Amyloid Arthropathy in the Course of Multiple Myeloma

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ABSTRACT. ***Objective.*** Primary amyloidosis is classical in the course of multiple myeloma (MM), but peripheral amyloid arthropathy is unusual. We evaluated the frequency and effect of amyloid arthropathy in a single center series of patients with MM.

Methods. Retrospective analysis of cases of peripheral joint amyloidosis in a cohort of patients with MM.

Results. Between 1978 and 1996, 11 patients (6 women, 5 men, mean age 59 yrs) were diagnosed with biopsy proven amyloid arthropathy in a cohort of 311 patients with MM. Arthritis was the first symptom of amyloidosis in all patients and occurred within the 6 months after MM diagnosis in most patients (7/11). Nine patients had light chain MM and λ light chain was more common than κ (6 vs 5). Shoulder hypertrophic arthropathy and rheumatoid arthritis-like polyarthritis were the 2 most common involved sites. In most cases, joint involvement was responsible for major limitations in activities of daily living. Amyloid deposits were clearly visible on magnetic resonance images (MRI), which also showed inflammatory synovitis in some cases. Control of MM was often associated with improvement of amyloid arthropathy, but additional rheumatological treatment — oral low dose prednisone or joint steroid injection — was often needed to achieve more complete relief. Amyloid arthropathy was not associated with decreased survival, except for patients with concomitant cardiac involvement.

Conclusion. This series provides reliable information on amyloid arthropathy, especially regarding functional effects, anatomical lesions on MRI, and therapeutic options. (J Rheumatol 2002;29:1473–81)

Key Indexing Terms:
MULTIPLE MYELOMA PRIMARY AMYLOIDOSIS ARTHRITIS
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Primary (AL) amyloidosis, first described by Magnus-Levy[1], is a rare condition, with an estimated annual incidence rate in the United States of 10 per million person-years[2,3]. The disease is due to the deposition of serum amyloid protein and a monoclonal light chain in different tissues or organs, related to plasma cell dyscrasia. A monoclonal component is identified on serum or urine immunoelectrophoresis in about 70% of cases, corresponding to a definite multiple myeloma (MM) in 15 to 21%[3-5]. Conversely, AL amyloidosis is observed in about 15% of MM[6,7].

AL amyloid deposition is a systemic process. Rheumatological involvement is possible, and carpal tunnel syndrome is the most common feature, present in 14 to 24% of patients with AL amyloidosis[3,4,8]. In contrast, peripheral arthritis is rare; Wiernick, *et al* found only 24 cases in the literature between 1873 and 1972[9], and Vuillaumey, *et al* reported only 2 cases of biopsy proven AL amyloid arthropathy among 1953 cases of MM[8]. No explanation is available for the very low incidence of joint involvement, compared to renal, cardiac, or neurological involvement. However, underestimation of its frequency is possible since no data from prospective studies or autopsy series specifically addressing this question are available to yield more accurate estimates. The spectrum of possible rheumatological manifestations varies from indolent arthritis (either erosive or not) to painful and rapidly destructive inflammatory arthritis. Some are suggestive of AL amyloidosis, such as hypertrophic shoulder arthropathy, called "shoulder pad," related to amyloid deposition within the joint and the subacromial bursa. Others are more misleading, especially polyarticular involvement; it may mimic rheumatoid

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arthritis (RA) when amyloid arthropathies are symmetrical and involve hands, or polymyalgia rheumatica when amyloid arthropathy predominates in shoulders and hips[3,4,6,9-17]. The clinical effects of amyloid arthropathy have not been extensively studied, especially regarding its influence on activities of daily living. Moreover, there is only limited data on therapeutic aspects of amyloid arthropathy. Although the combination of melphalan and prednisone has been shown to be efficacious in AL amyloidosis[3,18], there are no specific data on its efficacy in amyloid arthropathy, except from isolated case reports.

We summarize 11 observations of biopsy proven MM related amyloid arthropathy, diagnosed in our units between 1978 and 1996. Clinical and radiological aspects of this uncommon pathology are presented, with attention to the functional consequences for patients and therapeutic options.

MATERIALS AND METHODS

Between 1978 and 1996, 311 patients of the Rheumatology Institute of Cochin Hospital were diagnosed as having MM and were investigated according to a standardized protocol. At time of diagnosis, evaluation included: (1) general physical examination; (2) laboratory tests with white blood cell count, hemoglobin, serum creatinine, calcium, C-reactive protein (CRP), $ß_2$-microglobulin and lactate dehydrogenase levels, serum protein and 24 h urinary protein for Bence-Jones proteins, serum and urine immunoelectrophoresis; (3) bone marrow aspiration or biopsy; and (4) bone radiographs (half of the skeleton). MM stage was evaluated according to the Durie and Salmon classification.

During followup, the consultation included the general physical examination and laboratory tests, except immunoelectrophoreses and serum $ß_2$-microglobulin level. All rheumatological symptoms — joint pain, joint swelling or stiffening, arthritis — reported by the patients, other than bone pain, were noted and signs of extraarticular or systemic amyloidosis were sought. When joint symptoms were present, radiographs of the involved joint were performed, supported by either computed tomography (CT) or magnetic resonance imaging (MRI) when available. Synovial fluid (SF) analysis was done if an effusion was present, including cell count, bacteriological analysis, and a systematic search for urate or calcium pyrophosphate crystals. For some patients, a Congo red or thioflavin T staining of SF was also performed. If the diagnosis of joint symptoms was still uncertain, a synovium biopsy was performed; pathological analysis used optical microscopy and included a search for AL amyloid deposition by Congo red or thioflavin T stain.

RESULTS

Eleven (3%) cases of amyloid arthropathy were diagnosed among the 311 patients with MM treated in our unit between 1978 and 1996; this constitutes the largest and the most homogeneous series in the literature. The patients were 6 women and 5 men. Nine of these 11 patients had light chain MM. This rate is dramatically different from MM patients without amyloid arthropathy, for whom light chain MM represents only 43/300 cases (14%) (Table 1). The monoclonal component was IgA λ and IgG λ for the 2 other patients. κ light chain was found in 6/11 patients, λ in 5/11. The κ:λ ratio was 1.2:1, lower than that of patients without amyloid arthropathy (ratio 2:1). All patients had massive Bence-Jones proteinuria, and all but one had aggressive MM, stage III A or B of the Salmon and Durie classification. The MM characteristics for each patient are detailed in Table 2.

Table 1. Characteristics of patients with multiple myeloma (MM) with or without articular amyloidosis (ALA).

	Without ALA, n = 300	With ALA, n = 11
Age at MM diagnosis, (yrs), mean ± SD (95% CI)	63.8 ± 15.6 (62.0–65.6)	56.1 ± 9.2 (50.7–61.5)
M/F ratio	1.2:1	1:1.2
M component, % (no. of cases)		
IgG	54.7 (164)	9 (1)
IgA	25.7 (77)	9 (1)
Light chain	14.3 (43)	82 (9)
Other	5.3 (16)	0 (0)
Bence-Jones proteinuria +, %	65	100
Kappa/lambda ratio	2:1	1.2:1
Stage, %		
I	14	0
II	26	9
III	60	91
Survival, yrs, mean ± SD (95% CI)	4.1 ± 3.3 (3.7–4.5)	3.8 ± 3.0 (2.0–5.6)

Onset of amyloid arthropathy. The clinical manifestations of amyloid arthropathy never preceded the clinical onset of MM (Table 2). In 6 cases, the diagnosis of amyloid arthropathy was made concomitantly with that of MM or within a very few weeks thereafter (cases 1–5, 11). For one patient (case 9), there was a 6 month interval between the diagnosis of MM and onset of amyloid arthropathy. In other patients, the interval was even longer: 2 years (case 6), 4 years (case 8), and 7 years (case 7). In one case (case 10), this interval was impossible to identify; the patient was followed for several years in Africa for symptoms potentially related to MM before his referral in France, where the diagnosis of MM was made in 1994, one year before onset of amyloid arthropathy. Of course, since no information is available to determine the beginning of monoclonal overproduction and the amyloid deposition process, it is impossible to compare the chronology of joint amyloidosis and that of MM.

Clinical expression and functional impairment. For all patients, amyloid arthropathy was the first clinical manifestation of AL amyloidosis (Table 3). The first involved joint was variable: unilateral or bilateral wrist arthritis with associated carpal tunnel syndrome in 5 patients, peripheral arthritis in 5 (shoulder in 2, hip in 2, knee in one), and RA-like polyarthritis in one. During the disease course, other articular manifestations occurred (Table 4). The most frequent was bilateral shoulder arthritis, each time associated with the pathognomonic shoulder pad pattern. One of the 4 patients with RA-like polyarthritis had a huge C1–C2

Table 2. Main characteristics of MM and amyloidosis.

Patient	Sex	ALA Onset		Multiple Myeloma			Amyloidosis	Survival After Diagnosis of ALA/MM, mo	Cause of Death
		Age, yrs	Delay After MM Diagnosis, mo	Type	Stage	BJ, g/d			
1	M	62	0	κ	IIIA	5.2	Joint only	42/42	MM progression
2	F	68	2	IgA λ	IIIB	11.8	Joint only	22/24	Septic shock
3	F	56	0	λ	IIIB	20.0	Joint, macroglossia periorbital purpura, spleen, pancreas and kidney (post-mortem)	73/71	MM progression
4	M	57	0	λ	IIIB	5.1	Joint, macroglossia, heart, gut	48/48	Acute leukemia
5	F	60	0	κ	IIIB	3.3	Joint, macroglossia, heart	10/10	Cardiac failure
6	M	68	32	λ	IIIB	4.6	Joint, skin ecchymosa	6/36	Acute leukemia (plasmablastic)
7	F	59	80	κ	IIIB	9.9	Joint, macroglossia, parotidomegaly, skin nodules	40/120	MM progression
8	F	64	47	κ	IIIB	5.0	Joint, skin nodules	51/98	MM progression
9	F	56	6	κ	IIIB	27.0	Joint only	26/32	MM progression
10	M	34	NA	κ	IIIB	12.8	Joint only	12/12§	Unknown
11	M	47	0	IgGλ	IIA	6.9	Joint, heart	11/11	Cardiac failure

NA: not available. BJ: Bence-Jones protein.

synovitis, responsible for destruction of the odontoid process and subluxation of the atlantoaxial joint (Patient 4).

Whatever the location, patients complained of limitation of activities of daily living because of joint pain or stiffening. When isolated, shoulder arthritis was mainly responsible for painful joint stiffness, impairing patients in common activities such as housekeeping, cooking or cutting food, or carrying children or heavy things. Hip involvement was mainly responsible for walking pain and rapid reduction of walking distance; in case 7, the rapid joint destruction led to bilateral total hip replacement within one year. When polyarthritis was present, pain was present at night and prolonged (> 30 min) morning stiffness was common, as in RA. Patients for whom amyloid arthropathy occurred after onset of MM reported substantial worsening of their physical condition because of amyloid arthropathy, and often felt depressed by having their diagnosis upgraded from life-threatening (MM) to a very disabling disease (amyloid arthropathy).

Other amyloid involvement. Extraarticular amyloidosis was observed in 6 patients after peripheral joint involvement (Table 2). Five of them presented with cutaneous and mucous amyloid infiltration. Three were diagnosed with cardiac amyloidosis on echocardiography (cases 4, 5, and 11); in 2 patients (cases 5 and 11), rapidly progressive cardiac insufficiency developed that was responsible for death 10 and 11 months later, respectively.

Laboratory findings. SF analysis was performed in 6 patients (Table 3). SF cellularity varied greatly, from 200 to 12,400 cells/mm^3. Congo red staining of SF was positive for only one of the 11 patients. Whatever the results of SF analysis, synovium biopsy was performed in all 11 patients and joint amyloidosis diagnosis was based on Congo red or thioflavin T staining. Immunohistochemical analysis was performed in only 2 patients (Cases 3 and 6), confirming the AL nature of amyloidosis. In the other cases, the synovium samples had been fixed in paraffin, rather than frozen, which rendered impossible the recognition of light chain deposits by specific antibodies. In four cases (Cases 4, 8, 10 and 11), immunostaining by anti-SAA antibodies was nevertheless possible but failed to reveal SAA deposits.

Radiology findings. Although often normal, radiographs of the involved joints disclosed either joint space thickening related to synovium hypertrophy (frequent in shoulder arthropathy) or narrowing with or without cysts due to erosion by synovitis (especially for hip involvement) (Table 3). In one case (case 7), shoulder arthrography was performed before the synovium biopsy; it showed a thick and heterogeneous deltoid bursa (Figure 1). The extension of amyloid deposit was easily visualized by MRI, as a nonspecific synovium hypertrophy, hypointense on T1 weighted sequence and hyperintense on T2 weighted sequence (Figure 2). A dynamic enhancement was sometimes seen after gadolinium injection, revealing an inflammatory process associated with amyloid deposition. Joint or bursal effusion was sometimes noted. When performed,

Table 3. Features of amyloid joint involvement.

Patient	Amyloidosis						
	Sex	1st Joint Involved	Other Joint Involved	Synovial Fluid, cells	Radiographs	MRI	Specific Treatment: Efficacy
1	M	Shoulder pad	Wrists, knee*, polyarthritis	200/mm^3	Shoulders: Inc. joint space	ND	
2	F	Knee arthritis*	Wrists, MCP, PIP, right hip, ankles	12,400/mm^3 PMN 98% Congo red+	Knees, hips: degenerative changes	ND	
3	F	Wrist arthritis* + carpal tunnel	Shoulder, elbow, MCP, hips, RA-like polyarthritis,	ND	Hips: cystic lesions	ND	LD prednisone: +
4	M	Wrist arthritis + carpal tunnel	Shoulders, MCP, knees*, RA-like polyarthritis, cervical spine	9200/mm^3 PMN 78%	Wrists, hips: cystic lesions	ND	
5	F	RA-like polyarthritis	Shoulder pad, elbows, wrists + carpal tunnel, knee*	450/mm^3	Wrists: cystic lesions	ND	LD prednisone: +
6	M	Hip arthritis*	Femoral fracture	ND	Normal	ND	
7	F	Hip arthritis*	Shoulder pad, elbows, wrists + carpal tunnel	ND	Shoulders: cystic lesions Hips: cystic lesions, dec. joint space	Hip: articular and periarticular synovitis	Local steroids: +
8	F	Wrist arthritis* + carpal tunnel	Shoulder pad, elbows, MCP, hips, knees	2400/mm^3 PMN 8%	Shoulders, wrists: cystic lesions	Wrist: carpal tenosynovitis	LD prednisone: – Local steroids: + Colchicine: –
9	F	Wrist arthritis* + carpal tunnel	Shoulder pad,	ND	Shoulders: cystic lesions,	Shoulder: articular and periarticular synovitis	LD: prednisone: + Local steroids: +
10	M	Wrists arthritis* + carpal tunnel	Shoulder pad, hips	ND	Shoulders: cystic lesions, inc. joint space, humeral head moved down	Shoulder: articular and periarticular synovitis	
11	M	Shoulder pad*	Wrists + carpal tunnel, ankles	800/mm^3	Normal	Shoulder: articular and periarticular synovitis	LD prednisone: +

* Joint on which synovium biopsy had been performed. ND: not done, LD: low dose. +: response to therapy, i.e., improvement of pain and stiffness.

shoulder MRI disclosed either articular synovitis or deltoid bursitis. In some patients (cases 7 and 11), deltoid bursitis seemed more extensive and more intense than the gleno-humeral synovitis (Figure 3). In others (cases 9 and 10), joint synovitis was similar to periarticular bursitis (Figure 4). Similar observations were noted on hip MRI, between the hip synovium and the peritrochanteric bursa. Although MRI did not reveal pathognomonic signs of amyloidosis, it provided a clear visualization of synovial inflammation intensity and helped to determine the best site to perform the biopsy.

Treatment and evolution. When effective for MM, chemotherapy, either conventional or intensified, often led to improvement of joint symptoms. In 6 patients, additional rheumatological treatment was needed. Low dose oral prednisone was used in 5 patients (cases 3, 5, 8, 9, 11), with improvement of pain and stiffness; the effect on shoulder hypertrophy when present was less obvious. Three patients with inflammatory arthritis, defined as inflammatory pain, high SF cellularity, or gadolinium enhanced synovitis on MRI were treated with intra- or periarticular steroid injections, with substantial improvement. Colchicine was tried in one patient, without success.

Table 4. Amyloid articular localization in our patients and in 3 other series.

Site	Present Series, 11 cases, n (%)	Wiernik[9] 24 cases, n (%)	Cohen[10] 22 cases, n (%)	Hickling[6], 3 cases, n (%)
Carpal tunnel syndrome	8 (73)	8 (33)	10 (45)	3 (100)
Shoulder	10 (91)	18 (75)	15 (68)	3 (100)
Elbow	4 (36)	10 (42)	11 (50)	0 (–)
Wrist/MCP/PIP	8 (73)	17 (71)	16 (73)	3 (100)
Hip	5 (45)	8 (33)	3 (14)	0 (–)
Knee	5 (45)	15 (63)	16 (73)	3 (100)
Ankle	3 (27)	3 (13)	7 (32)	0 (–)
RA-like polyarthritis	4 (36)	1 (4)	1 (5)	3 (100)
Sternoclavicular joint	0 (–)	1 (4)	1 (5)	NA NA
Temporomandibular joint	0 (–)	0 (–)	1 (5)	NA NA
Cervical spine	1 (9)	1 (4)	1 (5)	0 (–)
Back	0 (–)	4 (17)	4 (18)	NA NA

MCP: metacarpal joint, PIP: proximal interphalangeal joint, NA: not available.

Overall survival was not different between patients with or without amyloid arthropathy (Table 2). The most rapidly fatal outcome was observed for the 2 patients with cardiac amyloidosis (cases 5 and 11). For the other patients, the causes of death were related to MM or to MM treatment rather than to amyloidosis. No relation was found between the clinical, laboratory, and radiological patterns of amyloid arthropathy and the duration of survival.

DISCUSSION

Joint AL amyloidosis is a rare event during MM, which is often more disabling for the patient than MM itself, even if not life-threatening. Our investigation is the largest single-center case series ever reported; moreover, in all our cases, joint involvement revealed amyloidosis, and was not a feature of an already widespread deposition. The estimated prevalence is 3% in our series, which is either higher than or close to previously reported levels — 0.1–0.2% in a series of 1953 MM[8], 6% in another series of 43 MM patients[6]. However, no cases were reported by Kyle, *et al* in their cohort of 2225 cases[3,4]. Our findings concerning MM characteristics are consistent with previously published data on AL joint amyloidosis. There was an overrepresentation of light chain MM, and no predominance of the λ isotype was found[9,11], in contrast to series describing patients with extraarticular AL amyloidosis[3,4,19-23]. The majority of patients had a stage III MM by the classification of Salmon

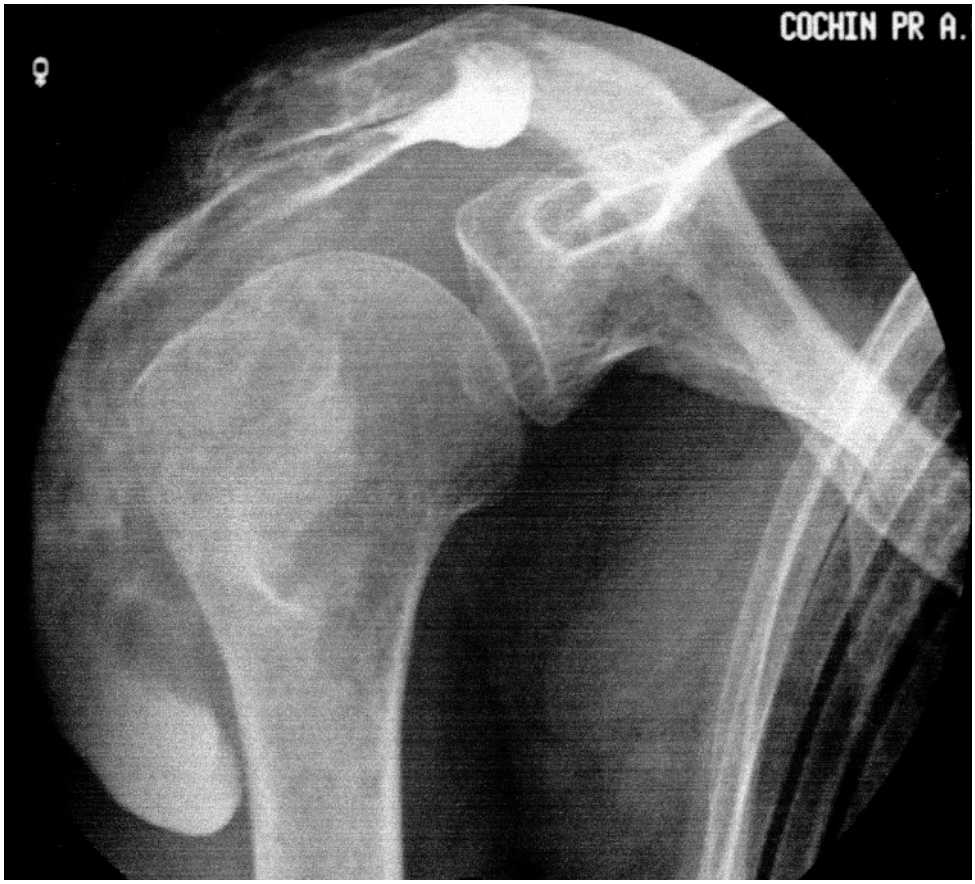

Figure 1. Shoulder bursography before bursal biopsy, case 7. Opacification of the enlarged deltoid bursa. The synovium appeared heterogenous, which corresponded to the synovial thickening provoked by amyloid deposition.

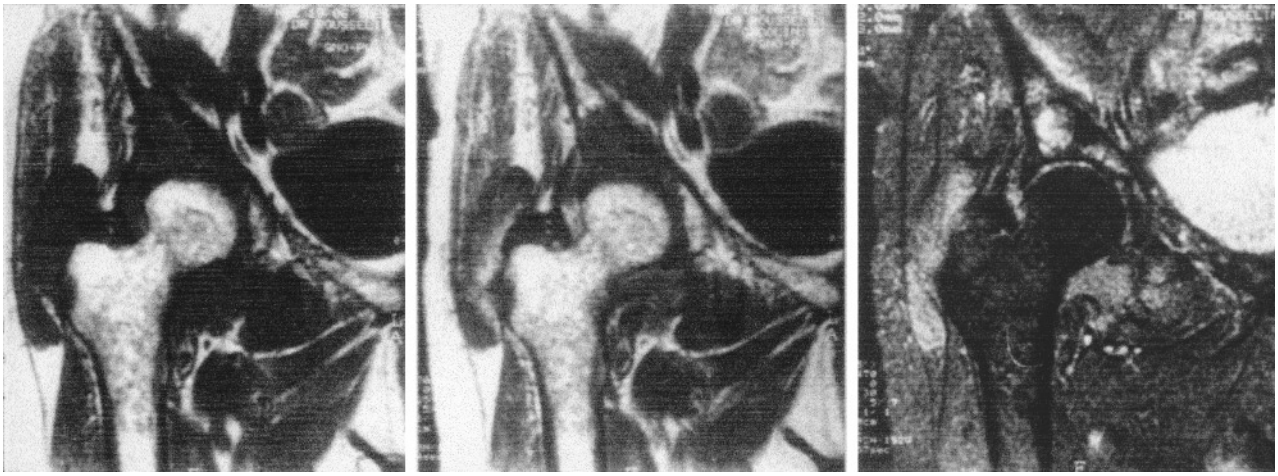

Figure 2. Hip MRI, case 7. Coronal section (left to right: T1, T1 with gadolinium, T2). Slight articular synovitis and a huge peritrochanteric bursa were noted. The signal revealed an inflammatory phenomenon with an isointense pattern on T1 weighted sequence, gadolinium enhancement, and hyperintense aspect on T2 weighted sequence. There was slight joint effusion of the hip. A cystic lesion of the right femoral head appeared as a T1 hypointense, T2 hyperintense, nongadolinium enhanced signal.

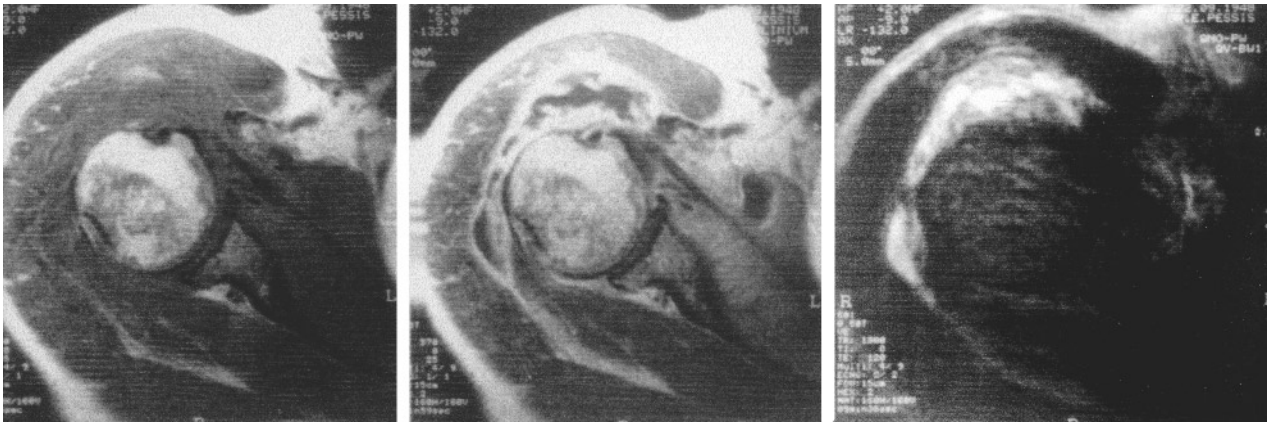

Figure 3. Shoulder MRI, case 11. Axial section (left to right: T1, T1 with gadolinium, T2). A huge deltoid bursitis was noted. The signal of the hypertrophic synovium was as described in Figure 2, with more intense enhancement with gadolinium. Extensive effusion of the deltoid bursa was observed, but no abnormal feature was present within the joint.

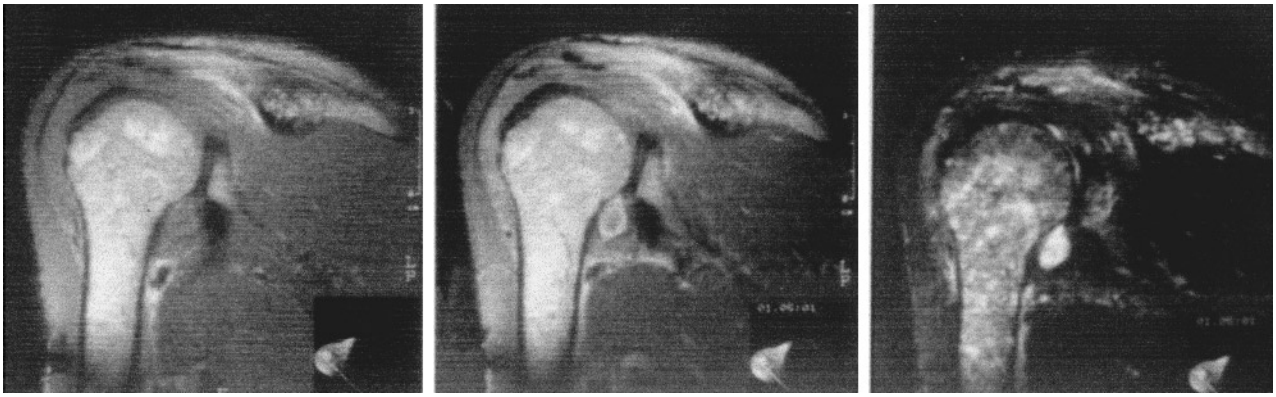

Figure 4. Shoulder MRI, case 9. Coronal section (left to right: T1, T1 with gadolinium, T2). Joint effusion was present and the articular synovium appeared hypertrophic in the inferior recessus, with an isointense signal on T1 weighted sequence, gadolinium enhancement, and hyperintense on T2 weighted sequence. The deltoid bursa was hypertrophic, isointense on T1 weighted sequence, gadolinium enhancement, and hyperintense on T2 weighted sequence. No effusion was seen in the bursa.

and Durie, MM related renal insufficiency was common[8–11,24], and Bence-Jones proteinuria was always present[9,10]. However, our study does not provide evidence for better understanding of pathogenic links between MM and AL amyloidosis, especially with regard to AL amyloidosis without an identifiable monoclonal component as reported[25-28] or to the predominant amyloid deposition in joints in our patients, for which light chain sequences or biochemical properties could play a substantial role[29-32]. Clinical onset of amyloid arthropathy is often concomitant with or subsequent to that of MM, but some cases of amyloid arthropathy preceding MM are reported[13]. However, joint amyloid deposition kinetics and its relation to that of monoclonal gammopathy remain poorly understood.

In this series and in the literature, the joints most frequently involved by AL amyloidosis are shoulders and wrists (Table 4)[6,9,10]. The shoulder pad sign was always associated with shoulder amyloid arthropathy, which reinforced its pathognomonic value[12,33]. Hip involvement is common, but there was one case revealed by a femoral neck fracture in our series — a huge cyst caused by amyloid deposition progressively eroded the bone. The ability of amyloid arthropathy to mimic RA should be more widely known, as it may be the first symptom of both joint AL amyloidosis and MM. The confusion between the 2 diseases is understandable: joint symptoms are similar and cutaneous nodules are possible in both[9]; a case of amyloid C1–C2 synovitis with subluxation of atlantoaxial joint occurred in one of our patients. Some features may be more suggestive of amyloidosis: shoulder pad sign, subcutaneous swelling of the fingers sometimes associated with tendon retraction, swelling of the tongue, and periorbital purpura[11,24,34]. No case of polymyalgia rheumatica-like amyloid arthropathy was found in our series. These findings have been described in elderly patients complaining of shoulder arthritis[14-17]. In 3 cases, cephalic signs of Horton's disease were also present: temporal artery biopsy revealed amyloid vasculitis in 2 cases[15,16] and association of amyloid vasculitis and giant cell arteritis in one case[17]. Whatever the presentation, the functional impairment due to amyloid arthropathy was substantial. This observation has not been noted in previous reports and needs to be emphasized. In our experience, joint pain and stiffening was comparable to that seen with inflammatory arthritis.

Low cell counts, between 100 and 1500/mm^3, are usually reported in SF[6,8-10]. Inflammatory arthritis with higher cell counts (> 2500/mm^3) is possible, reaching > 10,000 cells/mm^3 in rare cases[10,11]. Diagnosis of amyloid arthropathy was by SF analysis for only one of our patients, although it has been proposed as a reliable method for diagnosis[35]. The gold standard remains the synovium histology, mainly based on light microscopy of Congo red or thioflavin T staining. Immunohistochemical studies are required to characterize the amyloid deposit and to ascertain the primary (AL) nature of amyloidosis in difficult cases. This technique was performed for 2 patients, but not for the others, since no frozen synovium samples were available. This led to a debate concerning Patient 8, who underwent hemodialysis in the course of MM; since manifestations of amyloid arthropathy preceded the beginning of hemodialysis and ß$_2$-microglobulin amyloidosis usually appears after several years of hemodialysis, primary amyloidosis was the likely cause of the amyloid arthropathy. However, in the following years, a mixed (ß$_2$-microglobulin and AL) amyloidosis was considered for this patient, as described[13].

Some radiological features may suggest amyloid arthropathy. Extensive cysts are common in juxtaarticular areas, at the site of synovium insertion, which distinguishes them from subchondral cysts observed in other types of arthropathy[6,10,24,36]. These lesions are linked to the ability of the amyloid synovium to mechanically erode bone; moreover, inhibition of bone formation by the amyloid deposit has also been described[37]. Joint space enlargement provoked by synovium hypertrophy is also a common feature of amyloid arthropathy; it may not be considered pathognomonic, since it may be observed in acromegaly and osteochondromatosis. Joint space narrowing is also possible in very inflammatory joint amyloidosis or in late stages of the disease[34]. Currently, MRI seems to be the most informative method to explore amyloid arthropathy; although it does not provide specific images of amyloid deposits, it can indicate their extension[38,39]. Amyloid synovium usually discloses T1 hypointense and T2 hyperintense signal, often associated with enhancement after gadolinium injection, with a highly variable intensity. These findings, associated with the observation of inflammatory pain and high SF cell counts in some patients, contrast with the traditional belief that amyloid deposits are not phlogogenic, and favor the existence of an amyloid inflammatory synovitis.

Heterogeneity of treatment in our patients is explained by the lack of standardization until recently. Now the efficacy of a melphalan-prednisone regimen[18,40] or intensive chemotherapy followed by stem cell injection[41] is well established. In our experience, there was a relation between the evolution of joint amyloidosis and MM, even if they were not strictly parallel; joint symptoms tended to improve or to disappear when chemotherapy was effective in MM, and preceded or reappeared with a relapse of MM. We often observed substantial improvement of pain, but rarely of shoulder hypertrophy and stiffness. Continuous treatment with low dose prednisone (10 to 20 mg daily) was also often used for improving pain and function in some patients, but no reliable data are available for this.

Intra- or periarticular steroid injections in joint amyloidosis have been performed on an empirical basis. They were effective in patients with intense synovitis on MRI; in the other cases, the effect of such treatment seemed limited.

Other local treatments have been mentioned in isolated cases, such as isotopic synoviorthesis[42]. Whatever treatments were considered, there is no evidence they were able to reduce or stop the amyloid deposition within joints. From the present series and data in the literature, joint AL amyloidosis does not seem to influence survival[3,4,18,40], and the amyloid involvement with the poorest prognosis remains that of the heart and neurological system[5,43].

Even if articular amyloidosis is a rare event during the course of multiple myeloma, physicians should be able to recognize this confusing disease, especially in patients with light chain multiple myelomas. Special attention should be paid to the dramatic functional impairment engendered by this condition. Since both local and systemic treatments are at least partly efficacious, the diagnosis of joint amyloidosis should lead to substantial improvement in quality of life of patients with MM, who already face a serious and life-threatening disease.

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