Clinical and genetic heterogeneity in hereditary haemochromatosis: association between lymphocyte counts andexpression of iron overload.

Porto G[1], Cardoso CS, Gordeuk V, Cruz E, Fraga J, Areias J, Oliveira JC, Bravo F, Gangaidzo IT, MacPhail AP, Gomo ZA, Moyo VM, Melo G, Silva C, Justiça B, de Sousa M.

[1]Haematology, Santo António General Hospital, Porto, Portugal. gporto@ibmc.up.pt

Eur J Haematol. 2001 Aug;67(2):110-8.

Abstract

To identify a new marker of expression of disease, independent of HFE genotype in patients with hereditary haemochromatosis (HHC), the total peripheral blood lymphocyte counts were analysed according to iron status in two groups of subjects with HFE mutations. The groups consisted of 38 homozygotes for C282Y, and 107 heterozygotes for the C282Y or compound heterozygotes for C282Y and H63D. For control purposes, totallymphocyte counts and iron status were also examined in 20 index patients with African dietary iron overload, a condition not associated with HFE mutations, and in 144 members of their families and communities. Mean lymphocyte numbers were lower in C282Y homozygous HHC index subjects with cirrhosis and higher iron stores than in those without cirrhosis and with lower iron burdens [(1.65 +/- 0.43) x 10(6)/mL vs. (2.27 +/- 0.49) x 10(6)/mL; p = 0.008]. Similarly, mean lymphocyte counts were significantly lower in C282Y heterozygotes and C282Y/H63D compound heterozygotes with iron overload and increased serum ferritin concentrations compared to those with normal serum ferritin concentrations ($p < 0.05$). Statistically significant negative correlations were found, in males, between lymphocyte counts and the total body iron stores, either in C282Y homozygous HHC patients ($p = 0.031$ in a multiple regression model dependent on age) and in C282Y heterozygotes or C282Y/H63D compound heterozygotes with iron overload ($p = 0.029$ in a simple linear model). In contrast, lymphocyte counts increased with increasing serum ferritin concentrations among the index subjects with African iron overload ($r = 0.324$, not statistically significant) and among the members of their families and communities ($r = 0.170$, $p = 0.042$). These results suggest that a lower peripheral blood lymphocyte count is associated with a greater degree ofiron loading in HFE haemochromatosis but not in African iron overload, and they support the notion that the lymphocyte count may serve as a marker of a non-HFE gene that influences the clinical expression of HFE haemochromatosis.