ly. CD158a and b were not expressed by these cells. Natural killer activity was normal.

This case report describes an unusual context for the development of persistent NK lymphocytosis, i.e. more than one year post-transplantation, after infectious episodes not unusual in transplantation. This patient differs from the 26 $CD8^-/CD4^-/NKa^+$ cases reported by Scott *et al.*,[2] since nearly all lymphocytes were LGL, yet the absolute counts were lower than 4.5×10^9/L. NK-LGL leukemia[3] can also be ruled out in the absence of neutropenia, visceral involvement or coagulopathy. The long term and indolent character of this immunohematologic rarity is more reminiscent of the chronic NK cell lymphocytoses described after infectious episodes by several authors,[4,5] and given diagnosis criteria by Semenzato *et al.*[6] According to the latter, the patient described here appears to be another case of the very rare post infectious low count $CD3^-$ LDGL, only observed in 2 out of 195 patients by those authors. The indolent evolution of this patient's disease could be related to the immunosuppression he receives as rejection prevention, which matches attempted therapeutic approaches in NK lymphocytosis.[3]

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Colorectal cancer and HFE gene mutations

Sir,

Hereditary hemochromatosis (HH) is characterized by an increased absorption of iron resulting in excess deposition of this metal in parenchymal cells of the liver, heart, and certain endocrine organs.[1-3] Patients with HH have an increased risk, in relation to their increased iron stores, of suffering liver and esophageal cancer and skin melanoma.[4] The relative risk of subjects with moderately high levels of serum transferrin saturation and high serum ferritin (laboratory abnormalities similar to those found in HH heterozygotes) suffering from colorectal cancer is three times higher than in the normal population.[5,6]

Whether HH heterozygotes have a higher incidence of colorectal cancer is not known, although a slightly higher RR (1.28) in these subjects was found in one study.[7]

In 1996 Feder *et al.*[8] identified a gene strongly linked to HH, which is now known as HFE. A change in a single base pair of this gene (C282Y) is clearly associated with HH, and subjects who share a normal haplotype with C282Y are considered heterozygotes for the disease.[9] The relationship between a second genomic change (H63D) and HH is currently unclear. We investigated both substitutions in 116 patients with colorectal cancer and in 108 healthy subjects in order to compare the frequencies of the substitutions and determine whether there is higher than expected proportion of HH heterozygotes in patients with colorectal cancer.

A total of 116 DNA samples which had been stored at 4°C were thawed from a colorectal cancer DNA bank. DNA samples from 108 healthy blood donors were used as normal controls. The distribution of sexes was similar in both groups (54.3% males in the cancer group, 57.4% males in the control group), but that of age was heterogeneous (mean age 66.9 years in cases vs 40 in controls, $p<0.05$). C282Y and H63D mutations were screened for by using enzymatic digestion of PCR products encompassing the mutation sites as described elsewhere.[10] The frequencies of mutations in

Table 1. Genotype frequencies of mutations in the HFE gene in patients with colorectal cancer anf healthy controls.

Genotypes	*Cases n=116*	*Controls n=108*
HH/CC	68	70
HH/CY	5	6
HD/CC	36	28
DD/CC	6	2
HD/CY	1	2
C282Y*	2.6 (1-5.5)	3.7 (1.6-7.2)
H63D*	21.1 (16.1-26.9)	15.7 (11.2-21.3)

**Allelic frequencies (%; 95%CI). Genotypes are given for aminoacid 63 (H63D)/aminoacid 282 (C282Y) of protein. CC/HH corresponds to the wild type.*

both groups were compared using Fisher's exact test.

The genotypic frequencies for mutations of the HFE gene are shown in Table 1. The frequencies in cases and controls were similar to those found in previously published studies. The observed differences were not statistically significant. We found no homozygotes for C282Y (HH patient) in either group. These results rule out the existence of a strong association (OR ≥3) between HFE mutations and colorectal cancer. Patients with colorectal cancer do not appear to have a higher prevalence of HH heterozygosity than normal blood donors. A criticism to this study is that the groups were heterogeneous for age, and it is possible that some controls may develop colorectal cancer in the future, but this subgroup will be very small with little influence on the overall results. Our study suggests that the epidemiologic relationship between colorectal cancer and increased body iron is probably more the result of dietary and environmental factors than genetic factors. New epidemiologic studies specifically designed to prove this environmental relationship will be necessary to shed further light onto these observations.

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