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Letters to the Editor

Penicillamine induced pseudo-pseudoxanthoma elasticum in a patient with Wilson's disease, which role plays the hepatologist?

Key words: Wilson's disease. D-penicillamin. Toxicity. Adverse effect. Pseudoxanthoma elasticum.

Dear Editor,

Wilson's disease (WD) is an inherited disorder caused by a mutation in the ATP7B gene that produces copper accumulation in the liver and brain. Clinically, it is characterized by the presence of hepatic (1), neurological and/or neuropsychiatric disease. D- penicillamine is a copper chelator successfully used in the treatment of WD since 1956 (2). Its high therapeutic effectiveness has been undermined by the frequent occurrence of adverse effects.

Case report

A 30-year-old woman diagnosed at the age of 12 of WD with cirrhosis and portal hypertension without neuropsychiatric involvement. She had been treated with D-penicillamine (350 mg. *tid*, orally administered) since diagnosis. She consulted for loss of skin flexibility, apparition of whitish papules and redundant skin in cervical and axillary region (Fig. 1A). Skin biopsy was performed supporting the diagnosis of pseudo-pseudoxanthoma elasticum (PPXE) secondary to long term D -penicillamine treatment (Fig. 1 B and C). Treatment with D-penicillamine was discontinued and zinc acetate (50 mg. *tid*, orally administered) was started. Examination of the ocular fundus and echocardiography was performed to rule out involvement of the elastic tissue at these organs, being the study negative.

Discussion

According to the latest clinical practice guidelines of the European Association for the Study of the Liver (EASL) (3), the initial treatment of WD are chelating agents such as D-penicillamine, which increase the urinary excretion of copper. Approximately 50 % of patients will develop adverse effects in the first 6 months of treatment and up to a third of them will stop the treatment for this reason (4). Half of the patients treated with D-penicillamine have skin lesions, frequently characterized by the alteration of elastic fibers: PPXE, elastosis perforans serpinginosa, cutis laxa, and anetoderma. Several of these entities may coexist in the same patient (5). PPXE is characterized by the appearance of small yellowish papules in the sides of the neck and flexures. Over time, the skin may become lax forming redundant folds (6). Histologically, the PPXE is defined by the appearance of small, frayed and intensely basophilic elastic fibers in superficial reticular dermis. Specific stains for elastic tissue, as orcein show elastic fibers with irregular excrescences. Elastic fibers from other tissues and organs (7) (retina, lung, cardiovascular system...) may also be affected, so examination of the ocular fundus (8) and echocardiography (9) is recommended. If the patient presents dyspnea, it is recommended to perform radiography/chest CT, arterial gasometry and spirometry.

In the presence of a D-penicillamine-associated dermatosis, it is recommended to replace D-penicillamine for trientine or inhibitors of the intestinal absorption of copper (3): Ammonium tetrathiomolybdate or zinc salts. The resolution of PPXE after the change of treatment may take several years to correct due to the slow turnover of the elastic fibers. There is no medical treatment to expedite the resolution of the skin lesions and recover the elasticity (10). In our patient, treatment with

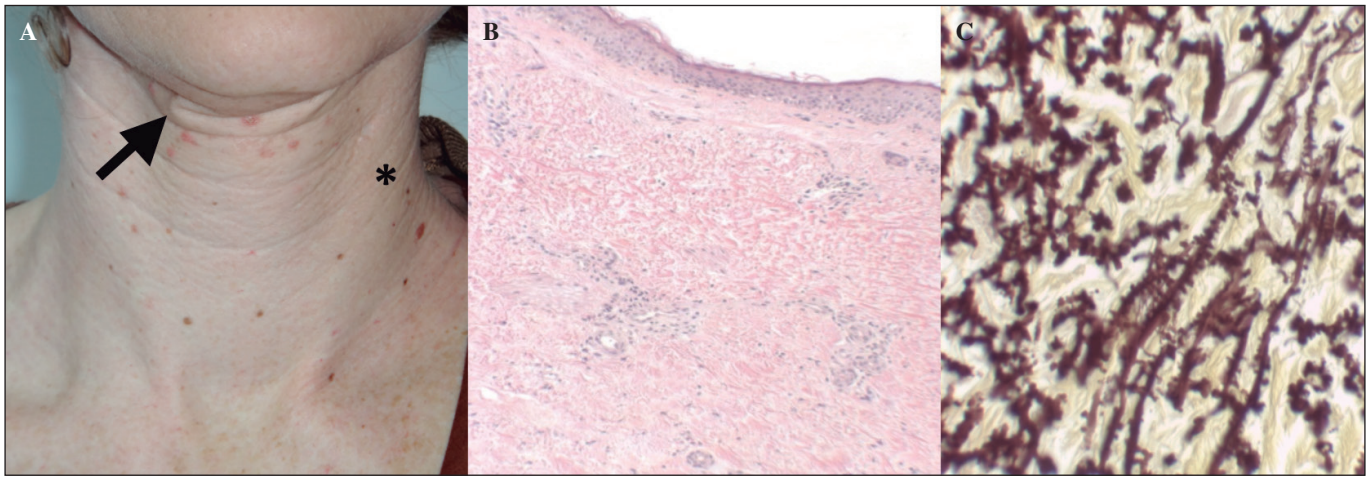

Fig. 1. A. Submental redundant skin fold (arrow). Anterolateral cervical skin surface with cobblestone appearance, micropapules with soft yellowish hue (asterisk). B. Panoramic view (hematoxylin-eosin x 10): The papillary dermis shows no significant changes and the epidermis is preserved, unaltered in any of its layers without areas of ulceration or transepidermal elimination. C. Orcein stain x 40: Elastic fibers with small irregularly shaped "brush" type excrescences.

zinc acetate was initiated without incidents. A year later the skin lesions persisted unchanged and liver disease was suitably controlled.

Luis Ibáñez-Samaniego, Alejandra Ochoa-Palominos, María Vega Catalina-Rodríguez, Magdalena Salcedo-Plaza and Gerardo Clemente-Ricote

Liver Unit. Hospital General Universitario Gregorio Marañón. Madrid, Spain

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