short report
Haematologica 1994; 79:364-366

AL-AMYLOIDOSIS IN MONOCLONAL GAMMOPATHIES

Anna Miliani, Franco Bergesio

*Clinica Medica IV, Università di Firenze, *Divisione di Nefrologia e Dialisi, Policlinico di Careggi, Florence, Italy*

ABSTRACT

Sixty-two patients affected by MGUS underwent fat tissue aspirate examination for diagnosis of AL amyloidosis. Nine out of the 62 were found to be Congo red positive. MGUS had already been diagnosed for quite a long time in about 60% of these patients, while this prevalence decreased to 24% among the Congo red negative patients. The follow-up of the positive patients is reported.

Key words: AL amyloidosis, MGUS, fat tissue aspirate, Congo red reaction

AL amyloidosis (AL-A) is found in about 6-15% of patients with multiple myeloma (MM);[1] this prevalence seems to be much lower in monoclonal gammopathy of undetermined significance (MGUS). In fact, among the 241 patients examined at the Mayo Clinic before January 1, 1971, and who underwent prospective follow-up for 20 to 35 years, evident systemic AL-A only developed in 8 patients (3.2%) at a median of 9 years after detection of the monoclonal protein.[2] A similar occurrence has also been reported by Blade et al.[3]

However, in clinically asymptomatic patients affected by MGUS fat aspirates from the periumbilical area may be Congo red positive. Few data are reported on this subject[4,5] and, furthermore, we do not presently know the natural history of these patients. We report our experience with periumbilical fat tissue aspiration (FTA) in 62 subjects affected by MGUS.

Patients and methods

We studied 62 patients (33 females and 29 males) with a serum monoclonal component (MC) without evidence of myeloma, Waldenstrom's macroglobulinemia or cryoglobulinemia. The patients were divided into two groups according to the type of monoclonal gammopathy (associated or not associated with another disease).

Group A. Forty-seven patients were completely asymptomatic. In 18 a MGUS had been diagnosed 16 to 145 months earlier (median 71 months); in the others the diagnosis of MGUS was made at the time of periumbilical FTA or preceded it by a short time (not more than 10 months).

Group B. Fifteen patients presented a MC associated with one of the following pathologies: lymphoproliferative diseases 5 patients; chronic liver disease 4 patients; epithelial neoplastic disease 2 patients; various inflammatory diseases 4 patients. In no case did discovery of the MC precede diagnosis of the other disease by more than 12 months, and discovery of the MC preceded FTA by more than 12 months (from 20 to 174 months; median 36 months) in only 5 subjects. No patient complained of symptoms that suggested amyloidosis.

The presence of amyloid was investigated by bilateral FTA using Congo red staining.[6] Congo red-positive patients underwent cardiac echotomography, full eye examination and detailed electroneurographic study. These and routine blood tests were repeated about once a year.

Results

The results of our investigation are reported in Tables 1 and 2. In 5 of the 9 Congo red-positive patients, the MC had been discovered, respectively, 28, 46, 134, 135 and 174 months before

Correspondence: Prof. Anna Miliani, Clinica Medica IV, viale Pieraccini 18, 50139 Florence, Italy. Tel. international +39.55.412178. Fax international +39.55.4223549.
Received December 21, 1993; accepted May 2, 1994.

©Ferrata Storti Foundation

Table 1. Light chain distribution in the overall population and in Congo red-positive patients (pts). The positive patient in group B suffered from chronic liver disease – patient #9 in Table 2.

group	no. of patients	Light chain type in overall population			Light chain type in Congo red positive pts.			% of positive pts.
		k	λ	kλ	k	λ	kλ	
A	47	23	23	1	2	5	1	14.5
B	15	9	6	—	1	—	—	

FTA. In the other four the diagnosis of MGUS was not more than 10 months old when the FTA was performed. MGUS had been diagnosed from a minimum of 18 months to a maximum of 125 months (median 73) before FTA in only 17 out of the 53 Congo red-negative patients.

Clinical tests were negative in 7 of the 9 Congo red-positive patients; cardiac echotomography was *suggestive* of amyloidosis in patient #1, and mild sensory-motor damage was linked to a slight sicca syndrome in patient #7.

To date, the follow-up of our Congo red-positive patients after demonstration of amyloid in FTA ranges between 8 to 58 months. In 5 pts physical examination and blood tests have remained unchanged; patient #1 died suddenly 8 months after FTA (autopsy not performed), while patient #7 remained clinically asymptomatic for amyloidosis for the next 47 months before dying of lung cancer. The autopsy revealed amyloid involvement of the myocardium. Patients #5 and #8 developed a clinically evident sicca syndrome two years after FTA; their respective follow-ups are 58 and 57 months.

Table 2. Follow-up of Congo red-positive patients (in months).

Pts.	*Time from diagnosis of MGUS*	*Time from FTA examination*	
1. LF	10	8	deceased
2. MF	11	11	
3. BC	48	46	
4. TG	63	53	
5. PI	86	58	
6. BA	103	57	
7. TT	190	45	deceased
8. BR	191	57	
9. DIF	225	51	

Conclusions

Conceivably, amyloid deposition takes a certain amount of time to occur and/or to become clinically apparent. This seems to be in agreement with Kyle's findings.[2] Accordingly, we observed a high prevalence (5/9) of Congo red-positive patients with a long history of MGUS. The overall high prevalence of AL-A found in our series (14%) could be explained by the fact that we only considered patients with a positive FTA regardless of clinically evident systemic AL-A (*subclinical amyloidosis ?*).

Since the amyloidogenicity of a monoclonal light chain is only partly evaluable and in any case it cannot be ascertained in every patient, all monoclonal gammopathies should be regarded as having the potential to develop into AL-A.

We think that routine study of periumbilical fat tissue is mandatory in all MGUS. In addition, Congo red-positive patients, even when asymptomatic, should be strictly monitored for early diagnosis of specific organ involvement because of the possible systemic evolution of the disease.

References

1. Ascari E, Merlini G, Riccardi A, et al. Amiloidosi AL. Proceedings of Società Italiana di Medicina Interna, 90th Meeting. Rome, 1989:361-75.
2. Kyle RA. "Benign" monoclonal gammopathy after 20 to 35 years of follow-up. Mayo Clin Proc 1993; 68:26-36.
3. Blade J, Lopez-Guillermo A, Rozman C, et al. Malignant

©Ferrata Storti Foundation

transformation and life expectancy in monoclonal gammopathy of undetermined significance. Br J Haematol 1992; 81:391-4.
4. Miliani A, Bergesio F, Salvadori M, et al. Gammapatie di significato indeterminato (MGUS) e amiloidosi AL (AL-A). (Abstract). 33th Meeting of the Società Italiana di Ematologia, Verona, 1991:240.
5. Curciarello G, Gentilini I, Amaddii G, et al. Discrasie plasmacellulari e amiloidosi AL: risultati preliminari di uno studio prospettico (Abstract). 34th meeting of the Società Italiana di Ematologia, Napoli, 1993:264.
6. Gertz MA, Li C, Shirahama T, et al. Utility of subcutaneous fat aspiration for the diagnosis of systemic amyloidosis (immunoglobulin light chain). Arch Intern Med 1988; 148: 929-33.

©Ferrata Storti Foundation