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Two Cases of Liver Angiosarcoma Among Polyvinyl Chloride (PVC) Extruders of an Italian Factory Producing PVC Bags and Other Containers

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Two cases are reported of liver angiosarcoma occurring among polyvinyl chloride (PVC) extruders from a small Italian factory producing PVC bags and other containers. The possibility that PVC extrusion carries a risk of liver angiosarcoma is important because of the very large number of people working with extruding, manufacturing and handling PVC, as compared with the number of people working in PVC polymerization and/or VC production. In the past, the level of vinyl chloride (VC) concentration in PVC extrusion workplaces has been thought to be "safe."

Key words: liver angiosarcoma, polyvinyl chloride, extruders

Vinyl chloride (VC) has been shown to be a multipotential carcinogen in experimental animals, producing a variety of tumours of different types, at different sites, one of which is liver angiosarcoma [Maltoni, 1974; Maltoni et al, 1981].

The early release, in 1973 [Maltoni, 1974], of the experimental results promoted epidemiological investigations that led to the discovery of the first three cases of liver angiosarcoma in PVC polymerization workers, in a U.S. VC-PVC factory [Creech and Johnson, 1974]. As predicted by the experimental studies, an excess of other tumours (brain, lung, and hemolymphoreticular tissues) were found among workers in the VC-PVC industry [IARC, 1979].

Since 1974, 102 cases of liver angiosarcoma have been reported among workers exposed to VC in various countries, as listed in the Liver Angiosarcoma Registry of ICI [Stafford, 1983]. Most cases were among polymerization workers, although a few cases were observed among VC producers and users.

In Italy four cases of liver angiosarcoma were reported in 1980 [Maltoni and Rondinella, 1980]. Three of these were found in workers from polymerization factories (cases 02, 03, 04) and were included in the Stafford list. The fourth Italian case of liver angiocarcinoma (case 01), observed in a PVC extruder from a small Italian factory producing PVC bags and other containers (PANSAC, Mira, Venice), was excluded from the list because it did not match the other cases on several counts:

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1) the latency time was short (6 yr); 2) the time of exposure was limited; 3) the tumour was observed at autopsy to have involved liver, lung, and pericardium, and although the primary tumour was probably in the liver, a multicentric origin could not be excluded; and 4) none of the other VC liver angiosarcomas were observed among extruders.

The possibility that PVC extrusion can entail a risk of developing liver angiosarcoma represents a great problem for two reasons: 1) the number of people extruding, manufacturing, and handling PVC is very high in comparison with the number of people working in PVC polymerization and/or VC production factories; 2) up to the present time the past concentrations of VC in PVC extrusion workplaces were thought to be "safe" (a sort of safeguard level), since no marker tumours (liver angiosarcomas) were observed among these workers.

In April 1983 an extruder from the same factory died of liver angiosarcoma. Two cases of this rare tumour in workers from the same small factory can in no way be considered coincidental.

These two cases of liver angiosarcoma in PVC extruders are herewith reported with the aim of promoting oriented experimental investigations and prompting adequate measures of prevention in extrusion factories.

CASE 01

De L. G. was born on June 15, 1935. He worked up to 1964 in a laundry. From 1965 to 1970, with only one year of interruption, he worked at PANSAC. In this factory he was initially employed as a PVC extruder for one year, and then as a packer of PVC bags.

In February 1970 he felt a diminution of "muscular strength," epigastric pain, and nausea.

In January 1971 he developed a cough, with mucous and hemorrhagic sputum. In February abdominal pain and vomiting developed and gradually worsened. At that time he was admitted to the hospital. In March pericardial and pleural effusions and ascites were evidenced. The cardiac silhouette appeared very enlarged on chest X-ray. A cytologic examination of pericardial fluid evidenced the presence of neoplastic cells of the lining type ("mesothelioma"?).

The patient died on April 16, 1971.

At autopsy, hemorrhagic nodular blebs of different dimensions were found in liver and lungs. The visceral and parietal pericardium were adherent in some areas and separated in other areas by hemorrhagic friable tissue 1 mm to 1 cm thick.

The histopathologic examination of liver, lungs, and pericardium showed the presence of an angiosarcoma.

CASE 02

D. G. was born on March 19, 1937. From 1967 to 1971 he had worked at PANSAC as an extruder of PVC and other plastic materials. From 1975 he worked elsewhere in the commercial field.

In the middle of March 1983 he felt a violent pain in the right hypochondrium that was particularly acute on right decubitus. Concurrently dyspnea at rest appeared. For this reason he entered the hospital.

The liver was found to be enlarged, hardened, with irregular surface and margins, but not dolent.

At that time a moderate ascites was also observed. Cytological examination of the ascitic fluid evidenced nontypical cells.

At the beginning of April 1983, a liver biopsy was performed; histopathological examination demonstrated a "cholangiocellular carcinoma."

On April 6, 1983, the patient died as a result of hemoperitoneum.

At autopsy the liver appeared enlarged with many nodules varying from 0.3 to 8 cm in diameter.

The histopathological examination performed by one of the authors (C.M.), as well as by the pathologist who had examined the biopsy, showed a *liver angiosarcoma* (Figs. 1–3; figures follow reference section). In the surrounding hepatic parenchyma, many lesions characteristic of the livers of VC-exposed workers [Thomas and Popper, 1975] were found. Among these were peliosis (Fig. 4), subcapsular, periportal, and intralobular fibrosis, with widening of the Disse spaces (Fig. 5), and hyperplasia and dysplasia (Fig. 6) of the sinusoid lining angioblastic cells.

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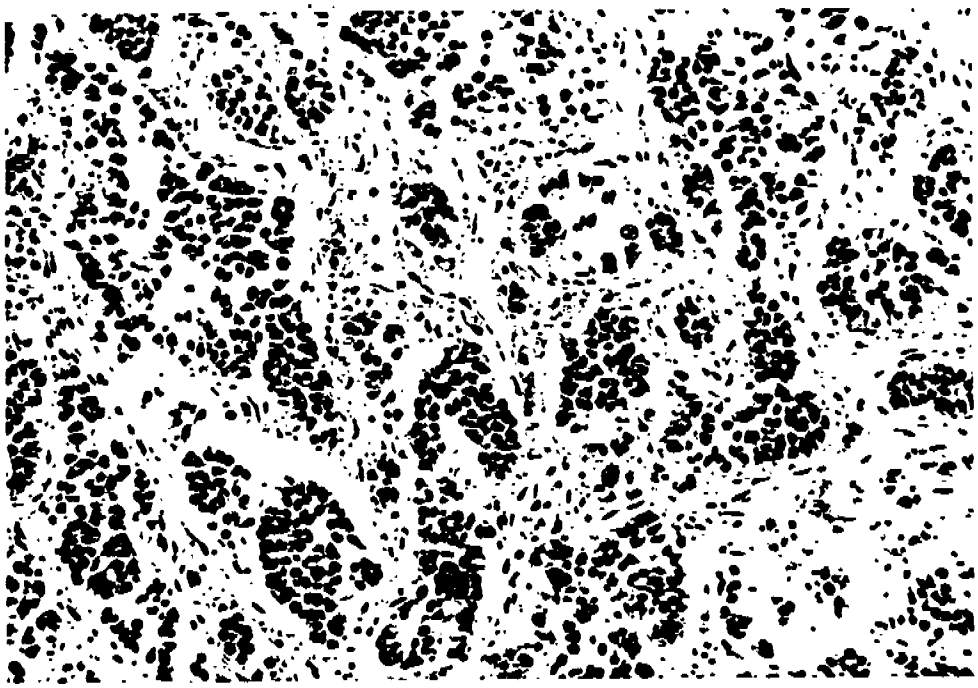

Fig. 1. *Case 02.* Liver angiosarcoma. Hematoxylin and eosin H & E ×200.

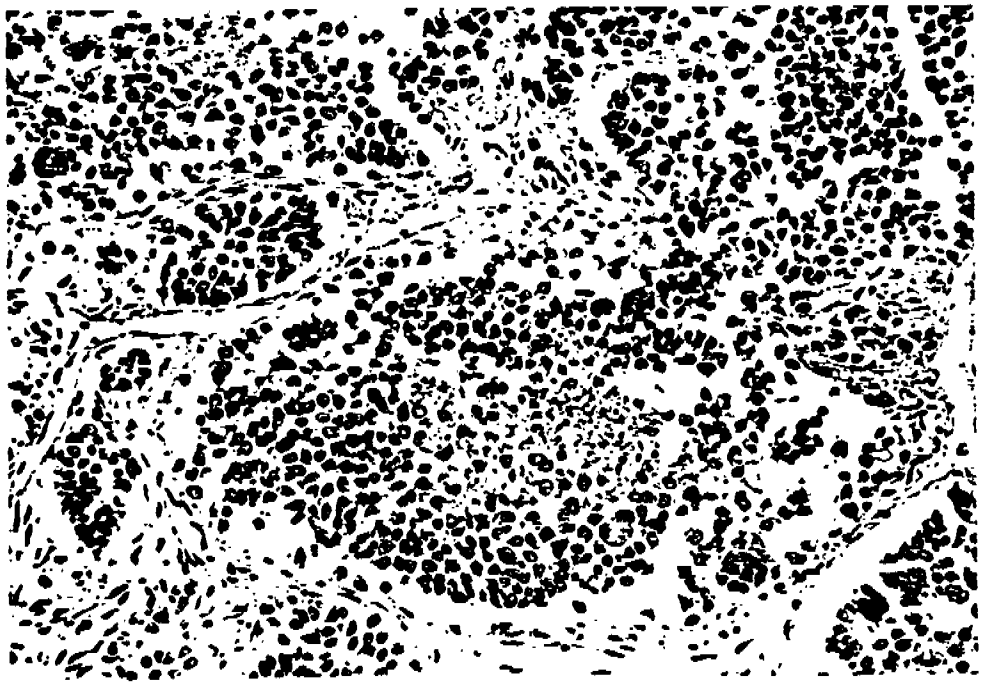

Fig. 2. *Case 02.* Area of liver angiosarcoma, with fibrous reaction. H & E ×200.

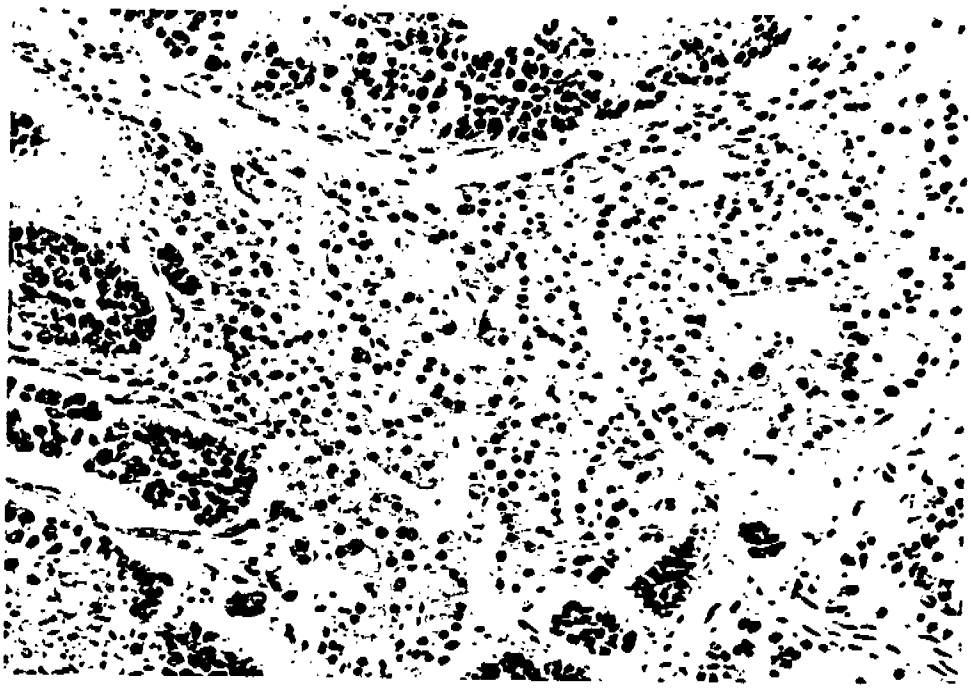

Fig. 3. *Case 02.* Liver angiosarcoma invading liver parenchyma. H & E ×200.

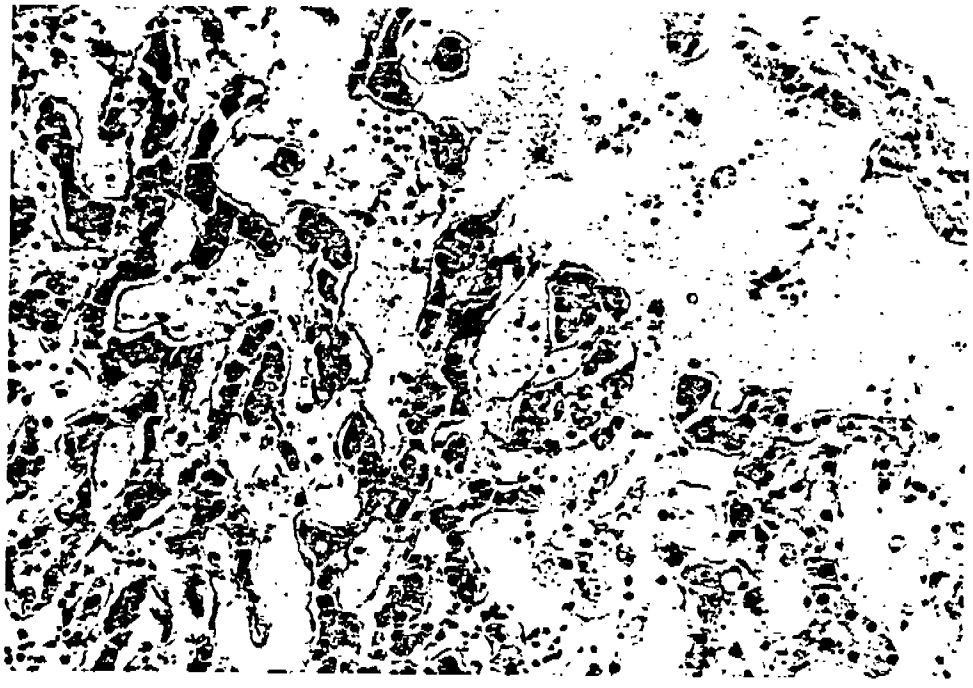

Fig. 4. *Case 02.* Peliosis in a subcapsular area of liver. H & E ×200.

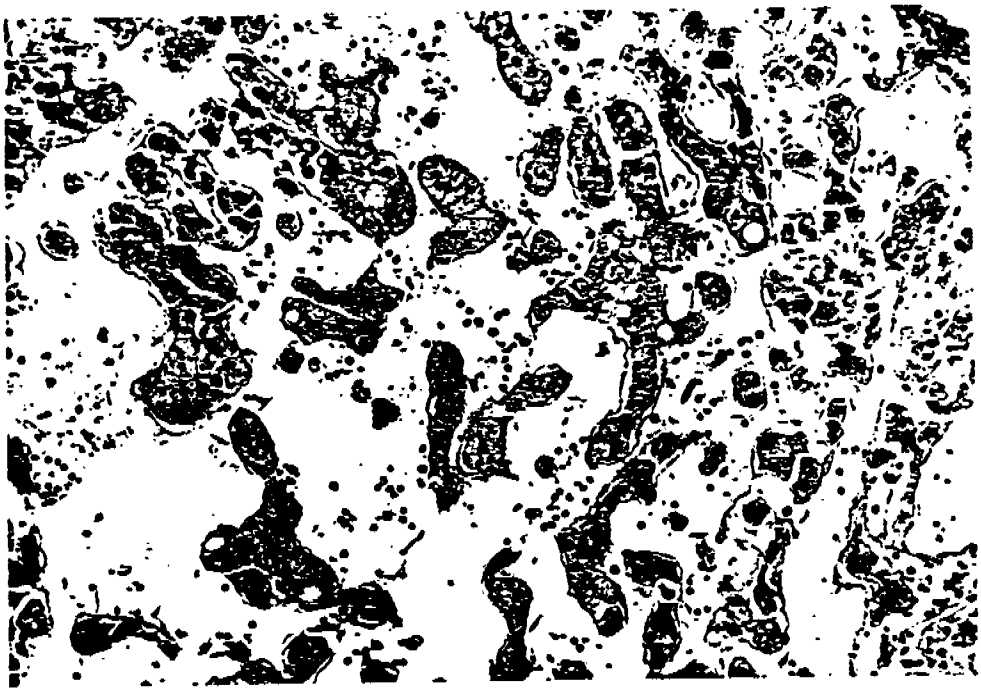

Fig. 5. *Case 02.* Peliosis with widening of Disse spaces. Mallory ×200.

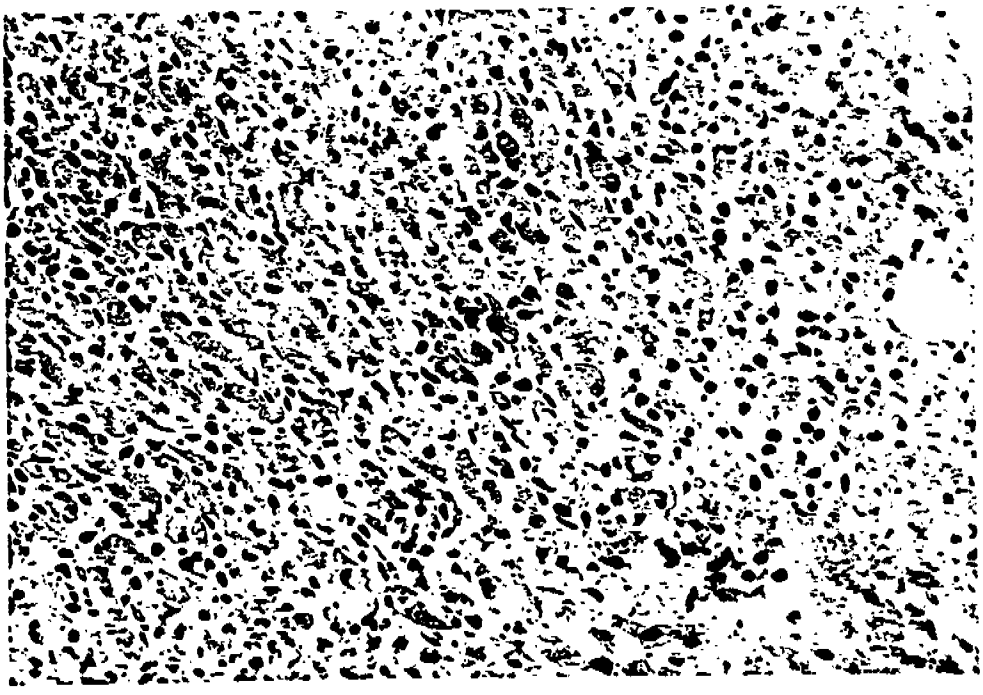

Fig. 6. *Case 02.* Area of liver showing dysplasia of angioblastic cells lining sinusoids. H & E ×200.