alkaline phosphatase (M 0.8–2.6, F 0.7–2.1 μkat/l)	2.93	2.85	3.25
Bone density (T score)	−3.8	−1.8	−2.5
CyA trough levels (ng/ml) onset/end of symptomatology	300/200	330/220	350/263
CyA dose (mg/kg per day) onset/end of symptomatology	7.0/3.5	5.1/3.4	6.5/5.3
Azathioprine (mg/day)	75	75	50
Prednisone (mg/day)	10	10	10

ferent degrees. The pain appeared principally during walking and the functional disability was often severe, necessitating the use of crutches.

Physical examination revealed marked hypersensitivity to touch (all three patients), mild periarticular soft tissue swelling (patients 1 and 2), and mild temperature increase in affected areas (patient 1). No changes in skin color or a joint effusion were present. There was a major quadricipital amyotrophy present in one case (patient 1).

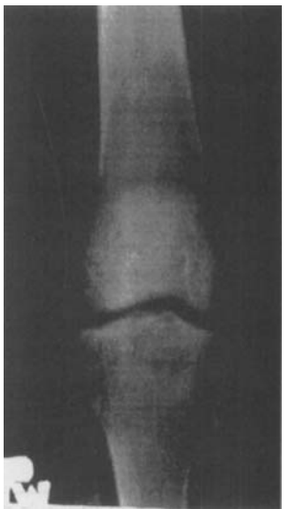

Fig. 1 X-ray of the right knee: a characteristic finding of patchy osteoporosis

Biochemical syndrome

Laboratory testing revealed no acute inflammatory syndrome (normal blood cell count, normal C reactive protein, no changes in erythrocyte sedimentation rate or plasma fibrinogen).

Radiological syndrome

Radiographs revealed a patchy osteoporosis in clinically affected areas of lower limbs and in one patient (1) also in the upper limbs (elbows and hands). Figure 1 documents an example of typical osteoporotic patterns. These changes were not present during hemodialysis treatment before transplantation.

Scintigraphic syndrome

Bone scanning with ^{99m}Tc methylene pyrophosphate showed an increased uptake of the agent with a periarticular distribution in affected joints in all three phases (Fig. 2).

Outcome

In all three cases, a complete recovery was achieved. Symptoms of RSDS improved when cyclosporine A doses were reduced and blood levels declined. Administration of calcitonin was deemed to have a favorable effect in patients 2 and 3 but no effect in patient 1. All patients were treated with calcium channel blockers simultaneously. Physiotherapy was provided to patient 1 only. Non-steroidal antiinflammatory drugs were adminis-

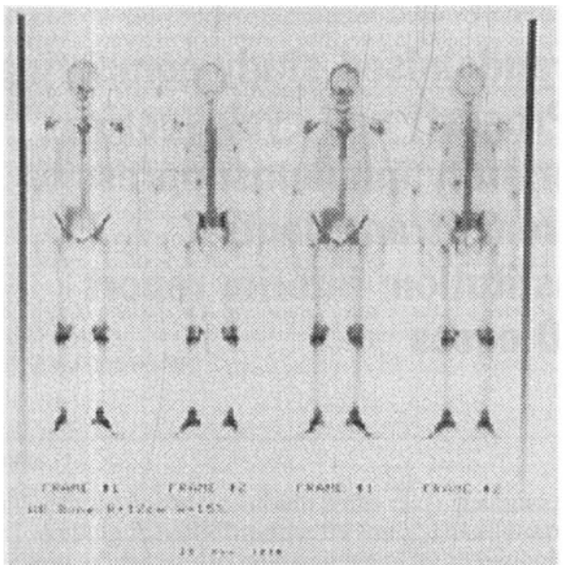

Fig. 2 Bone scanning with ^{99m}Tc methylene pyrophosphate: an increased uptake of the agent with a periarticular distribution in affected joints

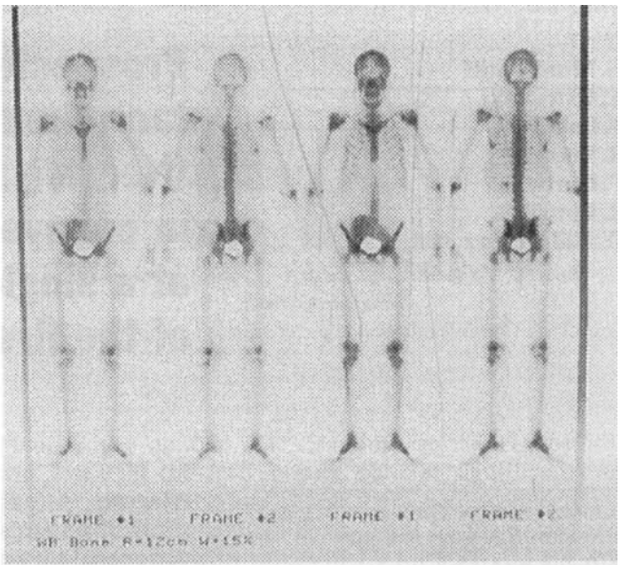

Fig. 3 Bone scanning with ^{99m}Tc methylene pyrophosphate: complete recovery of scintigraphic findings (the same patient as in Fig. 2)

tered too, but they did not relieve the symptoms. Time to complete clinical, radiological, and scintigraphic (Fig. 3) recovery, was 8 months (patient 1), 5 months (patient 2), and 2 months (patient 3). No one patient progressed to aseptic osteonecrosis.

Discussion

Clinical, biochemical, radiological, and scintigraphic findings in the three patients reported are reminiscent of sympathetic reflex algodystrophy. This syndrome was described after different types of organ transplantations [1, 3–5] and also after bone marrow transplantation [7]. In transplanted patients, the exact pathogenesis as well as the reasons why the lower limbs, predominantly, are affected are not known. Different factors possibly promote the occurrence of RSDS. Doses of cyclosporine A [1, 3–5], preexisting renal osteodystrophy with secondary hyperparathyroidism [3], pelvic surgery [3], and/or resumed physical activity [7] have all been considered as potential causative factors. We are not able to make definitive conclusions about etiopathogenesis according to our experience. However, the prognosis of all patients was favorable and the symptoms of algodystrophy subsided completely, most probably spontaneously over the course of time. No patient progressed to osteonecrosis.

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