Primary Amyloidosis: Short-Term Prognosis Is Not Always Unfavorable

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Dear Sir,

Primary amyloidosis is an uncommon disease characterized by the extracellular deposition of a fibrillic proteic substance consisting of immunoglobulin light chains [1] which in time leads to progressive impairment of the organ or tissue involved. The average survival of patients with this disease does not reach 15 months [2, 3] and the most common causes of death are renal and cardiac failure.

This case report concerns a 66-year-old man, diagnosed for primary amyloidosis in June 1984, who after 104 months of survival is apparently well. This patient, with no previous significant history of disease, was first seen at our department in June 1984 for edemas in his legs, general malaise and fatigue.

Objective examination revealed only slight hepatomegaly and small pretibial edemas. There were no macroglossia nor alterations in the nervous system. Arterial pressure was around 115/75 mm Hg and heart frequency was normal. Further investigation showed clear signs of nephrotic syndrome. Proteinuria was around 10 g/24 h, albuminemia was 2.5 g/dl and plasma triglyceride and cholesterol values were 618 and 634 mg/dl, respectively. Creatinemia was 1.6 and azotemia 51 mg/dl.

A renal biopsy was performed, and optical microscopy of the specimen showed an accumulation of eosinophilic material that was Congo red intensely positive, above all around the mesangium. Electron microscopy showed the typical fibrillar structure of amyloid. Biopsy of the rectal mucosa confirmed the diagnosis of amyloidosis. An examination of bone marrow aspirate revealed a plasma cell increase of 6.1%.

Plasma electrophoresis showed no monoclonal peak. The amounts of k light chains in the serum and urine were 555 and 40 mg/dl, respectively (700 mg in 24 h). Erythrocyte sedimentation rate was 94 mm/h. The Bence-Jones protein test was negative. Hemochrome showed no significant alterations. Complement and rheumatoid factor values were normal. Antinuclear and anti-DNA antibody tests were negative. Other routine laboratory tests were all normal. Serum β_2 microglobulin was 3.36 mg/l (normal: 0.86-3.94). Electrocardiogram showed a 1st-grade atrioventricular block and a left anterior partial block, echocardiogram a hypertrophic

cardiopathy with good contractility of the left ventricle, chest radiography revealed slight hepatomegaly, while abdominal ultrasound gave no abnormal findings.

The patient was given combined chemotherapy until August 1986: 6 4-day cycles with melphalan (0.25 mg/kg/day) and prednisone (2 mg/kg/day) and 21 cycles with vin-cristine (1 mg the 1st day of the cycle), cyclo-phosphamide (0.5 mg/kg/day for 4 days) and prednisone (0.7 mg/kg/day for 4 days). At the 7th cycle, vincristine, cyclophosphamide and prednisone were given instead of melphalan and prednisone, because of the lack of improvement in laboratory parameters. In March 1991, due to deterioration in renal function, the patient restarted treatment as above with vincristine, cyclophosphamide and prednisone. In August of the same year, after 4 cycles, this treatment was stopped, as not only had there been no reduction in creatinemia or proteinuria but, indeed, a progression of renal dysfunction.

In January 1992, creatinemia had reached a level of 7.2 mg/dl, proteinuria was 12 g/24 h, albuminemia was 3.3 g/dl, myelogram of plasma cells was 4% and the k light chain amount in the serum and urine was 294 and

39.8 mg/dl, respectively (597 mg in 24 h). During the following months, renal function deteriorated even further and at the beginning of July 1992, the patient started hemodialysis.

Figure 1 shows creatinemia and protein-uria trends from June 1984 to June 1992.

Rectal biopsy has been repeated, confirming the presence of amyloid, which, on the basis of light chains mostly of the k type, has been immunohistochemically classified as primary type.

An echocardiogram carried out in May

1992 showed slight dilation and moderate hypokinesia of the left ventricle and parietal thickening, while the ventricular myocardium had a granular appearance. The right ventricle showed just slight hypokinesia, and there was slight thickening of the interatrial septum.

Another echocardiogram in January

1993 showed no substantial variations. Despite these modest signs of myocardiopathy and ventricular low-frequency arrhythmia from atrial fibrillation and flutter, which arose in the past 2 years, the patient was completely asymptomatic and, therefore, bears dialysis well.

Reanalyzing the course of the disease, as far as renal involvement is concerned, the best results were obtained in 1989, when creatinemia was 2.1-2.2 mg/dl, proteinuria around 8 g/24 h, albuminemia was 3.6 g/dl and combined chemotherapy had already been suspended for about 3 years. That improvement could have been the result of a period of partial remission or quiescence of the amyloid disease.

Deterioration of renal function at the beginning of 1990 and in particular during the first half of 1991 could be connected to amyloidosis, shown also by the increase in the number of k light chains in the serum (1,140 mg/dl) and urine (42,5 mg/dl; 850 mg in 24 h). However, the subsequent rise in creatinemia observed some months before starting hemodialysis could not be blamed on amyloidosis, given that other parameters of the disease were unchanged. In fact, the myelogram percentage of plasma cells and

Fig. 1. Changes in creatinemia and proteinuria from June 1984 to June 1992.

the amount of paraprotein in the serum and urine are notably less. We did not feel like performing another biopsy, given the stage of advanced renal insufficiency, but inflammatory and/or hemodynamic factors cannot be excluded as having superimposed themselves over the basic disease.

Two studies carried out by Kyle et al. [2,3] on different groups of patients with primary amyloidosis report an average survival of 12 and 14.7 months.

Our patient has already lived over 104 months from the moment of diagnosis. This life span is one of the longest to be reported. The reason for this favorable course is not clear, but the lack of serious cardiac amyloidosis has probably played an important role. Also in the case reported by Fritz et al. [4], with the longest reported survival of 19 years, there was no severe cardiac damage.

Our patient's longevity and that of other cases described in the literature [4, 5] show how primary amyloidosis does not necessarily imply a short-term unfavorable prognosis.

– creatinemia (mg/dl) –proteinuria (g/24h) || chemotherapy

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