cositis and achieved some benefit with regard to the incidence and severity of mucositis.

We believe that we did not observe an individual or chance response to intravenous immunoglobulin. With regard to the interference of oral mucositis with the patient’s nutrition and quality of life and to the potential risk of systemic infection due to disrupted barriers, we believe that intravenous immunoglobulin might be effective in prophylaxis of this chemotherapy- and radiotherapy-induced toxicity.

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References


Notes

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Re: Excess Risk of Primary Liver Cancer in Patients With Diabetes Mellitus

Adami et al. (1) describe an increased risk of hepatoma among diabetics. In their Table 5, it is suggested that hereditary hemochromatosis (HH) is a risk factor for hepatoma in this diabetic cohort, although the magnitude of this association is probably underestimated because of underascertainment of HH within the cohort. The prevalence of homozygous HH in the general population has been estimated to be from 0.004 to 0.01, with a heterozygote frequency of 0.12-0.18 (2). In this large diabetic cohort, the prevalence of homozygous HH reported was only 0.00065.

HH is an autosomal recessive disease that is characterized in homozygotes by increased absorption of dietary iron with consequent iron deposition in many organs, including the liver, pancreas, and heart (3). This deposition eventually results in cirrhosis, diabetes, or heart failure (4). The gene most often associated with this disease is thought to be located on chromosome 6p in close association with the HLA-A locus (loss of heterozygosity scores as high as 4.1) (2). Hepatocellular carcinoma is frequent (200 times the national incidence) (5).

The prevalence of HH among diabetics has been estimated to be between three and five times the prevalence of HH in the general population (1.2%–5% of diabetics having HH) or 30-80 times greater than the prevalence reported by Phelps et al. (6) and Nelson et al. (7). In addition, we have demonstrated an increased risk of diabetes among the much more numerous HH heterozygotes (7,8), who also absorb iron abnormally. We have also reported an increased risk of hepatoma among HH heterozygotes (7). We believe that broader evaluation of body iron stores in this Swedish diabetic cohort would have demonstrated a much stronger relationship of HH with hepatoma in diabetics. It is also likely that heterozygous HH played a significant role in this relationship, although there is no rigorous means to evaluate this, because heterozygous HH cannot yet be diagnosed outside of known HH families.

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References


Notes

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Re: Excess Risk of Primary Liver Cancer in Patients With Diabetes Mellitus. Research alluded to in this letter and cited in references (7) and (8) was supported by the American Cancer Society, Illinois Division grant CCP16-92.

Response

As suggested by Dr. Nelson and his colleagues, homozygous hereditary hemochromatosis (HH) may be underascertained in our cohort of diabetic patients. Such underascertainment may be counterbalanced if patients with both HH and diabetes are more likely to be hospitalized than those with diabetes.