Primary Systemic Amyloidosis With Exclusive Involvement of the Tongue as an Exceptional Cause of Dysphagia

Fernando Mera Menéndez,[a] Solssiree Álvarez Carrillo,[a] Adolfo Hinojar Gutiérrez,[a] Santiago Nieto,[b] and Eduardo Raboso García-Baquero[a]
[a]Servicio de Otorrinolaringología, Hospital Universitario de La Princesa, Madrid, Spain
[b]Servicio de Anatomía Patológica, Hospital Universitario de La Princesa, Madrid, Spain

We present a 73-year-old woman with progressive dysphagia and dysarthria over 2 years associated with systemic symptoms including weight loss, asthenia, and dyspnoea. Biopsy of the tongue demonstrated amyloid AL deposits. The immunohistochemical study showed a notable positivity to antibodies for L-kappa chains. The patient died 6 months after diagnosis.

Key words: Primary systemic amyloidosis. Amyloidosis diagnosis. Amyloidosis treatment.

Amiloidosis primaria AL con afección exclusiva de la lengua como causa excepcional de disfagia
Se presenta el caso de una mujer de 73 años de edad con disfagia progresiva asociada a disartria de 2 años de evolución, con síntomas sistémicos que incluían disnea, astenia y pérdida de peso. Se realizó biopsia de la lengua que mostró amiloidosis primaria AL. En el estudio inmunohistoquímico se obtuvo una marcada positividad con anticuerpos frente a cadenas ligeras kappa. La paciente falleció a los 6 meses del diagnóstico.

Palabras clave: Amiloidosis primaria sistémica. Amiloidosis, diagnóstico. Amiloidosis, tratamiento.

CASE REPORT

Female, 73 years of age, with a history of seronegative oligoarthritis which evolved into symmetric polyarthritis (FR-HLA B27 +). Resistant to methotrexate and steroids, she was treated for 2 years with anakinra (IL-1 receptor antagonist). She was operated on for a severe carpian tunnel syndrome 1 year ago. She had a history of dysarthria and progressive dysphagia for liquids and solids over 2 years, accompanied in the last 6 months by asthenia and dyspnoea with moderate effort.

On examination, her tongue was hard, immobile, of normal size, and with reduction of the mouth opening due to temperomandibular joint ankylosis.

The analyses performed gave the following results: haemoglobin, 13.3 mg/dL; globular sedimentation velocity, 7; total bilirubin, 3.18 mg/dL; direct bilirubin, 1.53 mg/dL; indirect bilirubin, 1.75 mg/dL; total calcium, 9.5 mg/dL; creatinine, 1 mg/dL; creatinine clearance, 46 mL/min. Urine sediment was without significant alterations. Immunofixation in serum was negative for the M protein. Tumoural markers were negative. In the immunoglobulin analysis, a discrete fall in IgM to 33.3 mg/dL (normal count, 45-250) was observed, and the other immunoglobulins were normal. In blood, 0.01% of cells were seen to have a normal lymphoplasmocytoid phenotype.

The simple chest x-ray and abdominal ultrasound scan revealed cardiomegaly and dilatation of the vena cava and suprahepatic veins. The cervicofacial magnetic resonance image (MRI) showed a superficial alteration of the signal on the right free edge and the ventral portion of the tongue, without any other morphological alterations.

The biopsy of the ventral portion of the tongue identified an extensive accumulation of eosinophilic material that expanded the chorion affecting all of its thickness and was positive using the Congo red technique (Figure 1). In the immunohistochemistry tests, marked positivity was found for antibodies against light kappa chains and negativity for light lambda chains and AA amyloid (Figure 2).

A fine-needle aspiration puncture was then performed in the abdominal fat and turned out to be negative for amyloid material.

The biopsy of the bone marrow identified slight hypocellularity with atypical kappa clonal plasmocytosis; no accumulation of amyloid was seen in the biopsy.

Correspondence: Dr. F. Mera Menéndez.
Alción, 29, 2.º A. 28019 Madrid. España.
E-mail: fermera@yahoo.com

Received September 19, 2007.
Accepted for publication February 14, 2008.

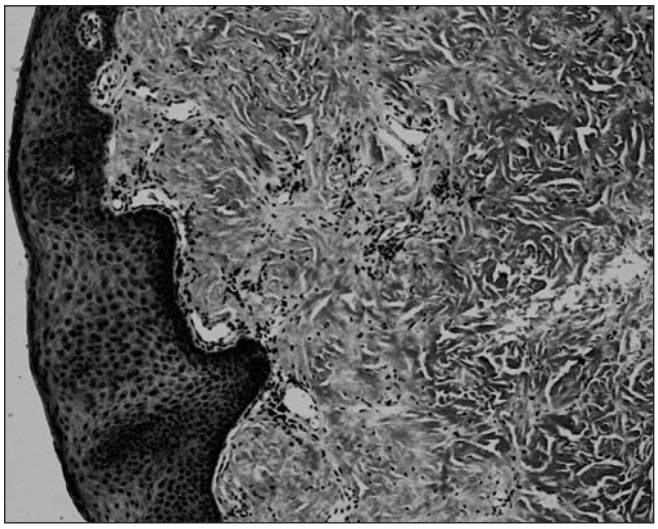

Figure 1. Appearance of the tongue under the microscope, showing the accumulation of amorphous material on the chorion. Congo red tincture.

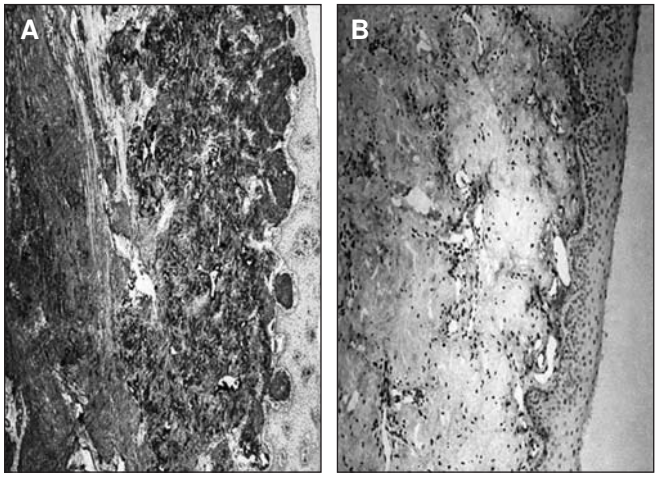

Figure 2. Accumulation of amyloid on the tongue where it is stained (A) positively with antibodies against light kappa chains and (B) negatively for light lambda chains.

The patient died from multiple organ failure 6 months after establishment of the diagnosis of primary AL kappa amyloidosis of the tongue.

DISCUSSION

Amyloidosis was first described by Karl Rokitansky, in 1842, as the pathological accumulation of intra- and extracellular fibrillar proteins, identified in the context of chronic illnesses and neoplasias.[1] The amyloid is classified by the chemical components in its fibrils as AL kappa and/or lambda, AA and ATTR. From a clinical perspective, the systemic or widespread pattern is sub-classified into primary amyloidosis, when the accumulation is associated with some kind of immunocytic dyscrasia, or secondary amyloidosis when it appears as a complication of chronic inflammatory processes.[2] Among patients with primary AL amyloidosis, 59% start with manifestations in the mouth, such as xerostomy, local pain, and dysphagia,[2,3] but local infiltration of AL amyloid into the tongue is very rare: the literature only contains 9 reports of cases such as the present one where the tongue was the only organ in which amyloid involvement was noted.[1,3,4]

Primary AL amyloidosis is a dyscrasia of plasma cells[5,6] that can divide into AL amyloidosis and AL amyloidosis with multiple myeloma (MM), depending on the number of bone marrow plasma cells, the amount of monoclonal protein in serum or urine and the presence or absence of bone lesions. Some authors believe that this differentiation is artificial and combine both entities into primary AL amyloidosis.[7]

The kidneys, heart, and liver are the organs most often involved in primary AL amyloidosis. Carpian tunnel syndrome is the initial manifestation in 20% of patients and may precede the illness by more than 1 year.[8]

Primary AL amyloidosis is a progressive illness with a poor prognosis, with a life expectancy of 6 to 12 months from the moment of diagnosis.[3,9]

Its systematic study comprises: electrocardiogram, Holter, plasma albumin, creatinine clearance, alkaline phosphatase, coagulation, bilirubin levels, cholinesterases, liver enzymes, thyroid hormones, and suprarenal assessment.[7] Patients with primary AL amyloidosis present an over-production of light kappa and/or lambda chains. In bone marrow biopsies, it is possible to detect the dominant clonal immunophenotype. Urine analyses contain Bence Jones protein and blood analyses show M protein and immunofixation of light chains.[5]

The definitive diagnosis consists in obtaining tissue that is positive for Congo red. In various series fine-needle aspiration puncture of abdominal fat and rectal biopsy shows sensitivity of between 54% and 82% and 100% specificity. If they are negative and there is a high suspicion of amyloidosis, a biopsy of the organ affected is indicated,[5,10] as in our case, in which the abdominal fat puncture was negative and the biopsy of the ventral surface of the tongue was positive for Congo red tincture.

The treatment has scant efficacy and is based on cytostatic drugs, alone or in combination, such as methotrexate, azatioprin, etanercept, anakinra, colchicine, melphalan with prednisone, and thalidomide.[8] Future therapeutic strategies to improve the prognosis for this illness include trials with the use of vaccines with the epitopes present in some kinds of amyloidosis.[5]

REFERENCES

1. Habelak M, Cieslik T, Lipiarz L, Zajecki W. Rare case of palatal amyloidosis. Wiad Lek. 2006;59:113-6.
2. Ramzi S, Vinay K, Robbins S. Clasificación de la amiloidosis en trastornos de la inmunidad. Patología estructural y funcional de Robbins. New York: McGraw-Hill; 2005. p. 263-9.
3. Basak PY, Ergin S, Sezer MT, Sari A. Amyloidosis of the tongue with kappa light chain desease. Australas J Dermatol. 2001;42:55-7.
4. Fahrner KS, Black CC, Gosselin BJ. Localized amyloidosis of the tongue: a review. Am J Otolaryngol. 2004;25:186-9.

5. Hazenberg BP, van Gameren II, Bijzet J, Jager PL, van Rijswijk MH. Diagnostic and therapeutic approach of systemic amyloidosis. Neth J Med. 2004;62:121-8.
6. Penner CR, Muller S. Head and Neck amyloidosis: a clinicopathologic study of 15 cases. Oral Oncol. 2006;42:421-9.
7. Pantoja L, Paniagua J, Megido M, Ortiz J. Forma de presentación de una amiloidosis primaria como polimialgia reumática y arteritis de células gigantes. An Med Interna (Madrid). 2001;18:205-7.
8. Palladini G, Perfetti V, Merlini G. Therapy and management of systemic AL (primary) amyloidosis. Swiss Med Wkly. 2006;136:715-20.
9. Hoefert S, Schilling E, Philippou S, Eufinger H. Amyloidosis of the tongue as a possible diagnostic manifestation of plasmocytoma. Mud Keiefer Gesichtschir. 1999;3:46-9.
10. Xavier SD, Bussoloti IF, Muller H. Macroglosia secondary to systemic amyloidosis: case report and literature review. Ear Nose Throat J. 2005;84:358-61.