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Sonographic findings in haemodialysis – related chronic arthropathy

G. Coari¹, A. Iagnocco¹, S. Maggi², M. Bracci¹, A. De Cata¹, M. Mastantuono³, M. Larciprete³, S. Persichetti²

¹ Department of Rheumatology, Rome University “La Sapienza”, I-00161 Rome, Italy

² Department of Urology, Rome University “La Sapienza”, I-00161 Rome, Italy

³ Department of Radiology, Rome University “La Sapienza”, I-00161 Rome, Italy

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Abstract. In 33 subjects receiving long-term haemodialysis sonographic examination of shoulders, hips and knees was performed. Changes of both joints and periarticular soft tissues were found in 60 shoulders, 16 hips and 42 knees. In the shoulder besides the presence of tenosynovitis and bursitis, even significant thickening of rotator cuff and increased distance between capsule and bone in transscapular scan were found. Also, in the hip the distance between capsule and bone was significantly increased. In the knee effusion was present in 14 cases and synovial hypertrophy in 20. Articular femoral cartilage was significantly thinned. Results obtained suggest the hypothesis of the presence of an important inflammatory component in the pathogenesis of arthropathy related to haemodialytic treatment. The production of cytokines by mononuclear cells stimulated by β -2 microglobulin may cause the inflammatory response. Sonographic findings of alterations in 42 symptomless joints show the importance of this diagnostic method to begin an early therapy.

Key words: Sonography – Haemodialytic chronic arthropathy

Introduction

Various articular symptoms develop in relation to long-term, intermittent dialysis as a treatment of terminal renal failure.

There are four clinical features related to this type of therapy: crystal-related arthritis, carpal tunnel syndrome, chronic arthropathy, destructive arthropathy.

Chronic arthropathy is reported more frequently and is characterized by joint pain. The shoulder is predominantly involved. In this joint sonography showed thickening of rotator cuff due to deposition of amyloid [1].

Some authors demonstrated also synovial hypertrophy in many joints [2], tenosynovitis of the fingers flexors, thickening of the capsule in the hip [1] and the presence of Baker's cysts [3]. All changes were related to deposition of β -2 microglobulin amyloid.

The early noninvasive diagnosis of dialysis-related amyloidosis is difficult [4]. Clinical signs, such as joint pain, are not specific [5], whereas typical radiological amyloid bone cysts, although specific, are a late event. Different studies observed that capsulosynovial swelling precedes the development of characteristic bone cysts [1, 6] hypothesizing that amyloid infiltration of synovial membrane and tendons [7–9] might be accessible to ultrasonographic assessment [10]. The present study was undertaken to evaluate the utility of real-time high-resolution ultrasound in showing and characterizing abnormalities [11], particularly previous ones, of patients who received long-term haemodialysis.

We studied the shoulder, hip and knee. This choice was justified by the good capability of sonography to examine articular and periarticular structures in those joints and to reveal the differences in comparison with normal subjects.

Materials and methods

Real-time sonography of the shoulders, hips and knees was performed in 33 patients receiving chronic haemodialysis as a treatment of terminal renal failure. All sonographic exams were carried out by two different operators using a 7.5 MHz linear transducer for the study of the knee and shoulder and a 3.5 MHz linear probe for the hip.

The patients were 19 males and 14 females. Their mean age was 46.8 years (range 20–75 years) and the mean disease duration was 7.3 years (range 0.5–27 years). Ten of them had rejection of renal transplant. Criteria for the clinical diagnosis of dialysis-related amyloidosis were: flexor tenosynovitis of the hand with diminished extension of the fingers, signs or symptoms

Table 1. List of the scans carried out in each joint

Joint	Scans	Examined structure
Shoulder	Anterior (longitudinal and transverse)	Biceps tendon
		Subacromialis bursa
	Posterior lateral	Joint space
		Subscapularis tendon
		Rotator cuff
Transascellar	Supraspinatus and infraspinatus tendons	
	Capsule-bone distance	
Hip	Anterior	Capsule-bone distance
	Lateral and posterior	Capsule
		Bursae
Knee	Anterior (suprapatellar recess)	Synovial membrane
	Anterior (flexed knee)	Synovial fluid
		Femoral cartilage
	Posterior	Baker's cysts

of carpal tunnel syndrome and shoulder pain with diminished range of motion [11, 12]. A total of 40 healthy subjects were studied for comparison (23 males and 17 females; mean age 43.3 years; range 34–57 years).

In each joint many scans were carried out to examine and evaluate the various articular and periarticular structures (Table 1). In the 66 shoulders tendons were examined, evaluating changes of their sonographic appearance, alterations of their margins, modifications of their thickness and the presence of peritendinous fluid collection; sonographic signs of bursitis were searched for; then the two different operators measured the thickness of the rotator cuff and the distance between the capsule and bone in transascellar scan, searching for the presence of intracapsular effusion [13].

In the 66 hips the distance between the capsule and bone was measured revealing the presence of joint effusion or synovitis [14]. Capsular thickening, irregularity of bone surface of femoral head or neck and the presence of bursitis were searched for.

In the 66 knees the thickness of synovial membrane measured in suprapatellar recess (mean value between longitudinal and transverse scans), and the thickness of articular condylar cartilage, were measured. The presence of joint effusion and of Baker's cysts were evaluated. Articular cartilage was measured according to Aisen's technique [15, 16]: In each knee six measurements were taken just above the superior margin of the patella (two laterally, two medially and two centrally). Then the mean value of each couple of results was calculated and the same measurements and calculations were repeated 2 cm above the patella.

Patients were divided into three groups according to the duration of haemodialysis treatment (Table 2): In group A the duration was less than 4 years (12 subjects), in group B it was between 4 and 10 years (12 subjects) and in group C it was more than 10 years (9 subjects).

Statistical analysis was applied to evaluate the differences between haemodialysis patients and normal subjects. The Student's *t*-test was used to evaluate the thickness of rotator cuff, the distance between capsule and

Table 2. Survey and structures involved in three groups of patients

Initials	Gender	Dialysis duration (years)	No. of structures involved at sonography	No. of joints involved at sonography	No. of joints involved at clinical examination
Group A					
NG	M	0.5	4	2	1
CR	F	1	6	3	2
SS	M	3.5	6	4	2
ML	M	3	13	4	3
MG	M	2.5	4	2	1
FM	M	2.5	4	4	2
PU	M	0.5	7	4	2
NM	M	3	4	2	2
VP	M	3	3	3	0
AB	M	2	2	2	0
OC	M	2	0	0	0
FM	F	2	10	5	4
Group B					
PL	M	9	0	0	0
TR	M	6	6	5	3
TQ	F	9	15	5	5
DD	F	7	3	3	0
GF	M	4.5	6	4	3
SD	M	4	9	4	2
MA	F	4	3	2	1
LQ	M	8	7	4	2
BT	F	6	11	5	4
PA	F	5	8	4	2
FL	F	9	8	4	2
VG	M	8	9	4	3
Group C					
FA	F	27	10	6	4
VA	F	20	12	5	3
FT	F	24	11	6	4
PD	M	11	7	4	3
CM	F	16	7	3	2
BML	F	13	9	4	3
PG	M	14	2	2	0
MI	F	14	9	5	3
NS	M	11	6	4	2

bone in the shoulder and hip, and the thickness of synovial membrane and articular condylar cartilage in the knee.

Results

Table 3 reports results obtained by sonographic examination of the shoulder. Sonography showed signs of tenosynovitis in 16 shoulders. Changes involved predominantly the biceps tendon with the presence of fluid peritendinous collection in all cases; in 5 of them even alterations of sonographic structure of the tendon were found. In 6 of the 16 cases with tenosynovitis articular effusion was also present. It is possible that in those cases a communication between tendon sheath and the joint was present. In the shoulder bursitis was shown in 30.3% of cases. Coracobrachial bursa was involved in 7 cases (10.6%) and subacromialis bursa in 13 (19.7%). In 4 of the 13 shoulders with subacromialis bursitis, joint effusion was present at the same time. Even in those cases a communication between bursa and articular cav-

Table 3. Shoulder (results)

	Normal joints (n = 80)	Joints of haemodialysis patients (n = 66)
Tenosynovitis of biceps tendon	0	9
Tenosynovitis of subscapularis tendon	0	3
Tenosynovitis of supraspinatus tendon	0	2
Tenosynovitis of infraspinatus tendon	0	2
Bursitis	0	20
Rotator cuff thickness (mm)	6.4	7.9 ($p < 0.005$)
Capsule-bone distance (mm)	2.3	3.5 ($p < 0.005$)

Table 4. Hip (results)

	Normal joints (n = 80)	Joints of haemodialysis patients (n = 66)
Distance capsule-bone (mm)	5.9	8.1 ($p < 0.0001$)
Capsular thickening	0	11
Irregularity of bone surface	0	17

Table 5. Knee (results)

	Measurement points	Normal joints (n = 80)	Joints of haemodialysis patients (n = 66)
Thickness of synovial membrane		3.6	4.1 (n.s.)
Thickness of articular femoral cartilage	a	2.3	1.6 ($p < 0.001$)
	b	2.7	1.9 ($p < 0.001$)
	c	2.4	1.8 ($p < 0.005$)
Effusion		0	14
Baker's cysts		0	1

ity was likely present. The thickness of rotator cuff was measured performing anterior scans beneath the acromion. Significant thickening ($p < 0.005$) was demonstrated confirming data reported by other authors [1]. The mean distance between capsule and bone surface in transacellar scan was significantly increased ($p < 0.005$) in the joints of haemodialysis patients with respect to normal joints, showing the presence of joint effusion [8]. The maximum value found was of 7 mm.

Table 4 reports results obtained by the study of the hip. The mean distance between joint capsule and bone surface was significantly increased in joints of haemodialysis patients in comparison with normal joints ($p < 0.0001$). This might be caused either by synovial hypertrophy or intra-articular effusion [15] or deposition of β -2 amyloid [1]. In addition to the measurement of the bone-capsule distance, it is important to evaluate even the sonographic appearance of articular space: When effusion is present, articular space between cap-

sule and bone is hypoechoic, whereas synovial hypertrophy causes a hyperechoic appearance. Increased value of capsule-bone distance with hypoechoic appearance of the space was found in 14 joints (21.2%). Thickening of the capsule was present in 11 cases (16.6%) and irregularities of bone surface of femoral head and neck were shown in 17 joints (25.7%).

Table 4 reports results obtained by sonographic evaluation of the knees. In this joint sonography showed the presence of nonsignificant synovial thickening. Articular femoral cartilage was significantly thinned in all points of measurements (a: $p < 0.001$); b: $p < 0.001$; c: $p < 0.005$). The involvement of the knee was confirmed by the presence of effusion in 12 joints (18.2%) and of one Baker's cyst.

An increasing number of lesions were observed according to dialytic age: In group A an average of 5.3 ± 3.5 changes were present, in group B 7.1 ± 3.7 and in group C 7.9 ± 2.7 (Table 2).

The difference in measurements between the two observers averaged 0.3 ± 0.2 mm for rotator cuff, 0.2 ± 0.2 mm for capsule-bone distance in the shoulder, 0.3 ± 0.4 mm for capsule-bone distance in the hip, 0.3 ± 0.4 mm for the thickness of synovial membrane of the knee and 0.2 ± 0.3 for the condylar cartilage of the knee.

Discussion

The present study showed the usefulness of sonography in the evaluation of changes due to chronic arthropathy of haemodialysis. In all three joints examined alterations were found. Particularly in 118 of 198 joints studied (59.6%) changes were present: Sonography showed alterations in 60 shoulders, 16 hips and 42 knees. The shoulder was the joint most frequently involved and changes were present mainly in tendons and bursae. The prevalent involvement of the shoulder has already been reported and it could be caused by local factors [17], vascular changes or the presence of many anatomical structures in this area (tendons, sheaths, bursae, articular structures). Opposite results were obtained in the hip and the knee where periarticular soft tissues were rarely involved and changes were present mainly in the articular structures.

In the knee different results were obtained with respect to previous reports [18], the present study showing effusion only in 14 of the 66 joints examined. Moreover, hypertrophy of synovial membrane was demonstrated in 20 cases, and this finding has never been reported in the literature before. Only in 2 patients (6.1%) did sonography not show any alteration; one of them had received dialytic treatment for 2 years and the other one for 9 years.

The wrist was not examined in the present study because 24 patients of 33 evaluated had received a surgical operation (9 of which bilaterally) for the presence of carpal tunnel syndrome [19].

Thickening of rotator cuff was confirmed [11] and this finding represents a further demonstration of the presence of amyloidosis in dialysis patients.

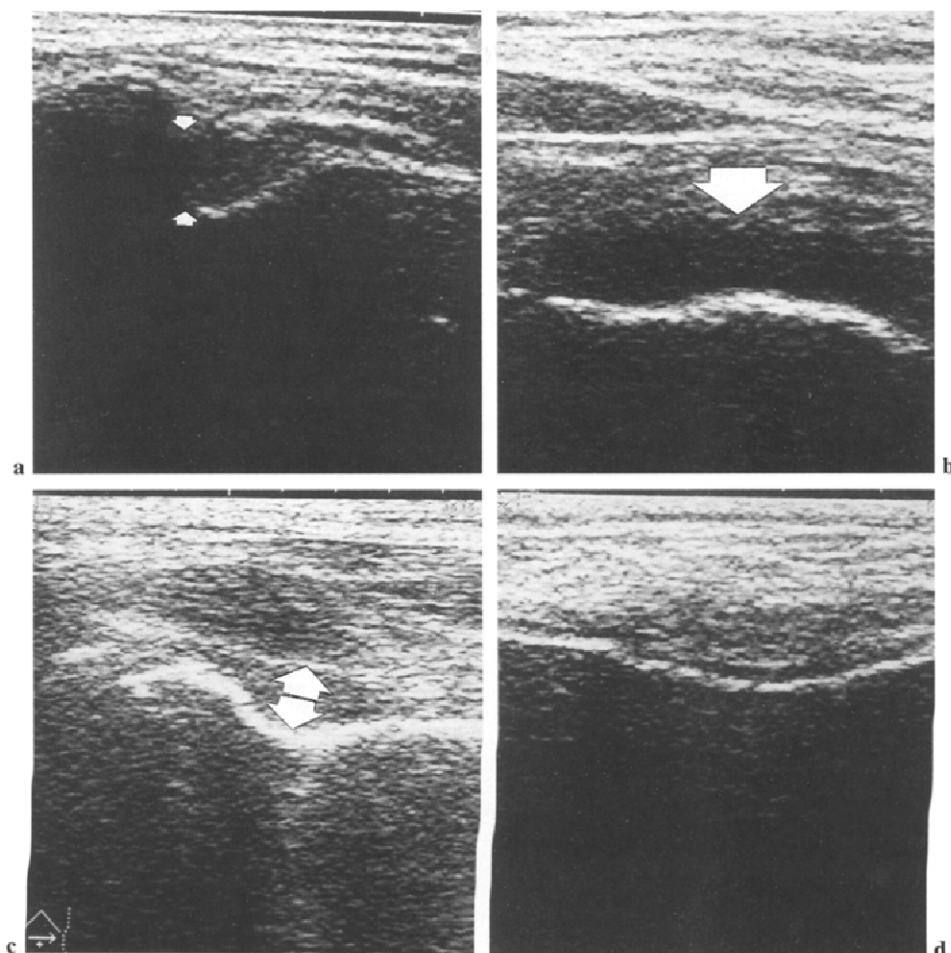


Fig. 1. **a** Measurement of thickened rotator cuff (*arrows*); **b** effusion (*arrow*) of the shoulder in transscapular scan; **c** measurement of increased-distance capsule-bone (*arrows*) in the hip; **d** thinned articular condylar cartilage in the knee (Aisen's technique)

The frequent finding of articular effusion shows the presence of inflammation in the joints of patients receiving chronic haemodialysis.

Pathogenesis of chronic dialysis-related arthropathy is considered to be multifactorial [20, 21]. The presence of fluid collection in tendons sheaths, bursae and articular space has been considered to be due to deposition of β -2 microglobulin, and this finding has been confirmed by postmortem studies [20]. The present study shows many cases of articular effusion in subjects with a short duration of haemodialytic treatment, the appearance of clinical symptoms of inflammation which disappear after corticosteroid therapy and sonographic demonstration of synovial membrane hypertrophy. Those findings suggest the presence of other important pathogenetic mechanisms.

Surely local factors such as changes of extracellular matrix composition, like crosslinking of collagen [17, 22], may be the cause of the frequent involvement of some structures in musculoskeletal apparatus. It is even possible that inflammatory mechanism is involved which may be the cause of synovial hypertrophy and consequent articular effusion.

Some authors suggest the intervention of a crystal-related inflammation due to the presence of hydroxyapatite and these data are confirmed by the good results obtained by treatment with colchicine [21]; nevertheless, in

most cases crystals were never found. Recently, production of IL-6 by peripheral blood mononuclear cells stimulated by β 2-microglobulin was demonstrated [23]. Particularly the β 2-microglobulin modified with advanced glycation end products is a major component in amyloid deposits and participates in the pathogenesis of haemodialysis-related amyloidosis as foci where monocyte and macrophage increase the secretion of IL-1 β , TNF- α [22] and IL-6 [26]. In this way an inflammatory response begins and leads to bone and joint destruction.

The presence of an inflammatory component in the pathogenesis of dialysis-related arthropathy with production of cytokines may justify even the significant reduction in the thickness of articular femoral cartilage, the important role of cytokines in the pathogenesis of cartilaginous damage in the course of chronic arthritis being known.

It is also possible that in the pathogenesis of inflammation, even an immune-complexes pathology is present, because many patients had an autoimmune disease with renal damage, whereas other subjects had had a rejection after renal transplantation with the intervention of autoimmune mechanisms.

Sonography showed changes in 118 of the 198 joints examined (59.6%), whereas clinical examination revealed alterations only in 69 joints (34.8%). These data confirm the importance of sonography, 41.5% of the

joints already damaged being symptomless. These findings may be useful to begin an early treatment. In fact, early detection of articular and periarticular alterations can surely indicate the most suitable treatment which tries to prevent the establishment of further changes. Moreover, in monoarticular involvement local intra-articular therapy may be indicated.

Dialysis duration seemed to be the most important factor in the development of chronic arthropathy [25], particularly for results obtained in the measurement of the distance between capsule and bone in the shoulder and hip. The study showed an increase in anatomical structures involved when the dialysis duration increased (Table 2); however, for the low number of cases examined differences were not statistically significant. Moreover, it was not possible to reveal any relationship between articular involvement and the dialysis membrane used [26], because in most parts of patients the dialysis duration was too long.

For the same reason it was not possible to establish any relationship between the presence of joint changes and the cause of haemodialysis treatment. No significant relationship was found with respect to the gender and age of the patients.

The present study showed that sonography is a useful and important diagnostic method in the detection and monitoring of dialysis-related arthropathy. Its noninvasiveness, repeatability and low cost surely justifies a widespread application of this technique.

References

- Jadaul M, Malghem J, Vande Berge B, Ypersele de Strihou C van (1993) Ultrasonographic detection of thickened joint capsule and tendons as marker of dialysis related amyloidosis: a cross sectional and longitudinal study. *Nephrol Dial Transplant* 8: 1104
- Hurst NP, Van den Berg R, Disney A, Alcock M, Albertin L, Green M, Pascoe V (1989) "Dialysis related arthropathy" a survey of 95 patients receiving chronic haemodialysis with special reference to β -2 microglobulin related amyloidosis. *Ann Rheum Dis* 48: 409
- Baldrati L, Docchi D, Balbi B, Rocchi A, Capponcini C, Turci F (1990) Popliteal cysts in chronic haemodialysis patients. *Nephron* 56: 444
- Kessler M, Netter P, Azoulay E, Mayeux D, Pere P, Gaucher A (1992) Dialysis-associated arthropathy: a multicentre survey of 171 patients receiving haemodialysis for over 10 years. *Br J Rheumatol* 31: 157
- Jadaul M, Vande Berge B, Malghem J (1994) Ultrasonography of the joints in β -2 microglobulin amyloidosis. *Rev Rheum* 61 (9) (Suppl): 43S
- Van Ypersele de Strihou C, Honon B, Vandenbroucke JM, Huaux JP, Noel H, Maldague B (1988) Dialysis amyloidosis. In: Grunfeld JP, Bach JF, Funck-Brentano JL, Maxwell MH (eds) *Advances in nephrology*. Year Book Medical Publishers, Chicago, pp 401–422
- Mack LA, Nyberg DA, Matsen FA (1988) Sonographic evaluation of the rotator cuff. *Radiol Clin North Am* 26 (n 1): 161
- Morita T, Suzuki M, Kamimura A, Hirasawa J (1985) Amyloidosis as a possible new type in patients receiving long-term haemodialysis. *Arch Pathol Lab Med* 109: 1029
- Lusenti T, Borgatti PP, Linder G, Anelli A, Brancaccio D (1991) Multiple tendineal tumoral amyloid masses in a patient on long-term dialysis. *Nephron* 57: 243
- Vandenbroucke JM, Jadoul M, Maldague B, Huaux JP, Noel H, Van Ypersele de Strihou C (1986) Possible role of dialysis membrane characteristics in amyloid arthropathy. *Lancet* 1: 1210
- Kay J, Benson CB, Lester S, Corson JM, Pinkus JS, Lazarus M, Owen WF (1992) Utility of high-resolution ultrasound for the diagnosis of dialysis-related amyloidosis. *Arthritis Rheum* 35: 926
- Owen WF (1989) Erosive spondyloarthropathy in a long-term dialysis patient. *Semin Dial* 2: 85
- Koski JM (1989) Axillar ultrasound of the glenohumeral joint. *J Rheumatol* 16: 664
- Koski JM (1989) Ultrasonographic evidence of hip synovitis in patients with rheumatoid arthritis. *Scand J Rheum* 18: 127
- Aisen AM, McCune WJ, MacGuire A, Carson P, Silver TM, Jafri SZ, Martel W (1984) Sonographic evaluation of the cartilage of the knee. *Radiology* 153: 781
- Iagnocco A, Coari G, Zoppini A (1992) Sonographic evaluation of femoral condylar cartilage in osteoarthritis and rheumatoid arthritis. *Scand J Rheumatol* 21: 201
- Floege J, Schaffer J, Koch KM, Sharon S (1992) Dialysis related amyloidosis: a disease of chronic retention and inflammation? *Kidney Int* 42: S-78
- Nessi R, Bolzoni S, Brancaccio D, Uslenghi C (1993) Amyloid osteoarthritis in dialyzed patients: integrate imaging. *Radiol Med* 85: 252
- Sivri A, Celiker R, Sungur C, Gokce Kutsal J (1994) Carpal tunnel syndrome: a major complication in haemodialysis patients. *Scand J Rheumatol* 23: 287
- Jadoul M, Malghem J, Vande Berg B, Van Ypersele de Strihou C (1993) Ultrasonography of joint capsules and tendons in dialysis-related amyloidosis. *Kidney Int* 43: S-106
- Bardin T, Kuntz D (1994) Dialysis arthropathy. In: Klippel JH, Dieppe PA (eds) *Rheumatology*. Mosby, London, pp 1–4, 7, 26
- Miyata T, Inagi R, Iida Y, Sato M, Yamada N, Oda O, Seo H (1994) Involvement of β -2 microglobulin modified with advanced glycation end products in the pathogenesis of haemodialysis-associated amyloidosis. Induction of human monocyte chemotaxis and macrophage secretion of tumor necrosis factor- α and interleukin-1. *J Clin Invest* 93: 521
- Memoli B, Libetta C, Rampino T, Dal Canton A, Conte G, Scala G, Ruocco MR, Andreucci VE (1992) Haemodialysis related induction of interleukin-6 production by peripheral blood mononuclear cells. *Kidney Int* 42: 320
- Iida Y, Miyata T, Inagi R, Sugiyama S, Maeda K (1994) β -2 microglobulin modified with advanced glycation end products induces interleukin-6 from human macrophages. Role in the pathogenesis of haemodialysis-associated amyloidosis. *Biochem Biophys Res Comm* 201: 1235
- Negi S, Kita Y, Uchita K, Abe T (1995) Ultrasonographic evaluation of shoulder joints in haemodialysis patients. *Nippon Jinzo Gakkai Shi* 37: 29
- Aoyagi R, Miura Y, Ishiyama T, Maruyama Y, Hasegawa (1993) Influence of dialysis membranes on the development of dialysis associated osteoarthritis. *Kidney Int* 43: S-111