Abstract

OBJECTIVE: To describe the evolution of biochemical and clinical features during a 17-year period in untreated subjects homozygous for the C282Y mutation in the hemochromatosis gene.

SUBJECTS AND METHODS: In 1998, 12 subjects from Busselton, Australia, were newly diagnosed as being homozygous for the C282Y mutation. We determined transferrin saturation and ferritin values and retrieved clinical information from the 1981, 1994, and 1998 population surveys for 10 of these subjects.

RESULTS: The median age of the 10 subjects in 1981 was 30 years. Between 1981 and 1998, the median transferrin saturation value increased from 42% to 76%. Six subjects with elevated transferrin saturation in 1998 had values less than 45% in 1981. Between 1981 and 1998, the median serum ferritin levels increased from 271 microg/L to 593 microg/L. Serum ferritin levels increased in 4 subjects, remained relatively constant in 4, and decreased in 2. Of 5 subjects with serum ferritin levels lower than 200 microg/L in 1981, 4 had no increase in these levels between 1981 and 1998. Of 4 subjects with persistently elevated serum ferritin levels greater than 500 microg/L, 3 developed stage III or IV fibrosis, based on the METAVIR scoring system.

CONCLUSIONS: Untreated C282Y homozygous subjects had progressively increasing transferrin saturation values but marked variation in serum ferritin levels during a 17-year period before diagnosis. A screening threshold for serum transferrin saturation values greater than 45% at an early stage in adult life could fail to detect 60% of C282Y homozygotes who subsequently develop biochemical features of hemochromatosis.