Clinical Note

Amyloidosis in the emergency department

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ABSTRACT

Primary systemic amyloidosis is a rare disorder caused by the deposition of immunoglobulin light chains in various tissues. The symptoms depend on the organs that have become infiltrated: kidney, skin, heart, etc. This diagnosis should be suspected in a patient with any of the following: proteinuria in the nephrotic range, heart failure, restrictive myocardiopathy, unexplained hepatomegaly, peripheral neuropathy or skin manifestations, the latter being quite often the index finding in this disease. Cardiac involvement occurs in almost one-half of the cases and is associated to a poor prognosis. We report the case of a 70-year-old female seen at the Emergency Outpatient Clinic with symptoms of heart failure and dermal lesions; a biopsy of the abdominal fat led to the diagnosis of primary amyloidosis.

Key Words: *Primary systemic amyloidosis. Heart failure. Diagnosis.*

RESUMEN

Amiloidosis en urgencias

La amiloidosis primaria sistémica (AL) es una patología rara, causada por el depósito de inmunoglobulinas de cadenas ligeras en diferentes tejidos. Su sintomatología depende de los órganos infiltrados: riñón, piel, corazón, etc. La sospecha diagnóstica se debe tener ante un paciente con alguno de estos datos: proteinuria en rango nefrótico, insuficiencia cardiaca (IC), miocardiopatía restrictiva, hepatomegalia no explicada, neuropatía periférica o manifestaciones cutáneas que pueden ser, en muchas ocasiones, el primer hallazgo de esta enfermedad. La afectación cardiaca sucede en casi la mitad de los casos y se asocia a un pobre pronóstico. En este artículo describimos el caso de una mujer de 70 años visitada en Urgencias con síntomas de insuficiencia cardiaca y lesiones dérmicas, que tras biopsia de grasa abdominal, se diagnosticó de amiloidosis primaria.

Palabras clave: *Amiloidosis sistémica primaria. Insuficiencia cardiaca. Diagnóstico.*

INTRODUCTION

Amyloidosis is a rare disease that is often underdiagnosed and has an incidence rate of approximately 8 cases (5.1-12.8) since per million people, per year[1]. The average survival rate for patients with systemic amyloidosis is approximately 13 months from the time the disease is diagnosed. Almost all organs can be affected by this disorder, however the low recovery rates are mainly a result of heart and kidney failure linked to the condition[1,2]. The aim of this study was to present the clinical case of an illness similar to heart failure that is frequently encountered in the emergency department and highlight the fact that however uncommon it may be to examine the substrate it should not be overlooked by emergency physicians rapid identification of the disease will allow better patients progress.

CLINICAL CASE

This is the case of a 70-year old woman with a history of high blood pressure which required no treatment at that time. She had had her gallbladder removed 20 years earlier after an episode of gallstone pancreatitis. She had been admitted to hospital a year earlier because of pleural effusions as a result of heart failure. She had been diagnosed with depression one

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and a half years earlier and had also become significantly less active over the last few months.

The patient came to the emergency department complaining of progressive dyspnoea (following minimal exertion) over the last fortnight, orthopnoea on 2-3 pillows and a small increase in the amount of urine she was passing but no oedema. She was not experiencing any thoracic pain or showing symptoms of a previous cold. She had noticed a loss of appetite, a general feeling of weakness, changes in her voice, dryness in the mouth, a lack of saliva and difficulty swallowing since she had last been admitted to hospital. She had been examined on two previous occasions by a dermatologist because of hair loss, changes in her nails and petechial lesions but no definitive diagnosis was made.

When the patient was examined she was conscious and oriented. Her breathing rate was slightly faster than normal and her oxygen saturation level was 92%. Her temperature and blood pressure were normal. Crepitations were present in both lungs during the cardiopulmonary examination and sounds were symmetrical but dull. The following symptoms were of note: a swollen, bright red tongue, lack of saliva, stiffening of the chin region and the upper lip, a lack of body hair, sparse eyebrows, petechial lesions on the upper back part of the thorax and legs, deteriorated nails and flaking of the skin on the fingers, ulcers on her legs and pressure sores but no oedema. Abdominal examination showed a scar from the cholecystectomy. The abdomen was soft and non-tender to palpation and the liver border measured 1.5 cm.

The ECG showed normal sinus rhythm at 100 bpm. Q waves in V1-V2, poor R wave progression in V3 and low voltage QRS complexes. The chest x-ray showed bilateral pleural effusions, which were larger on the right side. The gasometric results were as follows: pO_2 63.2 mmHg, pCO_2 35.6 mmHg, pH 7.52. saturation 95.1% glucose BM 6.3mmol/l. The results of the biochemistry were as follows: urea 94.4 mg/sl, creatinine 1.40 mg/dl, sodium 134 mEq/l, potassium 4.4 mEq/l, ESR 24. Albumin 3.4 g/dl, uric acid 7.99 mg/dl. Liver function was normal. Coagulation was normal. The blood test results were as follows: Hb 15.5 g, leucocytes 7,400 mm^3 (83.1% neutrophils, 8.2% lymphocytes). Platelets 230,000 mm^3. Iron and ferritin were normal. Urine sample results were as follows: pH5, density 1008, proteins were negative. When the patient was admitted she was examined by a dermatologist who carried out a biopsy of subcutaneous fat suspecting amyloidosis. Thorocentesis was carried out to aid evacuation and the pleural fluid was studied. The fluid had the characteristics of a discharge and grew nothing on cultures. The final test carried out was on the patient's serum, showing no antinuclear or antiDNA antibodies. The thyroid hormones were normal. CEA and CA 19.9 was normal. CA125: 247.3 U/ml. Immunologlobins IgG 2510 (751-1560). Serum immunofixation: monoclonal gammopathy 1 gG-λ. Urine immunofixation: the monoclonal elimination of immunoglobulins was negative. Proteins in a 24-hour urine sample: volume 1300, 0.05 g/l. Echocardiogram showed restrictive caridiomyopathy. There was minimal pericardial effusion. Helicoidal CT scan showed bilateral pleural effusion, signs of cardiomegaly, collapse of the posterior basal segments of both the inferior and superior lobes.

The fat biopsy confirmed the suspicion of amyloidosis. Any association with solid tumours, family history and monoclonal gammopathy was ruled out. Therefore, given the high level of the tumour markers a screening for undetected neoplasia was requested (gynaecological or abdominal), and a bone scan as well as a bone marrow aspiration were carried out.

The patient was given Malfalan and Prednisolone following suspected AL amyloidosis. However her condition worsened and she died one month after hospital admission.

CONCLUSION

The amyloidoses are a group of diseases characterised by an extracelular deposit of a fibrillar substance of protein origin in different tissues. These tissues lose their normal structure and begin to degenerate depending on the size of the deposit[2]. It generally affects people over the age of 65[1]. The most common type of amyloidosis is produced by immunoglobulin light chains or AL amyloidosis.

The annual global incidence rate of amyloidosis is 50,000 cases. The signs and symptoms of this disease are not specific and therefore rarely help the physician with the diagnosis. The most common symptoms are fatigue, weight loss, paresthesis, oedema, huskiness, Carpal tunnel syndrome, macroglossia, skin lesions and hepatomegaly[1].

Therefore, emergency physicians should consider the possibility of amyloidosis when they encounter a patient with at least one of the following four symptoms: nephrotic range proteinuria sometimes accompanied by kidney failure (proteinuria is present in over 90% of cases)[1,4], heart failure or fatigue as a result of restrictive cardiomyopathy, hepatomegaly and unexplained peripheral neuropathy.

In patients is with any of the aforementioned symptoms, serum and urine immunofixation should be requested. Monoclonal protein is detected in almost 90% of cases using this method, even though this should be carried out both in the serum and urine (given that in one third of cases a false negative result can be obtained from either sample).

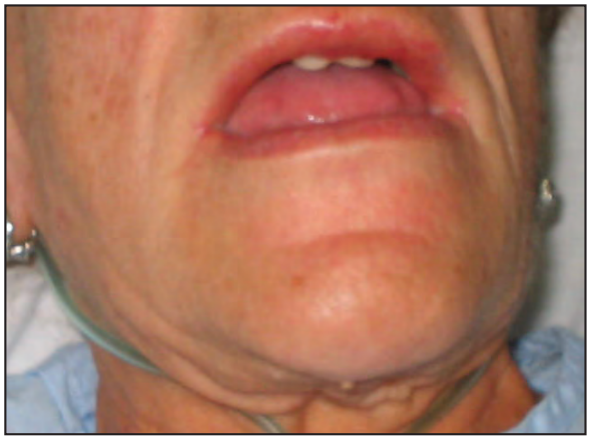

Figure 1. Swollen tongue and stiffness of the chin and lips as a result of amyloidosis.

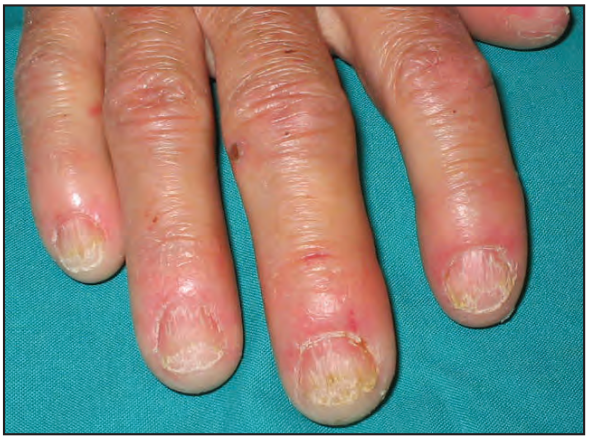

Figure 2. Brittle nails as seen in patients with amyloidosis.

The chest x-ray showed a normal size silhouette and some evidence of pulmonary congestion. The increase in the interventricular septum thickness, which can be observed in the echocardiogram and the diastolic dysfunction and low voltages in the electrocardiogram suggested restrictive cardiomyopathy. Skin complaints occur in up to 40% of cases and bring this undetected disease to light. The reddish purple lesions, petechias and ecchymosis (spontaneous or as a result of a slight trauma) are the most frequent symptoms (15%-20%)[1]. If the patient has fragile capillaries these lesions can be become ulcers if they affect the skin vessels. The most typical lesions are nodules, papules and plaques. They usually present no symptoms whether they are singular or multiple. They can be several centimetres in size and are generally found on the face, the extremities, torso or the genitals. They can merge and give the appearance of having affected a wide swollen area, similar to scleroderma or myxederma. It can affect the scalp resulting in hair loss. A dry mouth occurs when the saliva glands have been affected. Macroglossia was observed in 19% of cases. The nails of the patient also changed being deteriorated and brittle (Figures 1 and 2).

Amyloidosis is often suspected as a result of the symptoms that present themselves and laboratory tests and this should be confirmed by carrying out a biopsy with Congo red staining. The diagnosis depends on how the amyloid shows up in the tissues, and in other less common areas like the minor salivary glands, gums, rectum, bone marrow and subcutaneous tissue.

The natural progression of primary amyloidosis is death within two years of diagnosis in 80% of patients. However, if the disease is diagnosed quickly, treatment reducing the monoclonal immunoglobulin light chain can stabilise or regress the existing amyloid deposits and, in turn, preserve and improve the condition of the organs affected[3], with 75% of the patients responding to treatment within 12 months if no major organs are affected[3]. The prognosis of patients in whom the heart is affected by amyloidosis is not good[6]. Patients usually die as a result of progressive heart failure a within on year of the apperance of the symptoms[1,7-9].

Dermatologists and emergency physicians are often the first point of contact for these patients. It is important to recognise when a patient has systemic amyloidosis given that a quick diagnosis can improve their chances of survival.

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