PAPERS AND SHORT REPORTS

Dialysis arthropathy: complication of long term treatment with haemodialysis

E A BROWN, I R ARNOLD, P E GOWER

Abstract

Twenty eight patients who had received haemodialysis for more than 10 years were reviewed to establish the incidence of joint problems. Only six patients had no joint symptoms, one had avascular necrosis, one had had recent septic arthritis, and four had hyperparathyroidism. The remaining 16 patients had no evidence of hyperparathyroidism yet had an arthropathy causing pain and stiffness in many joints, particularly the shoulders. Ten of these 16 patients had a recurrent carpal tunnel syndrome requiring repeated surgical decompressions, which resulted in only partial improvement. Of the eight patients who had received dialysis for more than 15 years, seven had this "dialysis arthropathy" and six had recurrent carpal tunnel syndrome.

Dialysis arthropathy is a common and often severe and disabling complication of long term treatment with haemodialysis. The cause is not known, but amyloid was found in a synovial biopsy specimen from one patient.

Introduction

Patients receiving maintenance haemodialysis suffer from various problems of the joints, soft tissues, and tendons, including acute monoarthritis or polyarthritis due to periarticular calcification, ruptured tendons from gout or pseudogout, avascular necrosis, and carpal tunnel syndrome.[1-10] We previously published a survey showing that about half of our patients receiving dialysis had severe joint symptoms; many of these had evidence of hyperparathyroidism.[7] We also found that the incidence of joint symptoms was greater in those patients who had received dialysis for more than six years compared with those who had received dialysis for less than six years. In particular, we described a new syndrome of recurrent haemarthroses progressing to chronic capsulitis occurring in patients who had received dialysis for more than 10 years. Goldstein *et al* recently reported a group of 11 patients who had received haemodialysis for more than 10 years and found that eight of them had joint symptoms[11]; hyperparathyroidism was not excluded in these patients. To establish the incidence and nature of joint disease in patients receiving long term treatment with haemodialysis we surveyed all of our patients who had received dialysis for 10 years or more.

Department of Medicine, Charing Cross and Westminster Medical School, London W6 8RF

E A BROWN, DM, MRCP, senior registrar
I R ARNOLD, MB, MRCP, registrar
P E GOWER, MD, FRCP, consultant physician

Correspondence to: Dr Brown.

Patients and methods

All 28 patients (age range 29-67 years; five women, 23 men) who had received haemodialysis for 10 or more years at Charing Cross Hospital were studied. Only one patient had ever had a functioning transplant, and that patient had returned to dialysis treatment more than 10 years previously; in four other patients transplantations had not been successful, and two patients had received continuous ambulatory peritoneal dialysis for a few months. Until 1980 patients had used 1 m^2 Kiil dialysers and received dialysis for 10 hours twice weekly. Since 1980 they had used disposable Gambro dialysers (1·1 or 1·36 m^2) and received dialysis for six to eight hours twice weekly. Cuprophane membranes were used throughout.

All patients were seen at an extra clinic attendance when they were asked to evaluate pain and stiffness in each joint on a scale of 0 to 3 (0, no pain; 1, mild; 2, moderate; and 3, severe). An index of severity of joint disease was then calculated by adding the individual scores for pain and stiffness for each joint. Plasma urea, creatinine, haemoglobin, ferritin, calcium, phosphate, urate, and parathyroid hormone (C and N terminal) concentrations and alkaline phosphatase activity were measured before dialysis in all patients. Radiographs of the hands were obtained in all patients; in some patients painful joints were also examined by radiography. In one patient a synovial biopsy of a painful ankle joint was performed.

"Dialysis arthropathy" was defined as the presence of joint symptoms in the absence of evidence of hyperparathyroidism—that is, normal parathyroid hormone concentration and normal hand radiographs.

Results

Table I shows the nature of the different joint problems seen in the patients who had received long term treatment with haemodialysis. The 28 patients studied were divided into three groups (table II): group a (n=6) had

no joint symptoms (received dialysis for 10-12 years, age range 29-67, one woman, five men); group b (n=4) had joint symptoms accompanied by raised parathyroid hormone concentrations in all four and abnormal hand radiographs in two (received dialysis for 10-18 years, age range 40-62, four men); and group c (n=16) had joint symptoms but no evidence of hyperparathyroidism—that is, dialysis arthropathy (received dialysis for 10-18 years, age range 36-66, three women, 13 men). Ten of the patients from group c had had a previous parathyroidectomy but had normal or low parathyroid hormone concentrations and normal hand radiographs at the time of study. Two patients were excluded from these groups: one with recent septic arthritis complicating bacterial endocarditis and the other with avascular necrosis related to four unsuccessful transplantations.

There was no difference in creatinine, urate, and haemoglobin concentrations before dialysis between the group with no joint symptoms and the group with dialysis arthropathy. Parathyroid hormone concentration, alkaline phosphatase activity, and calcium phosphate product were also normal in patients with dialysis arthropathy (see table II). The mean (SEM) plasma ferritin concentration in patients with dialysis arthropathy (1132 (501) μg/l) was high, but plasma ferritin concentration was often normal (fig 2). The four patients with the most severe dialysis arthropathy had high ferritin concentrations of up to 7800 μg/l.

Hand radiography was performed in all patients with dialysis arthropathy (table IV); no radiographs showed subperiosteal erosions suggestive of hyperparathyroidism or evidence of chondrocalcinosis. Two patients had erosions at their interphalangeal joints, one also having appreciable subluxation. In one patient periarticular calcification was seen in his hand radiograph. Five patients' shoulders were examined by radiography: three were normal, one had erosions at the distal ends of the clavicles, and one had calcification in the supraspinous tendon on one side but not the other. Three patients' knees were examined by radiography: two were normal and one had marginal erosions at both tibial condyles. From these radiographs only three patients showed evidence of an "erosive arthropathy," and even these patients had normal parathyroid hormone concentrations.

TABLE I—*Nature of different joint problems in 28 patients receiving haemodialysis for more than 10 years. Values are numbers of patients*

Joint problem	Length of time receiving dialysis (years)								
	10	11	12	13	14	15	16	17	18
No joint symptoms	5		1						
Hyperparathyroidism	2				1				1
Dialysis arthropathy	2	3*	3†	1		2*	2*		3*
Carpal tunnel syndrome		2	1			2	2		2
Others	1		1						
Total No of patients	10	3	5	1	1	2	2		4

*Two patients also had carpal tunnel syndrome.
†One patient also had carpal tunnel syndrome.

TABLE II—*Clinical and biochemical characteristics of the three groups of patients receiving long term haemodialysis. Values are means (SEM)*

	Group a (n=6)	Group b (n=4)	Group c (n=16)
Men:women	5:1	4:0	13:3
Age (years)	46 (6)	50 (6)	51 (3)
No received parathyroidectomy	1	2	10
Joint severity index		2·0 (0·8)	20 (5)
No with carpal tunnel syndrome			9
No with trigger fingers			3
Parathyroid hormone (normal <0·5 μg/l)	0·37 (0·11)	1·30 (0·16)	0·24 (0·04)
No with hyperparathyroidism by hand radiography		2	
Ferritin (normal 20-200 μg/l)	345 (200)	314 (179)	1132 (501)
Calcium × phosphate (normal <5·2 mmol/l)	3·62 (0·59)	4·27 (0·49)	4·5 (0·4)
Alkaline phosphatase (normal 90-300 IU/l)	182 (26)	376 (76)	198 (20)
Urate (normal 100-400 μmol/l)	530 (19)	564 (96)	509 (23)
Creatinine (normal 42-130 μmol/l)	1275 (140)	1255 (124)	1179 (92)
Haemoglobin (normal 12-16 g/l)	9·2 (1·3)	9·7 (1·9)	8·3 (0·6)

Conversion: SI to traditional units—Calcium × phosphate: 1 mmol/l≈14 mg/100 ml. Urate: 1 mmol/l≈17 mg/100 ml. Creatinine: 1 μmol/l ≈0·01 mg/100 ml.

The joint disease of hyperparathyroidism was mild (mean (SEM) joint severity index 2·0 (0·8), range 1-4) compared with that of dialysis arthropathy (20 (5), range 4-67). The distribution of joints affected in hyperparathyroidism was non-specific, and stiffness was not a feature. Both pain and stiffness, often severe, occurred in patients with dialysis arthropathy. All joints could be affected, usually bilaterally, shoulders being the most commonly affected joint (table III). Fourteen of the 16 patients with dialysis arthropathy complained of painful or stiff shoulders, or both, the pain often being worse when receiving dialysis; haemarthrosis of the shoulder had been noted in five patients in the past.

Nine patients had carpal tunnel syndrome; all also had dialysis arthropathy. The incidence of carpal tunnel syndrome increased with the number of years that dialysis treatment had been given; six of the eight patients who had received dialysis for more than 15 years had had carpal tunnel syndrome (see table I). Patients presented with their first episode of carpal tunnel syndrome nine to 17 years after starting treatment with haemodialysis. The carpal tunnel syndrome is bilateral, and after decompression the symptoms recur, requiring further decompression. Having once developed the disease patients require decompression in one or other hand roughly once a year; one of our patients had six decompressions, three on each side (fig 1). One patient had no recurrence of carpal tunnel syndrome, but he had only had his first episode within the past year. Good relief of symptoms is obtained from the first decompression, but after subsequent operations there are residual symptoms and neurological signs; consequently, some of our patients had severely restricted hand movements.

Three patients had suffered from trigger fingers requiring operation. All three had dialysis arthropathy and two also had recurrent carpal tunnel syndrome.

TABLE III—*Distribution of affected joints in 16 patients with dialysis arthropathy. Values are numbers of patients*

Joint	Effect on joint			
	Pain	Stiffness	Unilateral	Bilateral
Hands	9	9	2	10
Wrists	6	7	1	8
Elbows	4	2		4
Shoulders	13	8	2	12
Neck	2			
Back	6	4		
Hips	5	3	1	5
Knees	4	7		8
Ankles	2	3		3
Feet	2	2		2

One patient underwent a synovial biopsy for a painful ankle joint. He had received dialysis for 18 years and had become severely disabled from dialysis arthropathy and recurrent carpal tunnel syndrome. His joint severity index was high at 67. The synovial biopsy of the ankle was performed after the had been painful for a month and showed evidence of gross amyloid infiltration.

Discussion

This study shows that dialysis arthropathy is a common and often disabling complication of long term treatment with haemodialysis. Dialysis arthropathy is characterised by pain and stiffness of the joints, predominantly bilateral and most commonly in the shoulders, though all joints can be affected. Often the pain in the shoulder is exacerbated by dialysis, and in some patients there is a history of haemarthrosis. Radiographs of the joints are usually normal, though a few show periarticular calcification or joint erosions. There was no evidence of hyperparathyroidism in our patients. Although plasma ferritin concentration is normal in many of the patients, it can be high, particularly in the presence of severe joint disease. Amyloid was found in a synovial biopsy specimen from one patient. Many of the patients with dialysis arthropathy also had bilateral recurrent carpal tunnel syndrome or trigger fingers, or both. Although symptoms responded to initial operation there were residual symptoms after subsequent operations.

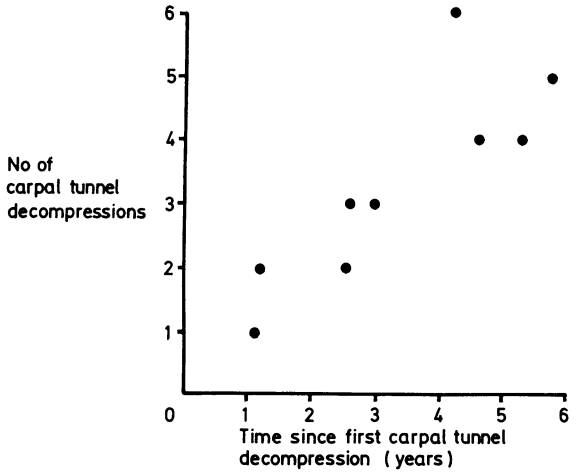

FIG 1—Rate of recurrence of carpal tunnel syndrome in nine patients.

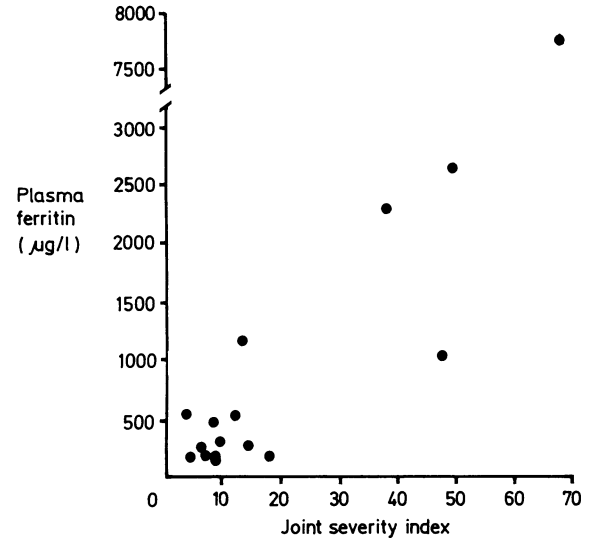

FIG 2—Relation between plasma ferritin concentration and joint severity index in 16 patients with dialysis arthropathy.

TABLE IV—*Radiographic findings in 16 patients with dialysis arthropathy*

	No of radiographs	Radiological findings		
		Normal	Periarticular calcification	Articular erosions
Hands	16	13	1	2
Shoulders	5	3	1	1
Knees	3	2		1

Carpal tunnel syndrome and other peripheral nerve entrapments are well recognised complications of haemodialysis[8 9] and are more common in patients who have received dialysis for a longer time.[7 10] Indeed, carpal tunnel syndrome appears to be an almost inevitable complication of long term treatment with haemodialysis. Six of eight patients who had received haemodialysis for more than 15 years were affected. Schwartz *et al* recently reported that five out of six patients who had received dialysis for more than 15 years developed carpal tunnel syndrome.[10] Although these studies also mention the bilateral nature of the carpal tunnel syndrome, they tend to imply that the response to operation is good and unlike our study do not describe the disabling recurrent course of the carpal tunnel syndrome that occurred in our patients.

In contrast with carpal tunnel syndrome chronic arthropathy is not well described as a common complication of long term treatment with dialysis. Charra *et al* report that shoulder pains along with carpal tunnel syndrome are found in patients receiving long term treatment with dialysis but do not mention pains in any other joints.[12] There has been only one other study of chronic arthropathy in patients receiving long term treatment with haemodialysis[11]; of 11 patients, five complained of shoulder pains and seven of knee pains and stiffness. Many of these patients had erosions or periarticular calcification on radiography, and as parathyroid hormone concentration was not measured hyperparathyroidism was not excluded as a cause of the arthralgias. Even so some of these patients had an arthropathy that appeared similar to the one described here.

The cause of this chronic progressive dialysis arthropathy and carpal tunnel syndrome is not clear. Biopsies have been performed at the time of carpal tunnel decompression in several centres, and amyloid is often, though not invariably, found.[9 10 12] Charra *et al* found that the incidence of shoulder pain was higher in patients with amyloid carpal tunnel syndrome (95%) compared with non-amyloid carpal tunnel syndrome (20%), suggesting that the pain in the shoulder may also be due to amyloid.[12] Bergada *et al* described two patients with polyarthralgias and carpal tunnel syndrome with amyloid found in both synovial and carpal tunnel biopsy specimens.[13] We performed one synovial biopsy and also found amyloid in the biopsy specimen.

Amyloid infiltration may be a marker of a more generalised inflammatory response concerning acute phase reactants including C reactive protein and ferritin. Interestingly, the highest ferritin concentrations (2000-7800 μg/l) are seen in patients with the most severe arthropathy. One patient with no joint symptoms also had a high plasma ferritin concentration (1250 μg/l). The higher concentrations found in patients with dialysis arthropathy may reflect both iron overload and chronic inflammation. Indeed, there is recent evidence in patients with rheumatoid arthritis that iron in a low valency state can promote the production of free radicals, resulting in peroxidation and consequent inflammation of synovial membranes.[14] The mechanism by which deposition of amyloid and other inflammatory responses occur is unclear but may concern activation of various inflammatory pathways by haemodialysis membranes mediated by interleukin 1.[15]

Although deposition of amyloid may be the cause of dialysis arthropathy, various other causes need to be considered. Hyperparathyroidism does cause an erosive arthropathy,[16 17] but in our patients with dialysis arthropathy there was no evidence of hyperparathyroidism, though many had previously had a parathyroidectomy. Deposition of crystals in the joints may also be responsible; calcium hydroxyapatite[18] and calcium oxalate[19] can both cause

chronic arthropathy. Periarticular calcification, which is a feature of both these conditions, is not, however, a feature of dialysis arthropathy. Similarly, there was no evidence of chondrocalcinosis or, hence, pseudogout in these patients. As bone biopsies were not performed in these patients the possibility that accumulation of aluminium in bone contributed to this arthropathy cannot be excluded.

The results of this study of patients receiving long term treatment with haemodialysis show that many patients develop a progressive and often severe arthropathy that is commonly complicated by recurrent carpal tunnel syndrome. Some of the patients became severely disabled from this arthropathy, which therefore must be regarded as a major complication of long term treatment with haemodialysis. As this arthropathy does not develop in patients with longstanding chronic renal failure who are not receiving dialysis it is probably due to the haemodialysis process itself rather than uraemia. Further studies are needed urgently to determine the cause of this dialysis arthropathy and establish whether inflammatory responses induced by dialysis could lead to this widespread deposition of amyloid.

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Internal urinary sphincter in maintenance of female continence

E VERSI, L D CARDOZO, J W W STUDD, M BRINCAT, T M O'DOWD, D J COOPER

Abstract

The integrity of the bladder neck was assessed in 98 continent women. Radiological and physiological evidence showed that half of these women had an incompetent bladder neck, but they were still continent. These data devalue the urodynamic finding of an incompetent bladder neck as an indication for surgery for incontinence and question the physiological importance of the internal sphincter.

Introduction

Traditionally, it has been taught that urinary continence is maintained by the internal and external sphincters. Ellis claims that in women the internal sphincter (the bladder neck) is the more important,[1] and in *Cunningham's Textbook of Anatomy* it is stated that "urine is held at the level of the bladder neck."[2] Opening of the bladder neck in response to stress—for example, increase in intra-abdominal pressure during a cough—has been considered to be abnormal[3] and has been used as an indication for surgery in patients complaining of stress incontinence (S Rees, T P Stephenson, C J Richards. The results of colposuspension. Proceedings of the International Continence Society's fourteenth meeting, Innsbruck, 1984). The aim of this paper is to show that incompetence of the bladder neck may be a common variant of normal and should not therefore be regarded as a urodynamic abnormality. This was achieved by radiological screening and interpretation of urethral pressure profilometry under stress.

Urodynamic Unit, King's College Hospital and Dulwich Hospital Menopause Clinic, Dulwich Hospital, London SE22

E VERSI, DPHIL, MB, research fellow
L D CARDOZO, MD, MRCOG, consultant gynaecologist
J W W STUDD, MD, MRCOG, consultant gynaecologist
M BRINCAT, MRCS, LRCP, research fellow
T M O'DOWD, BAO, MRCOG, research fellow

Computer Unit, King's College Hospital School of Medicine and Dentistry, London SE5

D J COOPER, MSC, DPHIL, senior analyst

Correspondence to: Dr L D Cardozo, Department of Obstetrics and Gynaecology, King's College Hospital School of Medicine and Dentistry, London SE5.

Patients and methods

Ninety eight women presenting with symptoms of the climacteric, not incontinence, were recruited for this study from the Dulwich Hospital Menopause Clinic. They were all found to be continent on pad testing (E Versi, L D Cardozo. One hour single pad test as a simple screening procedure. Proceedings of the International Continence Society's fourteenth meeting, Innsbruck, 1984) and normal urodynamically (uroflowmetry and videocystourethrography[4]).

Each patient had her bladder filled to capacity (400-600 ml) with Urografin 150 at room temperature, which was then screened radiologically using an image intensifier. The bladder neck was viewed in the erect oblique position. At the same time intravesical and intra-abdominal (rectal) pressures were recorded with the use of 1 mm manometer tubing, filled with saline, attached to Statham Gould transducers. This system enabled changes in detrusor pressure to be measured even during a cough (by subtracting the intra-abdominal pressure from the intravesical pressure). The integrity of the bladder neck was assessed radiologically and the image recorded on videotape while the patient was asked to cough six times as hard as possible. Incompetence of the internal sphincter was diagnosed when the bladder