

DEGENERATIVE OSTEO-ARTICULAR LESIONS AND AMYLOID INFILTRATION IN LONG-TERM HAEMODIALYSIS PATIENTS

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Summary

Duration of dialysis may have an important effect on the severity, the type and the progression of arthropathy in long-term haemodialysis patients. We report on seven patients, all on haemodialysis for more than 10 years, who were disabled by degenerative arthropathy. The main joints involved were shoulders, hips and knees. Associated pathology included carpal tunnel syndrome in all but one, aluminium intoxication in all and destructive spondylarthropathy in five of them. Prosthetic replacement was needed in four patients (3 hips, 1 knee). Histology revealed abundant deposits of amyloid substance similar to those found in the carpal tunnel synovium.

Introduction

With time on haemodialysis lengthening, uraemic patients develop joint problems with an increasing frequency [1]. Although some patients present articular complications of known origin such as septic arthritis or haemarthrosis, patients treated by haemodialysis for more than 10 years seem to present with a specific articular pathology. This type of arthropathy is particularly disabling. Its aetiology is still obscure.

Patients and methods

Amongst the haemodialysis patients referred to our department for various complications we selected for this report seven patients who presented with severe arthralgia and radiologically evident lesions of large joints. Septic patients or those suffering from corticoid induced avascular necrosis, were excluded from the study. Table I summarizes the principal data concerning these seven patients. It is noteworthy that none had amyloidosis as the primary renal disease. All were dialysed three times a week, all but one were home dialysis patients. Two patients had undergone subtotal parathyroidectomy several years ago; one other

TABLE I. Principal data concerning seven haemodialysis patients with severe arthropathy

Patients	Sex	Age	Duration of RDT	Renal disease
MJS	F	64	14	PKD
ML	F	63	14	CGN
TD	F	59	18	PKD (anephric)
MS	F	70	11	RVD
EN	M	70	10.5	CGN
JJ	F	52	14	CGN (anephric)
MG	F	56	12	PKD (anephric)

PKD: polycystic kidney disease CGN: chronic glomerulonephritis RVD: renal vascular disease RDT: regular dialysis treatment

had overt hyperparathyroidism. For each patient a radiological survey included X-rays of the hands (and wrists) shoulders, pelvis, hips and knees (and spinal column, when indicated). Besides routine biochemical analyses such as plasma calcium, phosphorus, and alkaline phosphatase activities, the patients underwent an aluminium mobilization test using a desferrioxamine (DFO) infusion. Recent bone histology was available in five of seven patients. Articular material obtained at surgery was fixed and paraffin-embedded. After specific staining for amyloid deposits 3–4 μ sections were observed under plain and polarized light microscopy. Transmission electron microscopy (TEM) analysis was available in three cases.

Results

Clinical and biochemical studies

All seven patients in the study suffered from severe shoulder pain and showed limited motion. In five, characteristic X-ray lesions were observed at the site of painful joints (Figures 1 and 2), i.e., subchondral bone translucencies, narrowing of the articular space, and small capsular calcifications. Similar lesions at the site of bearing joints (hip, knee) had more dramatic consequences since three out of the four patients suffering from hip pain, needed prosthetic replacement of the joint, and in one of the four patients who complained of knee pain a prosthesis had to be inserted. One of the remaining three who has a completely destroyed knee, is too ill to undergo surgery. One underwent synovial biopsy of the knee joint. Five out of the seven patients had destructive spondylarthropathy. All but one previously had a carpal tunnel syndrome associated in three with lacunae in carpal bones and degenerative arthropathy of the fingers. Surgical decompression of the median nerve had been performed in five of the six patients. No surgical stabilization of the vertebral column was performed in the patients suffering from spondylarthrititis-like lesions. All the patients were aluminium-overloaded as shown by the DFO mobilization test (mean \pm SEM of plasma

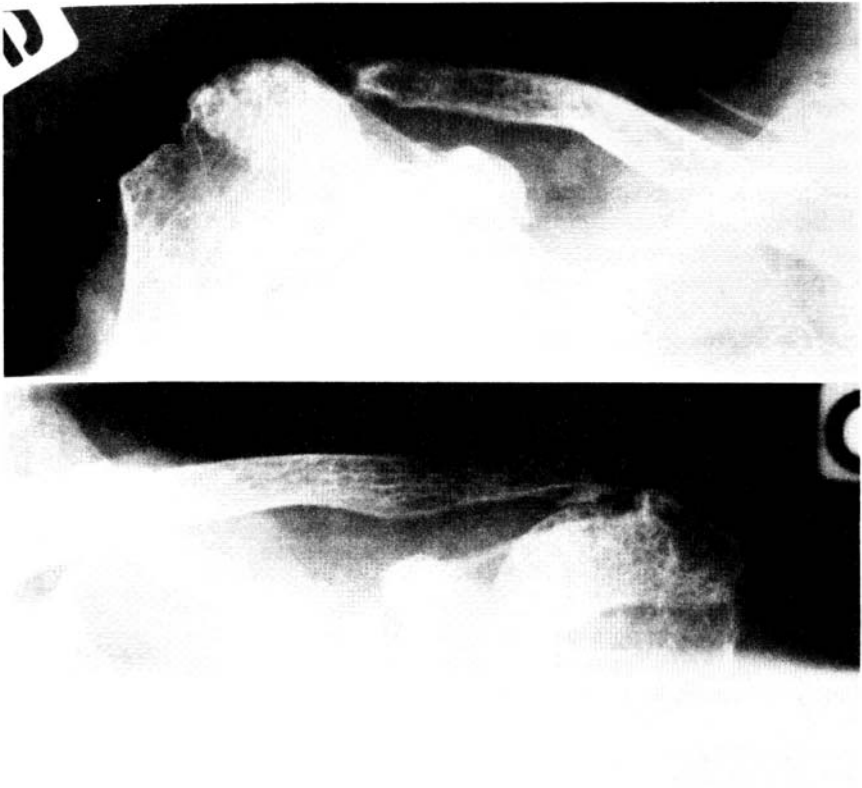


Figure 1. X-ray of shoulders of patient MS



Figure 2. X-rays of knees of patient MS

aluminium 24 hours after DFO, $21.6 \pm 2.6 \mu\text{mol}$, $n=5$) and/or evidence of abundant aluminium deposits in the bone revealed by histochemistry.

Microscopic studies

Light microscopy revealed the presence of amyloid substance in the synovial tissue of the three operated hips and in the transverse carpal tunnel ligament in four out of the five cases studied. In the fifth patient in whom the search for amyloid was negative at that site, amyloid deposits were found in her knee biopsy. On the operated knee of another patient the fragment obtained for histology was very small and did not allow demonstration of the presence of amyloid substance but analysis by TEM revealed apatite crystals. This patient had, however, abundant amyloid infiltration of her carpal synovium. Congo red-induced birefringence appeared to be resistant to potassium permanganate treatment in three cases but disappeared in one other case. TEM analysis of the amyloid deposits removed from two hips showed a characteristic fibrillar structure.

Discussion

It becomes increasingly evident that patients treated by haemodialysis for more than 10 years develop a new articular pathology distinct from previously described, well known types of arthropathy. Its frequency probably increases with time on treatment. It is characterized by shoulder pain in all patients and frequently also painful hips and/or knees. X-rays show narrowing of the articular space and subchondral lacunae almost similar to those recently described by Rubin et al [1] in terms of 'erosive azotaemic osteoarthropathy'. The term 'azotaemic' could be misleading because the lesions we described are never observed in end-stage renal failure prior to dialysis treatment. Rubin et al suggested on the one hand that hyperparathyroidism could be a major factor favouring the appearance of this type of arthropathy. This was clearly not a predominant feature in our patients since only one of them had patent osteitis fibrosa. On the other hand, we agree with these authors in that the duration of dialysis therapy has some importance in the incidence of joint symptoms. Goldstein et al [2] undertook a systematic evaluation of articular dysfunction and structure in eleven patients haemodialysed for more than 10 years. These authors reported a high incidence even in young patients, of joint complaints (8 of 11) and radiographic lesions (9 of 11), similar to ours. In their series hyperparathyroidism did not seem to play an important role since nine of the 11 patients had undergone parathyroidectomy several years earlier. Aluminium toxicity could not be formally excluded in their patients since aluminium burden was not evaluated.

The occurrence of microcrystalline-associated arthritis has been reported in end-stage renal disease either due to calcium oxalate [3] or to apatite [4] crystal deposition. However, these arthropathy types were not particularly related to the length of haemodialysis treatment.

The finding of amyloid substance in the articular synovium and carpal tunnel

structures represents a puzzling problem. Neither by its physico-chemical properties nor by its organ distribution does this observation fit any presently known pathological entity. We do not even know whether the presence of amyloid deposits bears any aetiological relation to this type of arthropathy or whether it is only the consequence of some non-specific degenerative process. The particular destructive arthropathy of dialysis patients clearly requires further investigation in order to elucidate its pathogenesis. This could eventually help to prevent the onset and progression of this recently discovered articular disorder that could well become one of the most frequent and most crippling complication observed in patients on prolonged haemodialysis treatment.

Acknowledgment

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