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TECHNICAL NOTE

Serum free light chains in the evaluation of the response to treatment and biological progression in primary amyloidosis

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Plasma cell dyscrasia;
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Abstract Primary amyloidosis is a rare condition characterised by the deposition of free light chains in different tissues and organs (e.g. kidney, heart, liver, gastrointestinal system). The aim of the therapy in patients with primary amyloidosis is to suppress the monoclonal plasma cells that produce the amyloidogenic free light chains and to preserve the organ function. Thus, the new criteria for the haematological disease response include the measurement of serum free light chains concentrations. The case is presented on a patient diagnosed with primary amyloidosis, where the difference between bound and free serum free light chains (dFLC) was used to evaluate the haematological response to the treatment, as well as any biological progression. In contrast to dFLC, Bence Jones Protein in urine was positive but ineffective to evaluate the response to the treatment.

PALABRAS CLAVE
Amiloidosis primaria;
Cadenas ligeras libres;
Proteinuria de Bence Jones;
Discrasia de células plasmáticas;

Cadenas ligeras libres séricas en la evaluación de la respuesta al tratamiento y progresión biológica en Amiloidosis Primaria

Resumen La amiloidosis primaria es una entidad rara caracterizada por el depósito de cadenas ligeras libres en diferentes tejidos y órganos (riñón, corazón, hígado, aparato gastrointestinal). El objetivo en la terapia de los pacientes con amiloidosis primaria consiste en suprimir las células plasmáticas monoclonales que producen las cadenas ligeras libres amiloidogénicas y preservar la función de los órganos afectados. Así, los nuevos criterios de respuesta hematológica de

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Respuesta al tratamiento

la enfermedad incorporan la medida de las concentraciones séricas de cadenas ligeras libres. Presentamos el caso de una paciente a quien se diagnosticó amiloidosis primaria y en la cual la diferencia de concentración en suero entre la cadena ligera libre monoclonal implicada y la no implicada (dFLC) nos permitió evaluar la respuesta hematológica al tratamiento y la presencia de progresión biológica. En contraste a la dFLC, la proteinuria de Bence Jones fue positiva pero ineficaz en la evaluación de la respuesta al tratamiento.

Introduction

Primary or systemic immunoglobulin light chain amyloidosis (AL amyloidosis) is a rare entity characterised by the deposition in different tissues and organs (e.g. kidney, heart, liver, gastrointestinal system) of amyloidogenic free light chains produced by a clonal population of plasma cells.[1] Importantly, the lethal consequences of AL amyloidosis are due to the toxic effect of amyloid deposits and not due to the malignant behaviour of the plasma cell clone in bone marrow. Therefore, an early diagnosis of AL amyloidosis is critical to facilitate swift access to effective chemotherapy, and consequently suppress the production of amyloidogenic free light chains before irreversible organ damage occurs. A strategy for the diagnosis and evaluation of amyloidosis includes tissue biopsy studies, investigation for paraproteinaemia and assessment for systemic disease or organ involvement.[2]

Recent evidence has shown that serum free light chains (sFLC) and, particularly, the difference between involved and uninvolved sFLC (dFLC) are a well-established method for monitoring the haematologic response to therapy in patients with AL amyloidosis.[3] We report the case of a patient diagnosed of AL amyloidosis that highlight the importance of dFLC as useful tool in the monitoring of patients with AL amyloidosis.

Case presentation

A 46 years old woman was admitted to the Hospital with acute kidney failure presenting a creatinine of 5.9 mg/L (biological reference interval (BRI): 0.6–1.2 mg/L). Suspecting a possible monoclonal gammopathy, the laboratory findings showed a beta-2-microglobulin of 17.8 mg/L (BRI: 0.8–2.4 mg/L), albumin of 3.19 g/dL (BRI: 3.0–5.2 g/dL), with no monoclonal protein detected in the serum protein electrophoresis (SPE) and negative serum immunofixation (sIFE). However, the sFLC concentrations were 94.8 mg/L for kappa (BRI: 3.3–19.4 mg/L), 23.2 mg/L for lambda (BRI: 5.7–26.3 mg/L) with a ratio K/L of 4.08 (BRI: 0.26–1.65) and a dFLC of 71.6 mg/L. The 24-h urine volume was 2990 mL (BRI: 1000–2500 mL) with a glomerular proteinuria of 5780 mg/24 h (BRI: <150 mg/24 h) described as nephrotic-range proteinuria. The 24-h urine study evidence a kappa positive Bence Jones Proteinuria (BJP) of 502 mg/24 h (BRI: negative). The imaging studies (x-rays and magnetic resonance imaging) did not showed evidence of lytic bone lesions and the bone marrow aspirate showed the presence of 7% of plasma cells. With these findings and the suspect of AL amyloidosis, renal biopsy and echocardiography study were done. In the renal biopsy, amyloid deposition was identified by a positive Congo-red staining and the immunohistochemical study of the amyloid material was strongly positive for kappa light chain. The echocardiography study showed septal hypertrophy and the serum concentrations of NTpro-BNP and cTnT were 479 pg/mL (BRI: <100 pg/mL) and 0.14 ng/mL (BRI: <0.025 ng/mL), respectively. The patient was finally diagnosed of AL amyloidosis in Mayo Clinic stage III and began treatment with Melphalan and Prednisone (MP). During the monitoring of the patient, the results of the sFLC were expressed as dFLC (Table 1 and Fig. 1). At diagnosis (day 0), dFLC was 71.6 mg/L and PBJ was 502 mg/24 h. After two cycles of MP (day +61), the patient achieved a status of very good partial response (VGPR) with dFLC value of 25.9 mg/L that corresponds to dFLC reduction of 64%. PBJ was 484 mg/24 h. After the fourth, fifth and sixth cycles of MP, the dFLC increased to 28.5 mg/L at day +120; 39.6 mg/L at day +150 and 43.0 mg/L at day +181. PBJ values were 260, 257 and 275 mg/24 h, respectively. The increase of dFLC showed the existence of biological progression of the disease and the haematologist decided to change the treatment to Bortezomib, Cyclophosphamide and Dexamethasone (VCD). The patient presented good tolerance at this new treatment with a dFLC of 28.0 mg/L at day +221 (after first cycle of VCD) and 8.3 mg/L at day +255 (after second cycle of VCD). The BJP were 219 and 270 mg/24 h, respectively. SPE and sIFE were negative during the two lines of treatment of the patient.

Discussion

The case presented illustrates the utility of sFLC in the diagnosis and monitoring of a patient with AL amyloidosis. At diagnosis, the International Myeloma Working Group (IMWG) guidelines recommends for the screening of monoclonal gammopathies a quick and easy protocol based on SPE, sIFE and sFLC, that enables a sensitive identification of the monoclonal component in the study of these patients. The addiction of sFLC analysis to SPE and sIFE avoids the inclusion of urine studies in the screening protocol. When the diagnosis of plasma cell disorder is made, a 24-h urine study is required for all patients. Nonetheless, in patients with a suspected AL amyloidosis, the study of 24-h urine IFE (uIFE) is essential in the protocol.[4,5] In this particular