Revised August 1954
Circular A-32 (Rev.)

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GPO 663—16—80034-1 380-793

CLINICAL RECORD	AUTOPSY PROTOCOL				
DATE AND HOUR DIED A. M. P. M.	DATE AND HOUR AUTOPSY PERFORMED A. M. P. M.	CHECK ONE		
		FULL AUTOPSY	HEAD ONLY	TRUNK ONLY
PROSECTOR	ASSISTANT			

CLINICAL DIAGNOSES *(Including operations)*

Patient is a part of the case review study on polyvinyl chloride production workers.

The diagnoses are based on a review of histological sections. A copy of the complete autopsy protocol was not available at the time of this review.

PATHOLOGICAL DIAGNOSES

1. Angiosarcoma of liver with extension through hepatic capsule and into diaphragm.
2. Angiosarcoma involving lung, myocardium, epicardium, kidney, peritoneum with extension into muscularis of small intestine, mesentery, retroperitoneum and mesenteric lymph node. (See summary of pathologic findings).
3. Progressive fibrosis of liver.
4. Megalocytosis of liver.
5. Sinusoidal dilatation of liver, (focal).
6. Bile stasis and jaundice (clinical).
7. Hepatomegaly (5,200 gms.)
8. Acute hemorrhage in peritoneal cavity
9. Acute hemorrhage into pleural cavity.
10. Congestion of spleen.
11. Plasmacytosis and ? extramedullary myelopoiesis of spleen.
12. Hyperplasia of Malphigian follicles of spleen.
13. Chronic hemorrhage, emphysema and anthracosis, lungs.
14. Hypertrophy of myocardial cells.

Reviewed by: OVER

[redacted]—SIGNATURE Hans Popper, M. D.

MILITARY ORGANIZATION *(When required)*	AGE	SEX	RACE	IDENTIFICATION NO.	AUTOPSY NO.
	52	M	W		

PATIENT'S IDENTIFICATION *(For typed or written entries give: Name—last, first, middle; grade; date; hospital or medical facility)*

REGISTER NO.	WARD NO.
00-00-00	

AUTOPSY PROTOCOL
Standard Form 503
503-104

BFG67407

15. Benign hyperplasia of prostate gland.
16. Focal chronic prostatitis.
17. Decreased spermatogenesis and moderate atrophy of seminiferous tubules.
18. Hyperplasia of bone marrow (increased myelopoiesis).

Louis B. Thomas, M. D.

Reg. #00-00-00

GROSS:

The specimen consists of 16 submitted slides bearing the label of the Methodist Evangelical Hospital in Louisville, Ky. and their accession number A-64-18.

(Note: Also received were submitted surgical slides which are accessioned under our number S74-823).

Microscopic:

Liver: Four sections of liver are reviewed. One section consists only of angiosarcoma which is composed of large vascular spaces filled with blood. Most of this portion of the tumor is hemorrhagic and necrotic. Along the capsular surface there is a zone of well-preserved angiosarcoma. Here the angiosarcoma cells, many of which are spindle-shaped with large irregular nuclei and elongated cytoplasmic processes, line irregular vascular spaces which are separated by fibrous trabeculae. Papillary protrusions of these trabeculae extend into the vascular spaces and in some areas the lining cells are detached and have proliferated as a mass of cells growing in the spaces. In these masses the angiosarcoma cells are rounded. In a few areas the angiosarcoma cells form a capillary pattern of more solid tissue and infiltrate the hepatic capsule. In fact, the section shows that the hepatic capsule is fused to the diaphragm and microscopically a few angiosarcoma cells appear to infiltrate the diaphragm.

The other sections show uninvolved liver and multifocal angiosarcoma. The separate foci of angiosarcoma are as small as one mm. and range in size up to the massive angiosarcoma described above. These smaller deposits of angiosarcoma are similar to the massive lesion but are different in two or three respects. The vascular channels are smaller, for example, and seem to be altered hepatic sinusoids lined by sarcoma cells. The walls between these spaces contain plates of hepatic parenchymal cells. Bile plugs are present in the canaliculi of hepatic plates within these small angiosarcomas and bile stasis and bile plugs are also noted in other portions of the liver. Invasion of portal vein branches by angiosarcoma cells is seen in the margin of some of these small angiosarcomas.

The uninvolved hepatic tissue, at a distance from the angiosarcomas, exhibit progressive fibrosis, sinusoidal dilatation, and slight chronic inflammation. All these features were described in detail in the report

of the surgical biopsy (see S74-823). Megalocytosis, i.e. variation in hepatic cell size was noted in the surgical but one of the autopsy slides shows a focus of hepatic cells which are enormously enlarged. These cells are 3-4 or even 5 times larger than normal hepatocytes and have nuclei 3-4 times larger than normal hepatocyte nuclei. Several cells have two or three nuclei and one has four large nuclei with prominent huge nucleoli. The cytoplasm of these cells is strongly eosinophilic, almost orangophilic and has a ground glass appearance. One hepatic cell in the area contains hyaline ("alcoholic") in its cytoplasm.

Lymph nodes and mesentery: One section shows a congested, hyperplastic lymph node with primary lymphoid follicles and occasional reaction centers. It contains anthracotic pigment and presumably is a tracheobronchial lymph node. This same slide includes a piece of mesenteric fat. Just below the peritoneal surface is a 2 mm. focus of capillary and cavernous angiosarcoma in the mesenteric fat. The histological features of the angiosarcoma cells are the same as seen in the angiosarcomas of the liver. Another slide contains a section, presumably of mesentery, which shows a 1 cm. nodule of angiosarcoma producing a bulging mass on the peritoneal surface. This fatty, mesenteric tissue also includes a small lymph node which is partially replaced by angiosarcoma. The angiosarcoma is in the cortex of the node and at one point extends through the capsule and into adjacent fatty tissue.

Small bowel: Sections show two or three nodules of angiosarcoma on the surface of the small intestine. One of these infiltrates through the muscularis propria but the submucosa and the mucosa are not involved.

Lung: The three sections of lung show hemorrhagic nodules of cavernous and capillary angiosarcoma varying from 2-3 mm. to several centimeters in size. There are numerous hemosiderinophages in adjacent lung tissue which also exhibits compression, anthracosis and emphysema with fibrosis of alveolar walls. The pleural surfaces over the larger tumor nodules are covered with hemorrhage and fibrinous adhesions.

Heart: Multiple deposits of angiosarcoma are seen in the myocardium and epicardium. These vary from 1 mm. up to 1 cm. in size and are discrete. The angiosarcoma cells surround and envelop cardiac muscle bundles so that these often appear to form papillary

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strands projecting into the interconnecting vascular channels. The cardiac muscle cells, so enclosed, are in part well preserved, but in other areas they are vacuolated and appear to be degenerating. In some areas of the angiosarcoma the cardiac muscle cells have disappeared and the angiosarcoma is supported on trabecular bands of fibrous connective tissue. Thus the structural pattern of the angiosarcoma in the heart is similar to the angiosarcome in the liver; in the heart the angiosarcoma cells use the cardiac bundles as a scaffold whereas in the liver the hepatic plates are surrounded and enveloped by angiosarcoma cells.

Elsewhere the cardiac muscle cells show moderate hypertrophy but there is no necrosis or interstitial fibrosis.

Kidney: The two sections of kidney show slight arterionephrosclerosis. There is a slight to moderate increase in the cells of the glomeruli. These appear to be mostly endothelial cells but special stains would be useful to rule out proliferation of mesangial cells as well.

Also present is a 1 mm. discrete nodule of cavernous angiosarcoma in the subcapsular cortex of the kidney. In this location the angiosarcoma cells use renal tubules as a scaffolding for growth. (See description of angiosarcoma in the liver and heart).

Pancreas: Not remarkable.

Spleen: The splenic red pulp is congested and diffusely hypercellular. This hypercellularity is partly due to a proliferation of sinusoidal lining cells and an increased number of lymphoreticular cells in the cords of Bilroth. Also the sinusoids are filled with cells, most of which appear to be mature plasma cells and plasma cell precursors. Numerous polymorphonuclear leukocytes are present and perhaps some immature myelocytes are also present. Special stains would be needed to show definitely that there is extramedullary myelopoiesis. No megakaryocytes are seen and there are no recognizable colonies of normoblasts.

The Malphigian follicles are enlarged and several reaction centers are seen in the "B" lymphocyte zone of the follicles. Many of the penicilliary arterioles are hyalinized.

Adrenal Gland: The adrenal gland is not remarkable. There is a discrete 2 mm. sized nodule of angiosarcoma in the retroperitoneal fat adjacent to the adrenal gland.

Thyroid gland: Not remarkable.

Prostate Gland: The section shows hyperplasia of prostatic glands and focal chronic inflammation.

Testis: There is decreased spermatogenesis with almost no spermia or spermatids and only a few secondary and tertiary spermatocytes being seen. There is slight atrophy of seminiferous tubules. A few groups of interstitial cells of Leydig are seen.

Bone and bone marrow: Two sections, one of rib and one of vertebra, are examined and the bone marrow of both is hyperplastic, principally due to increased myelopoiesis. Numerous colonies of erythropoietic cells are also seen, and megakaryocytes and megakaryoblasts are present in normal numbers.

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Summary and Comments about Pathologic Findings

1. The principal interest in this case from the standpoint of the VC-PVC study is, of course, the angiosarcoma. Clinically there appeared to be a large primary angiosarcoma of the liver and complications of this lesion, chiefly hemorrhage, were apparently the anatomical cause of death.

2. An important question is whether the angiosarcomas in other organs were primary or metastatic or partly metastatic and partly multicentric origin of angiosarcoma in several organs. This question cannot be resolved on histological observations. Some of the angiosarcomatous nodules on the serosal surface of the peritoneum could be implant metastases following rupture of the hepatic angiosarcoma. Other angiosarcoma deposits were, however, deep within the tissues of the organ involved (kidney, heart and mesenteric lymph node) and could be considered new primaries. Alternatively they could be explained by hematogenous spread of the angiosarcoma. A similar mechanism could explain the pulmonary nodules of angiosarcoma. Thus the question of multiple primary angiosarcomas versus metastatic angiosarcoma is not resolved. In the liver, there does appear to be multicentric origin of angiosarcomas.

3. The other hepatic lesions consisting of progressive fibrosis, etc. seen in Mr. Sims' liver are characteristic of changes seen in the liver of other patients, both with and without hepatic angiosarcomas, in the VC-PVC study. A most remarkable feature in this patient's liver was the marked degree of focal megalocytosis. The relationship of this unusual effect on hepatic cells and VC exposure needs to be studied further and, of course, the possible relationship of megalocytosis as a precursor change for the development of hepatocellular carcinoma needs to be looked for in other cases included in the study.

4. The splenic changes in this patient are interesting and in part have been observed in the spleens of other patients included in this study. However, additional sections and special stains are needed to establish definitely whether there is extramedullary hematopoiesis. We have seen this definitely in one other patient's spleen (? in two) but this and other changes in the spleens must be studied.

5. We are not certain whether the hyperplasia of lymph nodes and lymph nodules in the appendix are related to the hyperplasia of the Malphigian follicles. The Malphigian follicle changes have been seen in enlarged spleens of other patients in the VC-PVC study but we have

not examined enough material to know whether there is generalized hyperplasia of lymphoid tissue in all patients or whether it is chiefly confined to the Malphigian follicles and therefore related to hepatic lesions. Some information might be obtained from the clinical charts. Did any of the patients have enlarged peripheral lymph nodes?