

A 77-year-old female with macroglossia

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CASE REPORT

A 77-year-old woman was referred to the outpatient clinic because of a slowly progressive swelling of her neck and tongue in the last two years, causing difficulty with eating and speaking. She had never experienced respiratory problems. Her feet and hands were not enlarged. Furthermore, she had noticed spontaneous haematomas around her eyes and corners of her mouth which she blamed on her use of aspirin. Additionally, she complained of a numb feeling in digit V of her left hand. Physical examination indeed revealed macroglossia (*figure 1*), swelling of the mouth floor and haematomas around both eyes and mouth (*figure 2*). Hypesthesia of digit IV and V of her left hand was confirmed. Laboratory investigations showed an elevated erythrocyte sedimentation rate (25 mm/h) and total protein (95 g/l), normal blood count, a creatinine of 63 $\mu\text{mol/l}$, no proteinuria, normal calcium and normal liver enzymes. Thyroid-stimulating hormone and insulin-like growth factor 1 were 2.00 U/l and 10 nmol/l, respectively (normal).

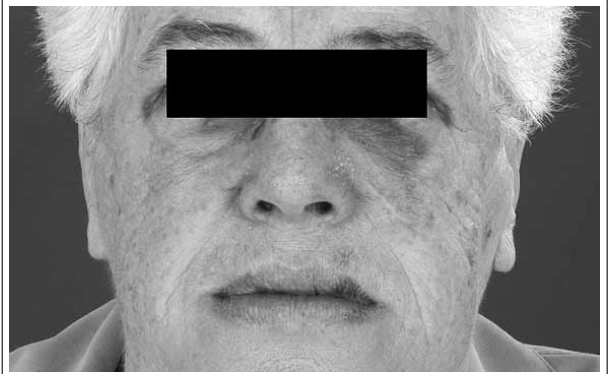
WHAT IS YOUR DIAGNOSIS?

See page 140 for the answer to this photo quiz.

Figure 1.



Figure 2.



ANSWER TO PHOTO QUIZ (PAGE 136)

A 77-YEAR-OLD FEMALE WITH MACROGLOSSIA

The combination of macroglossia, spontaneous haematomas around the eyes and mouth, neuropathy and elevated total protein are suggestive of amyloidosis. Additional laboratory investigation revealed paraprotein, IgG kappa (30.2 g/l), with a total IgG of 33.7 g/l and decreased IgA (0.37 g/l) and IgM (0.17 g/l). Paraprotein (free light chain kappa, 728 mg/l) was also found in the urine. Bone marrow biopsy showed 30% monoclonal plasma cells (IgG kappa). With X-ray, two osteolytic lesions were found in the skull and left femur, respectively. A tongue biopsy stained with Congo red was negative, but a lip biopsy demonstrated focal amyloid. Cardiac ultrasound was normal.

Under the diagnosis of AL amyloidosis accompanying multiple myeloma stage IIIa, she was treated with thalidomide, dexamethasone and clodronic acid. Treatment was complicated by an allergic reaction to thalidomide and medication was switched to melphalan and dexamethasone. Over time, the paraprotein IgG kappa decreased to 2.0 g/l and IgA and IgM normalised. Although her macroglossia did not disappear, her tongue did not enlarge further. She has now been stable for four years.

AL amyloidosis is a rare plasma cell disorder with overproduction of monoclonal immunoglobulin light chains with deposition of amyloid fibrils in various organs. The symptoms depend mainly on the localisation of depositions. Macroglossia is virtually pathognomonic of systemic AL amyloidosis and is present in 10 to 23% of patients.¹ The degree of macroglossia can vary from

slight tongue thickening to massive enlargement and interference with eating, swallowing, speaking, and breathing.² Amyloid deposits can infiltrate capillaries leading to weakening of microvascular tensile strength. In combination with factor X deficiency this is thought to be responsible for the haematomas. Factor X deficiency below 50% is present in less than 10% of patients with AL amyloidosis and presumably results from absorption of factor X by amyloid fibrils.³ Amyloid deposition in the nervous system can cause peripheral neuropathy and can progress from a distal sensory deficit to a motor neuropathy in advanced cases. Kidney involvement, cardiac amyloid deposition and hepatomegaly are common but absent in this case.

In only a minority of patients is the AL amyloidosis related to multiple myeloma. The prognosis of this is poor with a median survival of four years. In conclusion, macroglossia without other symptoms can be the first indication of AL amyloidosis in multiple myeloma.

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