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Clinical characteristics of patients with systemic amyloidosis from 2000–2010☆

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Abstract
Background: The epidemiology of systemic amyloidosis has been changing in the last decades. We aim to describe the clinical characteristics of the patients seen at our institution with systemic amyloidosis in 2000–2010 and compare them with previous Spanish series.
Patients and methods: An observational, retrospective study was performed on all the patients admitted to a tertiary hospital in Madrid, Spain who had been diagnosed of amyloidosis from January 2000 to December 2010. Patients without a proven diagnosis of amyloidosis, with dialysis-associated, senile, or localized forms of amyloidosis were excluded from the study. A systematic review was made of the clinical records, collecting the demographic, clinical and biochemical variables at diagnosis and patients' outcome.
Results: A total of 55 patients were studied, 24 (44%) of whom had AL amyloidosis, 30 (56%) AA amyloidosis, and 1 a familiar form. The most frequent underlying disorders were rheumatoid arthritis (9 patients, 30%) and ankylosing spondylitis (4 cases, 13%). The kidneys were the most frequently involved organ (36 patients, 67%) with nephrotic-range proteinuria during diagnosis (3.4 ± 3.7 g/24 h). Median time to diagnosis was 3 months (interquartile range [IQR]: 1–17). Median follow-up time was 24 months (IQR: 10–91). During follow-up 31 patients died; 18 of those deaths were related to amyloidosis.
Conclusions: Renal dysfunction dominates the course of systemic amyloidosis, which does not seem to have changed in the last decades. We have observed an important delay in the diagnosis of these processes. Therefore, it is necessary to maintain a high degree of clinical suspicion regarding these conditions.

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PALABRAS CLAVE
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Características clínicas de los pacientes con amiloidosis sistémicas en el periodo 2000–2010

Resumen
Antecedentes: La epidemiología de las amiloidosis sistémicas está cambiando en las últimas décadas. Describimos las características clínicas de los pacientes con amiloidosis sistémicas atendidos en nuestro centro en el periodo 2000-2010 y las comparamos con las anteriores series españolas.
Pacientes y métodos: Estudio observacional retrospectivo de pacientes con diagnóstico de amiloidosis sistémica en un hospital terciario entre enero de 2000 y diciembre de 2010. Se excluyó a los pacientes sin diagnóstico histológico y a aquellos con formas asociada a diálisis, seniles o localizadas. Mediante revisión sistemática de las historias clínicas se recogieron las variables demográficas, clínicas, de diagnóstico, seguimiento y mortalidad.
Resultados: Se estudió a 55 pacientes, 24 (44%) tenían amiloidosis AL, 30 (56%), amiloidosis AA y un paciente, una forma familiar. Las enfermedades inflamatorias subyacentes más frecuentes fueron la artritis reumatoide (9 pacientes, 30%) y la espondilitis anquilosante (4 enfermos, 13%). El órgano más frecuentemente afectado fue el riñón (36 pacientes, 67%), con una proteinuria al diagnóstico de $3{,}4 \pm 3{,}7$ g/24 h. El tiempo hasta el diagnóstico fue de 3 meses (rango intercuartílico [RIC]: 1-17). La mediana de seguimiento fue de 24 meses (RIC: 10-94). Durante el seguimiento fallecieron 31 pacientes y 18 muertes fueron atribuíbles a la amiloidosis.
Conclusiones: La afectación renal es la presentación más prevalente de las amiloidosis sistémicas, sin cambios en las últimas décadas. Observamos un largo tiempo de latencia hasta el diagnóstico, por lo que es preciso mantener un alto grado de sospecha clínica de estos procesos.

Introduction

Amyloidosis represents a heterogeneous group of diseases characterized, from the pathogenic standpoint, by an extracellular deposit of proteins in the form of insoluble fibers. These proteins aggregate in a characteristic three-dimensional configuration in beta-sheets, which when stained with Congo red exhibits birefringence under polarized light.[1] To date, 25 structurally unrelated proteins capable of causing amyloidosis are known.[2] The various forms of amyloidosis are classified according to these precursor proteins and by the distribution of the amyloid deposit in the body.[3] The main types of systemic amyloidosis are primary (AL) amyloidosis, secondary (AA) amyloidosis, familial amyloidosis, senile amyloidosis and amyloidosis associated with the deposit of beta-2-microglobulin in patients with end-stage chronic kidney disease.[4]

Amyloidoses are classified as rare diseases, despite the fact that our knowledge of their epidemiology is based only on small retrospective series and they are probably underdiagnosed conditions.[5,6] The last Spanish series of patients with amyloidosis was published more than 20 years ago. These series have reported a predominance of secondary systemic forms combined with a high prevalence of tuberculosis and other chronic infections.[7–11] Various authors have indicated that the epidemiology of systemic amyloidosis, particularly secondary forms, has changed in recent decades as a result of earlier diagnoses, more potent and active treatments against the baseline diseases and a reduction in the comorbidity associated with the underlying inflammatory diseases.[12,13] At the same time, there is concern that the low diagnosis of these conditions is a reflection of less clinical suspicion due to a change in the type of presentation of systemic amyloidosis and a more indolent course.[13]

The aim of this study is two-fold. It seeks to describe the clinical characteristics of patients diagnosed with systemic amyloidosis who were treated in a tertiary hospital in Madrid during the period 2000–2010 and compare these with previously published Spanish series.

Patients and methods

Study design and patient selection

We conducted a retrospective observational study on patients admitted to the University Hospital La Princesa of Madrid in the period between January 2000 and December 2010 who had a diagnosis (primary or secondary) of amyloidosis. The diagnosis of amyloidosis was accepted if it met the clinical, laboratory and histopathological criteria in terms of the personal and family history, the history of inflammatory disease, organ involvement and/or the presence of a monoclonal component in serum or urine, according to the currently accepted diagnostic criteria for amyloidosis.[14] Using a computerized review of medical records, we conducted patients follow-up until death, to loss or to the present.

We excluded from the final analysis those patients with senile forms of amyloidosis (cerebral amyloid angiopathy and senile cardiac amyloidosis), nodular localized amyloidosis and amyloidosis associated with beta-2-microglobulin. We also excluded from the final analysis those with a presumptive clinical diagnosis (lacking histological confirmation) and those who, with a positive result for amyloids in an abdominal fat biopsy, did not develop symptoms of amyloidosis during the follow-up period. We only analyzed those