

AL amyloidosis in a young adult: remission with autologous stem cell transplantation

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ABSTRACT

Autologous stem cell transplant is one of the therapies employed in the treatment of primary amyloidosis or AL. The authors report on a 46-year-old patient with bilateral periorbital hematomas, macroglossia who presented, during the investigation, IgG-Kappa paraprotein in serum. The diagnosis of primary amyloidosis or AL was confirmed and the treatment proposed consisted of high-dose melphalan as conditioning regimen before autologous stem cell transplant, which determined complete remission of the disease, along with the disappearance of clinical signs and absence of the monoclonal component.

Keywords: amyloidosis, autologous transplantation, melphalan.

INTRODUCTION

AL Amyloidosis is a deposition disease in tissues of fragments of light chain, with spatial and tinctorial disposition of amyloid fibrillar material.¹ The amyloid deposition affects several organs and both the deposition extension and the affected organ are related with worse prognosis, such as cardiovascular involvement. The therapeutic difficulty in these cases motivated the authors to report the results obtained with autologous stem cell transplant.

We recently assessed a young patient. For 2 years, the clinical picture consisted of periorbital hematomas, carpal tunnel syndrome and presence of serum monoclonal protein at the protein electrophoresis. After the assessment, AL amyloidosis was identified. The proposed treatment consisted of chemotherapy associated with autologous stem cell transplant.

CASE REPORT

M.M.V.F., a 46-year-old male patient, sought medical attention complaining of hand paresthesia, myalgia, periorbital hematomas and macroglossia. The symptoms had been ongoing for 2 years, without a definitive diagnosis. At physical examination, he presented periorbital hematomas, macroglossia, signs suggestive of carpal tunnel syndrome in both hands and unspecific muscular pains.

The protein electrophoresis identified a monoclonal peak at the gamma-globulin region, which corresponded to 31.3% of the total proteins. The erythrocyte sedimentation rate (ESR) after the 1st hour was altered, at 39 mm (normal value \leq 15 mm). The whole blood count did not present any alterations at the following parameters: HB = 13.9 g/dL; HT = 41.9%, red blood cells = 4.91×10^6 μ /L, leukocytes = 9,100 μ /L and platelet count = 198,000 μ /L. Regarding the renal profile: urea = 44 mg/dL

Received on 02/18/2010. Approved on 08/26/2010. We declare no conflict of interest.
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and creatinina = 1.53 mg/dL. No alterations were identified at the partial urinalysis (urine I). The patient presented IgM level of 30 mg/dL (within normal range) and monoclonal IgG-Kappa light chain measurement of 3.6 g/100 mL at the serum protein immunofixation test. The echocardiogram with Doppler was considered normal.

The aspiration myelogram showed normal cellularity in the erythrocytic, monocytic and granulocytic series, with preserved cell maturation progress. The lymphoplasmacytic series presented 14% of mature plasmacytes. The patient was submitted to a rectal biopsy, of which result showed hyaline amorphous material positive for amyloid material with specific staining methods. Eighteen months later, the patient is in complete remission, with no clinical signs and the monoclonal component has disappeared.

The patient received, for a consecutive week, 0.4 mg of granulokine via subcutaneous route, followed by high-dose Melphalan via intravenous route, 200 mg/m². After the third day, he was submitted to apheresis, to obtain CD34-positive cells (stem cells) (Figures 1 and 2).

DISCUSSION

Amyloidosis is not a single disease. The term is currently used generically to refer to any pathological condition where there is extracellular deposition of fibrillar proteins, with special birefringence characteristics. The binding to certain stains such as Congo red or thioflavin is a common denominator in cases of amyloidosis. There are currently more than twenty proteins with these characteristics and each one of them must be seen as a distinct clinical entity.

The three most common forms, with a multiorgan system presentation, are the light-chain amyloidosis (AL), formed by kappa and lambda chain fibrils, reactive-form amyloidosis (AA), derived from the serum protein precursors and the hereditary form, caused by mutations in the plasma proteins. Although the amyloidosis form linked to Alzheimer's should be the most prevalent form of amyloidosis, it is not mentioned in the context of systemic disease, as it is a disease located in a single organ.²

In the AA and hereditary forms of amyloidosis, the course of the disease is slow and periods of survival present considerable variation.³ In the AL form, a combination of symptoms that affect kidneys, heart, gastrointestinal, neurological and hematological systems, or liver alterations are part of the clinical picture.

Before the 1970s, in a series of 42 patients from Boston University, nineteen patients who presented AL amyloidosis



Figure 1 – Presence of periorbital hematoma at diagnosis.

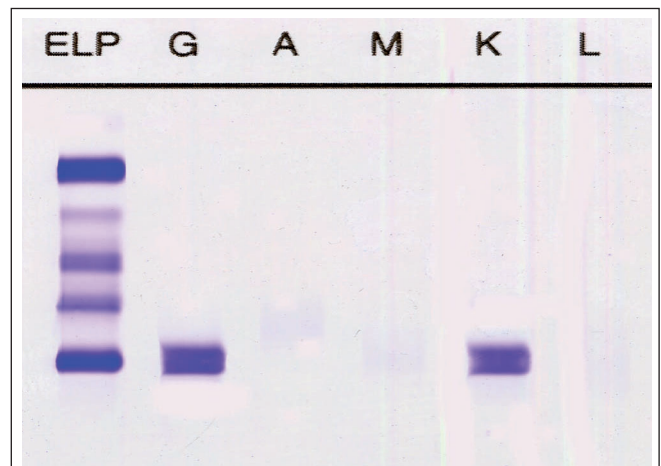


Figure 2 (A) – Presence of Kappa monoclonal protein.

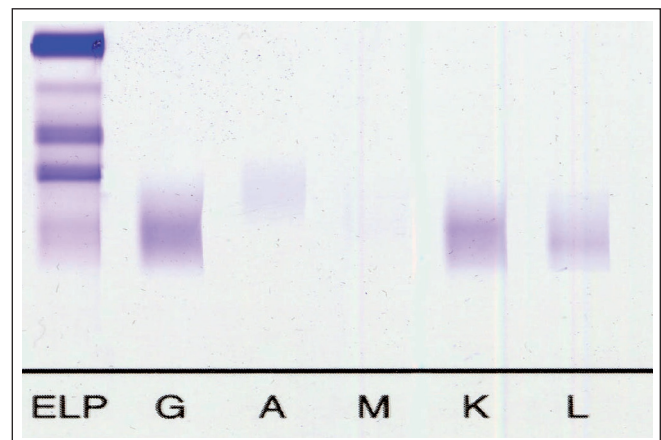


Figure 2 (B) – Disappearance of Kappa monoclonal protein.

were compared with 23 that presented AA amyloidosis. Approximately two-thirds of the patients presented Nephrotic Syndrome (NS) and cardiac involvement, the latter more frequently observed in AL amyloidosis⁴.

In another study, a review of 229 cases of AL amyloidosis from the Mayo Clinic assessed from 1970 to 1980 showed that one third of the patients presented NS, a little less presented heart failure and 10% presented orthostatic hypotension. Approximately half of the patients presented neuropathy and carpal tunnel syndrome.⁵

The present case went undiagnosed, in spite of the presence of the carpal tunnel syndrome, bilateral periorbital hematomas and presence of high levels of monoclonal protein in the peripheral blood. Periorbital hematomas, as seen in our case, can be the single isolated manifestation for several years, according to previous reports.⁶ The absence of anemia, bone lesions and presence of moderate plasmacytosis with mature forms, led to the hypothesis is amyloidosis, which was established by rectal biopsy.

As the patient was young (in the fourth decade of life), it became necessary to demonstrate that it was not a case involving some type of hereditary component, which was performed by attaining the diagnosis of AL amyloidosis through immunohistochemical techniques.

The treatment of AL amyloidosis depends in part of the clinical presentation and the involvement of visceral organs that are essential for survival.⁴ Although the conventional therapy with melphalan and prednisone leads to partial remissions, the duration of these depend on the intensity of the cardiac, hepatic and renal involvement.

The use of chemotherapy with high doses of melphalan and autologous stem cell transplant in the absence of cardiac involvement can result in prolonged remissions, which sometimes last longer than 2 years.

Survival in the AL form, in the absence of cardiac involvement, usually varies from around one year with conventional chemotherapy and 6 months with the opposite situation; that

seems to be the situation of the present case, as our patient has 24 months post-stem-cell transplant.^{7,8,9}

In brief, we reported on a case of a young male adult with AL amyloidosis, where the first-choice conventional therapy (melphalan and prednisone) was replaced by high doses of melphalan, followed by autologous stem cell transplant, with very favorable results, currently at 24 months post-transplant.

No studies on the regression of the amyloid material were performed, as scintigraphic techniques for this purpose are not available in our country.

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