An association of sarcoidosis with hepatocellular carcinoma

Sarcoidosis is a multisystem disease characterized by non-caseating granulomas. Liver involvement is common, with hepatomegaly and cholestasis; portal hypertension, cirrhosis and hepatic failure are rare.

We report a 42-year-old woman who presented with abdominal distension and pain for 1 month. At age 16 she had presented with jaundice and hepatosplenomegaly; biopsies of the liver and the right supraclavicular lymph node showed non-caseating granulomas. Sarcoidosis was diagnosed and she was treated with steroids with good clinical response. A year later, repeat liver biopsy showed cirrhosis. Over the next 9 years her steroids were tapered. She continued to do well for the next 13 years until she presented with the complaints mentioned above. She had not used alcohol or any illicit drugs. Work-up revealed an increase in \( \alpha \)-fetoprotein, \( \gamma \)-glutaryl transferase and angiotensin-converting enzyme levels. Hepatitis B and C antibodies, antinuclear antibody, antimitochondrial antibody, anti-Smith antibodies and antiparietal antibodies were negative. CT of the abdomen showed a diffusely nodular liver with peripheral masses in the right lobe. Fine-needle aspiration of the lesion showed atypical cells consistent with hepatocellular carcinoma (HCC). She was started on cisplatinum and doxorubicin which were later changed to etoposide and tamoxifen. She did well, but developed pancytopenia after 2 years of chemotherapy. Bone marrow biopsy revealed acute myeloid leukemia from which she died a few months later.

The association of hepatic sarcoidosis with HCC has been reported once before [1], in a 63-year-old man with a long-standing history of hepatic sarcoidosis who developed HCC; he apparently did not have cirrhosis. In view of the poor prognosis, chemotherapy was withheld and the patient died within 3 months. Two earlier studies [2, 3] showed an increased incidence of HCC in sarcoidosis; however, there was no mention of hepatitis B or C, alcohol use or the autoimmune status of the patients. Mechanisms of how sarcoidosis may cause lymphoma have been proposed [4]. How HCC might evolve is unknown. An early and essential step in carcinogenesis is hepatocyte injury by a potentially carcinogenic agent [5]. Sarcoidosis is presumed to cause hepatocellular injury either from direct contact damage or immunologically, leading to necrosis with subsequent regeneration and fibrosis. HCC and cirrhosis could be envisioned as two possible independent sequelae of sarcoid, but cirrhosis with resultant hepatocellular regenerative efforts is more likely to be the causal pathway between sarcoidosis and HCC. Thus HCC should be considered a possible cause of clinical deterioration in patients with long-standing sarcoidosis.
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doi:10.1093/annonc/mdi306
Published online 21 June 2005