

Special Communication

Angiosarcoma of Liver in the Manufacture of Polyvinyl Chloride

Three reported cases of angiosarcoma of the liver serve as an alert to the probability that this condition may, in some instances, be causally related to employment in the manufacture of polyvinyl chloride resins.

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On January 22-23, 1974, a manufacturer of polyvinyl chloride and copolymers notified its employees, the National Institute of Occupational Safety and Health, the Kentucky State Department of Labor, and the public, that three workers had died of angiosarcomas of the liver. These cases had as a common denominator employment in the manufacture of polyvinyl chloride resins.

A patient of one of the authors (J.L.C., Jr.) died on September 27, 1971 from an angiosarcoma of the liver. At that time the potential causal relation to the manufacture of polyvinyl chloride resins was not realized. Although other clinical manifestations of exposure to VCM were known (acroosteolysis), only one experimental paper¹ indicated that vinyl chloride may be a carcinogen. The tumors in rats that he described occurred primarily in the skin and were epidermoid in origin.

Eighteen months later on March 3, 1973, a second former employee in the Louisville plant died. Since he was not under our care, no connection was made that the two cases may have had a common origin. When a third patient died on December 19, 1973, the pathologist on gross examination diagnosed an angiosarcoma of the liver. Since all three patients were treated by different physicians, no relationship to exposure to polyvinyl chloride was surmised until the authors, recognizing the rarity of the tumor, and learning that all three had worked in the PVC plant, brought the matter to the at-

tention of the company. Further search indicates that a fourth death from angiosarcoma may have occurred five years earlier (1968), but the death certificate shows primary liver tumor as the cause of death. (Clinical, epidemiologic, toxicological and occupational investigations are being vigorously pursued with regard to other employees who may have been similarly exposed.)

A brief resume of the first case under our care is presented. The history, clinical course, and pathologic findings are consistent with the others who died of angiosarcoma. These cases will be presented in a group and in more detail at a future date.

Case Report

Patient one, a 36-year old white male, was hospitalized January 5, 1970 because of tarry stools.

Occupational History.— The patient had been employed from November 1955 until his illness, except for two lay-offs of nine months in 1958 and six months in 1959, as a chemical helper and operator in the Louisville plant of B. F. Goodrich Chemical Company in the manufacture of polyvinyl chloride resins.

Present Illness.— At the time of admission the patient had no complaints except passage of tarry stools. Past history was negative except for an operation for hemorrhoids four years earlier. Physical examination showed pallor, and black stool on rectal examination. Liver and spleen were not palpable. Although upper G-I series was interpreted as normal, a tentative diagnosis was made of bleeding duodenal ulcer.

On diet and medication, the patient had no recurrence of

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overt bleeding until May 1, 1970, four months later, when he was readmitted for tarry stools. Again he was found to have marked pallor, and tarry stool on rectal examination. At this time the liver was demonstrably enlarged and the spleen was palpable. Blood chemistry studies (SMA-12) were not significantly abnormal; total bilirubin, alkaline phosphatase, LDH, and SGOT were only slightly elevated. G-I series showed only anterior displacement of the stomach, but barium swallow suggested esophageal varices. Intravenous pyelogram was normal; barium enema was normal except for displacement of the splenic flexure by an enlarged spleen. Liver scan on May 4, 1970 was interpreted as being compatible with a large lesion in the left lobe of the liver, extending into the right lobe.

Operative Procedure and Findings. — On May 7, 1970 an exploratory laparotomy was carried out. Under anesthesia, the abdomen was entered through a vertical incision. Marked enlargement of the liver and spleen were noted, and the liver was adherent to the anterior surface of the stomach. The liver capsule was quite thickened and tough. There was a gelatinous-like material at the junction of the liver and the stomach. Retroperitoneal nodes were very soft, enlarged, and succulent in appearance. A biopsy of the liver was performed. There was marked degree of hemorrhage following this which was controlled with large sutures through the liver.

Report of Pathologic Findings

Gross. — Specimen is a portion of soft gray and light brown tissue that is 2.2 x 1.9 x 1 cms. at the present state. In some

areas it appears to be composed of liver and in others light beige, moderately firm tissue with areas of sponginess and softness.

Microscopic. — Most of the tissue pattern of liver is replaced by luxuriantly growing cells forming irregular spaces. These spaces display many trabeculations in their lumina and are lined by pleomorphic malignant endothelial cells. Here and there these cells grow in nearly solid sheets. Elsewhere they line capillaries. There is a newly formed stroma with various degrees of hyalinization here and there.

Diagnosis. — "Liver, biopsy of, angiosarcoma (malignant hemangioendothelioma)."

Clinical Course

Following the laparotomy and biopsy the patient was given 3600 R cobalt and several intra-arterial infusions of 5 FU. During this time there was marked distortion of his blood chemistry with severe diminution of albumin, and marked increase in total bilirubin, alkaline phosphatase, LDH, and SGOT. After a stormy course and several months of convalescence, including several abdominal paracenteses for recurrent ascites, he recovered sufficiently to return to work for a short time. He succumbed to the liver tumor fourteen months post-operatively and died on September 27, 1971.

Reference

1. Viola PL, Bigotti A and Caputo, A: Oncogenic response of rat skin, lungs, and bones to vinyl chloride. *Cancer Research* 31:516-519, 1971.

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Editor's Note

Professor Cesare Maltoni, Director of the Institute of Oncology of the University of Bologna Italy, presented the results of his unpublished experiments with vinyl chloride on February 15, 1974 at the U.S. Dept. of Labor hearing in Washington, D.C. on "Possible Hazards of Vinyl Chloride Manufacture and Use". His work, which is obviously original and innovative, demonstrated angiosarcoma of the liver and other tumors in experimental animals at air concentrations of vinyl chloride which are known to be present at times in workroom atmospheres. Professor Maltoni describes his methodology as predictive of the carcinogenic potential of airborne chemical contaminants. Professor Maltoni is apparently the first to show the relationship between exposure to vinyl chloride and the appearance of angiosarcoma in mammals.

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