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HEPATIC ANGIOSARCOMA IN A VINYL CHLORIDE WORKER

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More than 38 cases of angiosarcoma so far have been confirmed among workers exposed to vinyl chloride monomer gas (VCM) during the manufacture of polyvinyl chloride (PVC). The median interval from first exposure to diagnosis was 17 years; the average time of exposure was 16 years.[1] We are reporting on a patient whose exposure to VCM lasted only 3½ years.

A 36-year-old white male was admitted to the hospital for treatment of peptic ulcer pain that had recurred intermittently for 15 years. His health otherwise had been good; he did not smoke and he drank very little alcohol. For 3½ years he had worked as a "polycleaner," a cleaner of polymerization vessels in a factory where VCM is processed to PVC. After this he had worked for three years prior to admission as a storeman of raw materials, handling resins only.

On examination the patient looked well; the only abnormal physical sign was a liver palpable to 6 cm. Barium meal revealed the presence of

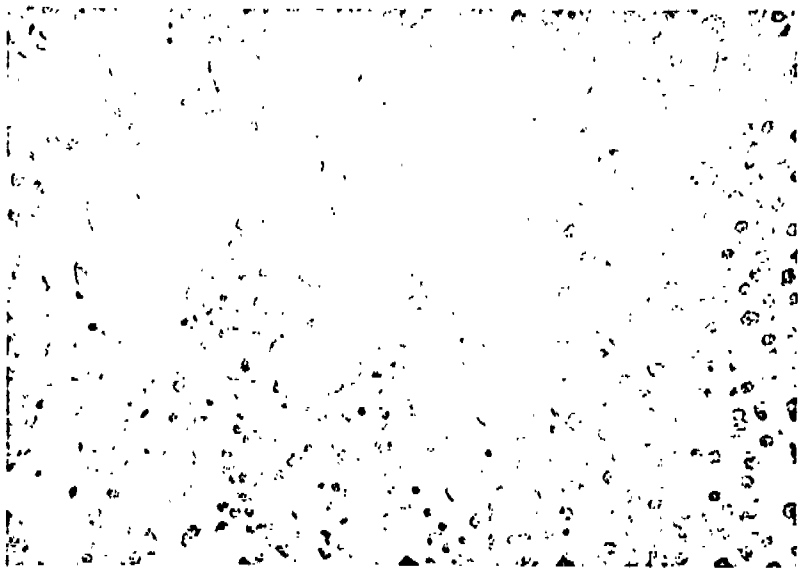

Fig. 1. Focal severe sinusoidal dilatation on liver biopsy (× 500)

a deformed duodenal cap. At operation a large duodenal ulcer was found, for which a Pólya partial gastrectomy was performed. The liver appeared cirrhotic, with grossly distended veins forming a collateral circulation in the anterior abdominal wall and the falciform ligament. Tests of liver function gave normal results, but an operative liver biopsy showed noncirrhotic fibrosis; there were several foci of severe dilatation of the sinusoids (Figure 1).

Recovery from operation was uneventful. The serum alkaline phosphatase level rose to 87 I.U./L (normal range: 15 to 40) after six weeks, but all other liver-function tests and the erythrocyte sedimentation rate were normal, apart from a bromsulphalein retention of 17% (45 min.). Tests for smooth-muscle and mitochondrial antibodies and for Australia antigen were negative.

One year after operation the patient was working full time as a dock laborer. There were no abnormal physical signs apart from the enlarged liver. Liver-function tests now showed a further rise in the serum alkaline phosphatase level to 115 I.U./L, with an elevated bilirubin value of 32 μmole/L (normal range: 5 to 17).

Fig. 2. Gross appearance of liver at postmortem

Four months later he was admitted to the hospital as an emergency patient. He now had dyspnea, ascites, ankle edema, and jaundice. He looked ill and wasted. Liver palms and numerous spider nevi were present. The liver extended 10 cm. below the costal margin. Diuretics caused an appreciable loss of edema, with great relief of the dyspnea. Results of the liver-function tests were grossly abnormal: serum bilirubin 103 μmole/L, alkaline phosphatase 120 I.U./L, serum glutamic oxalacetic transaminase 35 I.U./L, albumin 27 gm./L, globulin 40 gm./L. During the next month the bilirubin rose steadily to 390 μmole/L. A scan showed the liver to be massive, with numerous areas of decreased uptake. A hepatic arteriogram revealed a widespread pathological circulation, with multiple areas of tumor blush, suggestive of a highly vascular multicentric hepatic neoplasm. Tests for α-fetoprotein and carcinoembryonic antigen were negative. A barium-swallow test demonstrated varices.

Dilated veins appeared on the anterior abdominal wall, but at no time was a hepatic bruit heard. Soon afterward the patient lapsed int hepatic coma and died.

At necropsy there was edema of both lungs. The right lower lobe

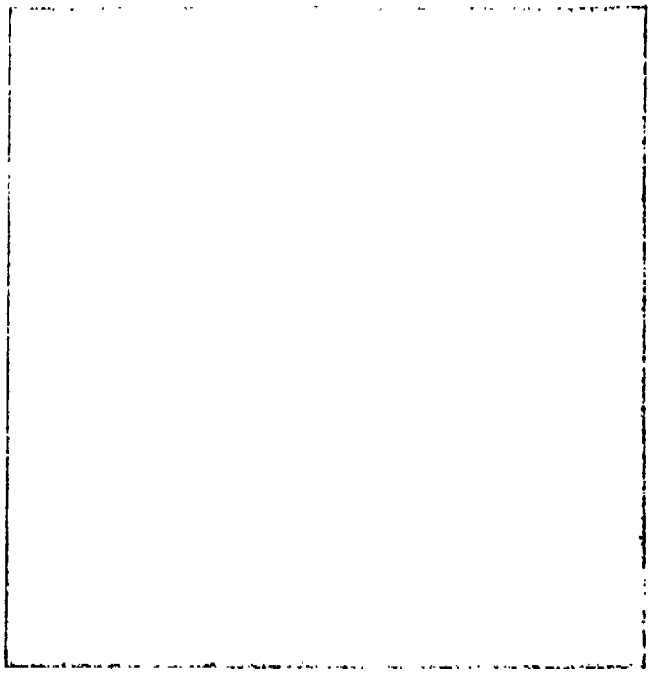

Fig. 3. Postmortem hepatic venogram

showed patchy collapse and consolidation and evidence of several hemorrhages. The pericardium contained clear yellow fluid but there was no significant ascites. Apart from the old partial gastrectomy, the alimentary tract was normal.

The liver weighed 3,240 gm. and was greatly enlarged by a vascular tumor which had almost completely replaced normal hepatic tissue (Figure 2). Large blood lakes and cavernous vascular spaces were shown well by injection of barium suspension into the hepatic vein after death (Figure 3). The spleen was congested and very firm, but weighed only 200 gm.

Microscopy showed replacement of much hepatic parenchyma by hemorrhagic and necrotic tumor tissue. The tumor consisted of vascular channels, varying greatly in size and shape, lined by plump endothelial cells and also by large multinucleate tumor cells (Figure 4), believed

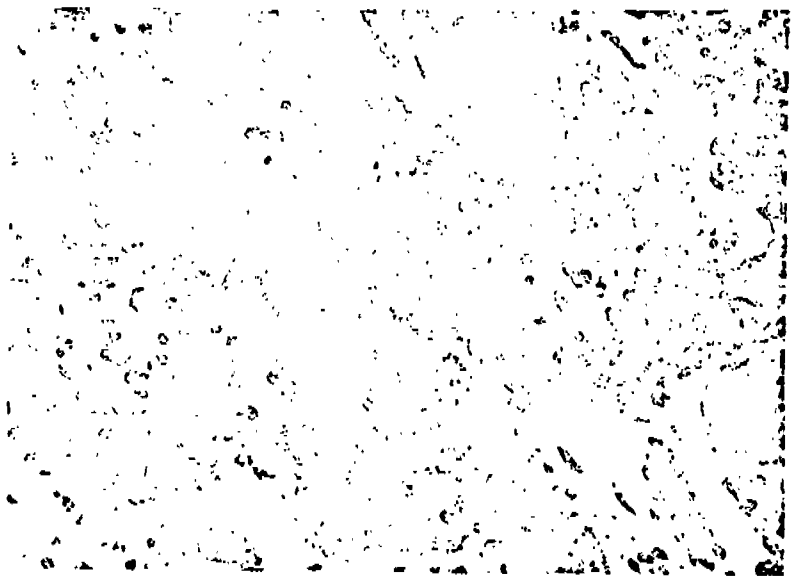

Fig. 4. Microscopy of tumor (× 500)

to be malignant Kupffer cells. In some parts of the tumor these cells were sparse and the dilated sinusoidal structure resembled that seen in the biopsy specimen, but in other parts these giant tumor cells were very numerous. A few had desquamated into the vascular channels and there was evidence of tumor-cell embolism in the pulmonary hemorrhages, although no cohesive metastatic tumor tissue was found in the lungs or other organs.

Discussion

This patient was remarkable in several respects. The duration of exposure to VCM of 3½ years, compared with the mean of 16 years for the previously reported 38 cases of angiosarcoma, was unusually short. Only one younger case has been described. The latent period from the first exposure to VCM to diagnosis was eight years, whereas for the other reported cases the mean interval was 17 years (range: 11 to 30 years).[1] We have no evidence that the exposure to VCM was in any way unusual; in particular, the patient had not been a gas "sniffer" and

his subsequent periods of employment had consisted of laboring and handling bananas. He had, however, been a polycleaner, and 84% of cases of VCM-treated angiosarcomas so far described have occurred in persons similarly employed.[1] He is only the second patient with angiosarcoma to be reported in Britain.

This patient also was unusual in that the liver biopsy performed 15 months prior to his death revealed striking focal dilatation of the sinusoids. This change has been described recently in the early stages of some other angiosarcomas linked to vinyl chloride.[2] We have performed liver biopsies on a number of other VCM workers with appreciable periods of exposure, but have seen only a noncirrhotic fibrosis[3] and are unable to confirm that the sinusoidal dilatation can be considered a precursor to the formation of tumor. It is to be hoped that stricter environmental controls will prevent further angiosarcomas arising *de novo*, but workers who have already developed portal hypertension and those who have been exposed to high concentrations of the chemical in the past must be monitored carefully in the future.

Summary

A man aged 36 years who had been a VCM process worker for only 3½ years was unexpectedly found at laparotomy for a peptic ulcer to have an enlarged liver and portal hypertension. Biopsy showed striking focal dilatation of the sinusoids. Fifteen months later the patient died of a hepatic angiosarcoma.

Acknowledgment

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