

Hepatic Angiosarcoma and Bronchioloalveolar Carcinoma Induced by Fowler's Solution

Michael L. Kasper, MD; Lynn Schoenfeld, MD; Robert L. Strom, MD; Athanasios Theologides, MD, PhD

THE MEDICINAL use of Fowler's solution reached its heyday during the Victorian age, but arsenical solutions continued to be prescribed for dermatological conditions until the 1960s. Following intake of arsenic, in the patient we describe, a hepatic angiosarcoma and a bronchioloalveolar carcinoma appeared simultaneously after a prolonged latent period.

Report of a Case

A 67-year-old man had been well until seven months before his death. At that time he was found to have ascites, abnormal liver function test results, and decreased hepatic uptake with multiple focal defects appearing on a liver-spleen isotope scan. Tests for carcinoembryonic antigen and α -fetoprotein gave negative results, and the results of a liver biopsy were not diagnostic.

On referral to our hospital, he was cachectic, with scleral icterus, asterixis, fetor hepaticus, and rales in the base of the right lung. He had ascites without abdominal organomegaly or masses. His palms and soles had hyperkeratotic papules.

His medical history included treatment with 10 g of arsenic trioxide (Fowler's solution) for dermatitis herpetiformis

(1936 through 1942). He had a 30-pack-year smoking history, but he had quit smoking ten years before we saw him. He had been smoking two packs per week while taking Fowler's solution. He drank one or two drinks each day.

Laboratory studies disclosed the following values: serum urea nitrogen, 74 mg/dL (reference range, 10 to 26 mg/dL); alkaline phosphatase, 130 mU/mL (reference range, 24 to 80 mU/mL); SGOT, 34 IU/L (reference range, 11 to 22 IU/L); total bilirubin, 8.5 mg/dL (reference range, up to 1.3 mg/dL); ammonia, 184 μ mol/L (reference range, 11 to 35 μ mol/L); albumin, 2.3 g/dL (reference range, 3.5 to 5.1 g/dL); prothrombin time, 15.4 s (reference range, 10 to 13.5 s); partial thromboplastin time, 38.4 s (reference range, 28 to 40 s); WBCs, 14,800/cu mm (reference range, 5,000 to 10,000/cu mm); and hemoglobin, 13.7 g/dL (reference range, 14 to 18 g/dL). Hepatitis B surface antigen was nonreactive. A chest roentgenogram showed a density in the base of the right lung.

Because of the patient's progressive ascites, a peritoneovenous shunt was inserted. His clinical condition deteriorated, and the hepatorenal syndrome ensued, followed by sepsis and death. At autopsy, the liver was found to be red-brown and diffusely nodular; it weighed 2,450 g. The nodularity comprised pale-yellow nodules measuring 0.2 to 4 cm in diameter and dark-red nodules measuring 0.1 to 0.2 cm in diameter. Histopathologically, the tumor islands consisted of dilated sinusoids lined by anaplastic endothelial cells. This composition created a scaffolding pattern in which cords of hepatocytes stood out in branching arrays against a background of proliferating endothelial cells (Fig 1). These latter cells were spindle shaped, with eosinophilic cytoplasm, large pleomorphic nuclei, and

small nucleoli. Immunoperoxidase staining for factor VIII-related antigen yielded positive results.

The lower lobe of the right lung contained a solitary 2-cm peripheral tumor nodule. Microscopically examined, the nodule showed fibrosis and solid tumor masses with tall columnar cells lining the alveoli but preserving the basic alveolar architecture (Fig 2). These cells showed marked anaplasia, with hyperchromatic nuclei and prominent, often multiple, eosinophilic nucleoli. Bizarre giant cells and multinucleated cells were also present. These histopathologic observations were believed to be most indicative of a bronchioloalveolar carcinoma. The cells, however, showed more anaplasia and pleomorphism than is usually seen in this type of tumor. No other epithelial tumors were present in the patient, eliminating the possibility of a lung metastasis. There was invasion of fibrotic areas by cords of tumor cells as well as invasion of blood vessels. Mucicarmine staining showed slight positive results. Immunoperoxidase staining for factor VIII-related antigen produced negative results. No metastases from either of the two tumors were found at autopsy. The splenic vein was thrombosed. The hepatic portal system was grossly normal.

Comment

Hepatic angiosarcomas are rare tumors that make up 1% to 3% of hepatic tumors, with approximately 200 cases reported.¹ The association of nonmedicinal long-term arsenic exposure and angiosarcoma of the liver was first made by Roth in an autopsy series of Moselle vintners. Three of the 27 subjects were found at necrop-

From the Section of Hematology (Dr Kasper) and Department of Internal Medicine (Drs Kasper and Theologides), University of Minnesota; and the Department of Pathology (Drs Schoenfeld and Strom) and Section of Hematology/Oncology (Dr Theologides), Hennepin County Medical Center, Minneapolis.

Reprint requests to University of Minnesota Hospitals, Box 480, Mayo Memorial Building, 420 Western St SE, Minneapolis, MN 55455 (Dr Kasper).

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