Letters to the Editor

Periorbital Ecchymoses Are Not Pathognomonic of the Light-chain Type of Amyloidosis

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Accepted March 23, 2007.

Sir,

Up to now, periorbital ecchymoses have been considered virtually pathognomonic of acquired monoclonal immunoglobulin (Ig) light-chain (AL) amyloidosis. (1) We report here a case of transthyretin (TTR) familial amyloid polyneuropathy that disproves the absolute specificity of this clinical sign.

CASE REPORT

A 52-year-old man presented with a progressive 16-month course of severe sensorimotor polyneuropathy. He had no personal or familial medical past history. Clinical manifestations appeared in July 2003 and were characterized by decreased sensation and painful paraesthesia of the upper extremities, followed 4 months later by distal weakness. Then, decreased sensation, painful paraesthesia and distal weakness of the lower limbs progressively appeared. Alternating diarrhoea and constipation, Raynaud’s syndrome and erectile dysfunction were noted at the same time. The patient also complained of effort dyspnoea and orthopnoea. Electromyography demonstrated a severe axonal sensorimotor polyneuropathy involving all 4 limbs. Investigations revealed a normal blood count and serum glucose, creatinine, and urea, electrolytes and liver function test. There were no inflammatory biological markers. Classical causes of axonal polyneuropathy, such as alcoholism, vitamin deficiency, diabetes mellitus, dysthyroidism and auto-immune diseases, were ruled out. The suspected dysautonomia was confirmed by an abnormal heart-rate variability on electrophysiological tests. Echocardiography showed thickened ventricular walls with a granular sparkling appearance and impaired diastolic dysfunction. The patient developed periorbital and scleral ecchymoses after vomiting (Fig. 1). Periorbital ecchymoses are due to the fragility of capillary blood vessels induced by amyloid deposits. It may be a spontaneous phenomenon, but most often occurs after physical activity or trivial trauma (2) such as coughing or vomiting. They have already been described in different circumstances: in skull trauma; in a patient who died after attempted cardiopulmonary resuscitation (3); in cerebral vein thrombosis (4); and in migraine. (5) Various cutaneous manifestations may occur during AL amyloidosis, including purpura (frequently periorbital), nail dystrophy, skin thickening and pruritus (2). In 1998, Dubrey et al. (2) reviewed the clinical features of 232 patients with AL cardiac amyloidosis. Ecchymoses were present in 40.9% of patients and periorbital purpura in 12.5%. Ocular manifestations in AL amyloidosis include sicca syndrome (2) and ophthalmoplegia associated with biopsy-proven amy-
Amyloid infiltration of extra-ocular muscles. In 2002, Lachmann et al. (1) studied 350 patients with systemic amyloidosis and concluded that a genetic cause should be sought in patients with systemic amyloidosis in whom confirmation of the AL type cannot be obtained, as in our case. In the same study, amyloidogenic mutations were present in 34 of the 350 patients with systemic amyloidosis in whom the clinical and laboratory findings had suggested a diagnosis of AL type of the disorder. In our patient, the only argument in favour of AL amyloidosis was the presence of periorbital ecchymoses. However, no circulating paraproteins, urinary light chains or immunohistochemical staining of amyloid deposits with anti-light-chain (lambda or kappa) antibodies were detected.

Cutaneous manifestations occurring during TTR amyloidosis, such as xerosis, ulcers, trauma or burn lesions (7), seem to be the consequence of the involvement of small fibres and are not specific of TTR amyloidosis. Ocular manifestations in hereditary TTR amyloid polyneuropathy include vitreous opacities, glaucoma, papillary disorders, keratoconjunctivitis sicca (8) and conjunctival and retinal microangiopathy (9).

As far as we are aware, periorbital ecchymoses have previously been reported only once in TTR familial amyloid polyneuropathy. In 2005, Kim et al. (10) described an aggressive form of familial amyloid polyneuropathy, caused by a heterozygous Glu54Gly mutation in the TTR gene, in which a spontaneous bruise arose on both periocular areas at onset. However, the author did not emphasize the interest of this sign as a feature of TTR familial amyloid polyneuropathy.

ACKNOWLEDGEMENT

We thank Dr G. Bassez (département de Pathologie, Hôpital Henri Mondor, Créteil, France) for immunohistochemistry and fruitful comments on the manuscript.

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