Idiopathic familial hemochromatosis: limited disease extent with prolonged survival and arthritis

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SUMMARY Three siblings with idiopathic hemochromatosis are presented. They are remarkable because of the particularly benign disease and absence of typical HLA phenotype in the index case. In only one of the patients is the glucose tolerance disturbed. This case also has an HLA A3 phenotype. A typical hemochromatosis arthropathy is described in two patients. Following venesection a subjective improvement of the arthritis was reported by one patient.

Key words: Hemochromatosis, Ferritine, Arthritis, Cirrhosis.

INTRODUCTION

Idiopathic hemochromatosis is a rare familial disorder of unknown etiology (1). We report three siblings, the index case having an unusually long survival with limited extent of disease without treatment. In two patients typical signs of arthropathy associated with hemochromatosis were present.

REPORT OF CASES

Case 1

A 56-year old man was admitted because of weakness, anorexia, slight dyspnoea on exertion, stiffness and pain in the low back, hips and lower extremities. The second and third metacarpophalangeal (MCP) and third proximal interphalangeal (PIP) joints were painful in both hands with episodic swelling and slight redness since more than one year.

The diagnosis of hemochromatosis had been made at the age of 37 years, based on total saturation of the iron binding capacity (IBC), hepatomegaly, macroscopically beginning hepatic cirrhosis and limited portal fibrosis with important hepatocellular iron deposition on histologic examination. The family history revealed the two additional cases reported below.
Physical examination showed grayish-brown skin pigmentation, pulmonary emphysema and bilateral cataract. The liver span was 12 cm on the midclavicular line. The wrists, malleoli and second and third MCP joints were tender and slightly swollen. The mobility of the right wrist, both thumbs and the fingers were moderately impaired. The grip strength was decreased. The cervical and lumbar spine were tender on pressure, with a practically normal range of movements. The mobility of hips and knees was normal, the latter being painful on movement. A slight anteroposterior ligamentous laxity was noted in both knees, with no local inflammatory signs. Flexion and extension movements of the ankles were decreased.

Laboratory evaluation revealed normal hematological tests, and normal ESR, with negative RA-latex test and CRP. The prothrombin time was 82% of normal. Serum iron and IBC were 244 µg per 100 ml. During the desferrioxamine test less than 2 mg iron was found in the urine of 24 hrs. Ferritin was elevated to 1200 µg per ml. Oral glucose tolerance and bromosulphophhtaleine tests were normal. The HLA phenotype was A1 A11 B8 BW35 BW6 CW4. The liver was denser than normal and heterogenic on echography; its volume was normal on computerized axial tomography (CAT)-scan of the abdomen with a density of 100 to 110 Units (Hounsfield). The density of the spleen was 36 U and the portal vessels 32 U. The pancreas was enlarged but of normal density.

Radiographic examination revealed narrowing of the intervertebral discs C5-C6 and C6-C7 with small osteophytes at the same level. The lumbar spine was normal. In both knees, the internal femorotibial joint space was narrowed, with osteocondensation of the corresponding tibial plateau. The patella was slightly subluxated externally, with small lateral osteophytes. Joint space narrowing, marginal bony sclerosis and small osteophytes were present in the first MTP joints bilaterally. In the hands, irregular narrowing was observed of the first, second and third MCP joints, especially of the second (Fig. 1), with subluxation, slight osteophytosis and cystic subchondral lesions. No clear osteopenia was described in this patient and no intra-articular calcifi-