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Digestive System

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microscopy and immunologic markers may be necessary to make the distinction between the more anaplastic hemangiosarcoma and Kupffer cell sarcoma (see Kupffer cell sarcoma, p. 73). Primary hemangiosarcomas must be distinguished from metastatic hemangiosarcomas from other sites.

Biologic Features

Hemangiosarcoma of the liver tends to invade locally by first extending along hepatic cords. As they become larger and more cellular, extension across hepatic cords and other normal structures is noted. Primary hepatic hemangiosarcomas metastasize to other organs, primarily the lung. Although they are induced by various chemical carcinogens, hemangiosarcomas are rare spontaneous neoplasms.

Comparison with Other Species

The histology of primary hepatic hemangiosarcomas is similar in most species including humans (Popper et al. 1977; Wayss et al. 1979). The development and various histologic stages of the lesion appear to be equivalent in man and animals when the lesions are caused by exposure to vinyl chloride, inorganic arsenicals, and thorium dioxide (Thorotrast) (Popper et al. 1977).

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Hemangioma, Liver, Rat

Paul N. Brooks and Francis J. C. Roe

Synonym. Hemangioendothelioma.

Gross Appearance

Hemangiomas appear macroscopically as dark, raised foci and are generally soft in texture. They occasionally occur in association with hepatocellular neoplasms and tend to hemorrhage easily, which may result in fatal intraabdominal bleeding. Hemangioma of the rat liver is a relatively rare spontaneous neoplasm.

Microscopic Features

The diagnosis of hemangioma is made upon evidence of a primary proliferation of endothelial cells, which is initially apparent in association with cords of liver cells, but, subsequently, hepatocytes are exluded from the neoplasm except for clumps of liver cells trapped during expansive growth. Eventually, these trapped hepatocytes become atrophic and degenerate and are replaced by fibrous tissue. In other areas a definite connective tissue stroma is evident in association with the proliferating endothelial cells.

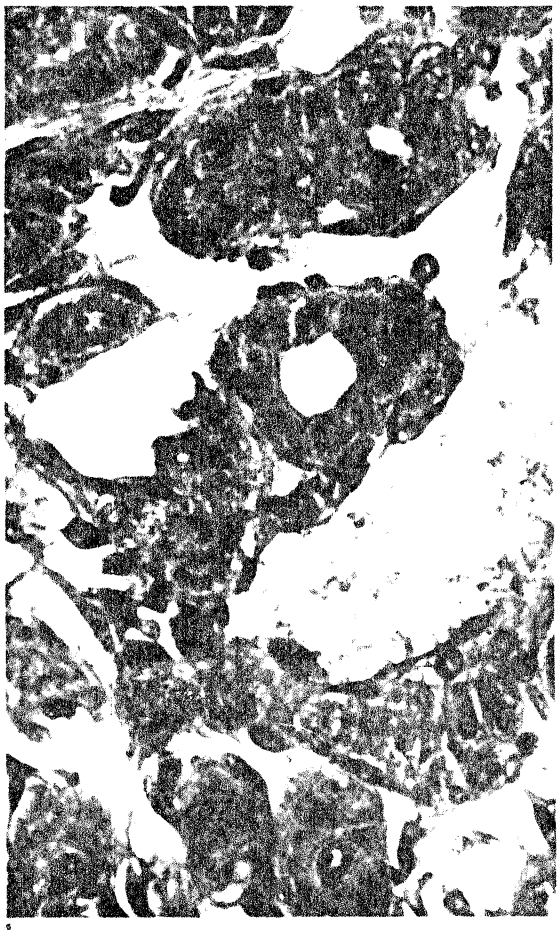

Fig. 56. Hemangioma, liver, rat. Cords of hepatocytes are lined by plump, but otherwise normal, endothelial cells. H and E, × 1720

Fig. 57. Hemangioma, liver, rat. Vascular spaces lined by endothelium; hepatocytes are sparse, and those present are atrophic. H and E, × 1720

There is considerable variability in the micromorphology of hemangiomas of the liver, even within individual tumors. Frequently, there are areas in which cords of liver cells, lined by neoplastic endothelium, give rise to pseudoglandular, papillary, and cystic structures. These areas contrast with those of more solid appearance containing no or only a very few hepatocytes, but characterized by a prominent connective tissue stroma. The endothelial lining is usually only one cell thick, but locally the depth can be greater than this.

Sinusoids within the neoplasm develop to a variable degree and become filled with blood. In some instances, cystic blood-filled spaces are a prominent feature.

Neoplastic endothelial cells are larger than normal, but are occasionally oval or round rather than flattened. The nucleus is generally large in proportion to cell size, with only scant cytoplasm in most cases. Benign neoplastic endothelial cells are easily recognizable as endothelial in origin, in contrast to the malignant variants, which have a more diverse morphology. Mitotic figures are only rarely observed within the neoplasm and there is never invasive growth, although such lesions are not always clearly delineated from surrouding tissue by any distinct capsule (Figs. 56, 57).

Differential Diagnosis

The differential diagnosis of hemangioma can be quite difficult when such neoplasms occur in the liver. In particular, hemangioma must be distinguished from morphologic forms of hepatocellular proliferation, those of hepatocellular alteration, and hemangiosarcoma. Usually, the characteristic epithelial appearance of cholangioma does not lead to confusion in the diagnosis of hemangioma.

Within hepatocellular adenomas and carcinomas, there are occasionally "hemangiomatous" areas in which sinusoidal dilatation is conspicuous. The associated endothelial cells are, however, quite normal and exhibit no neoplastic features.

Foci or areas of telangiectasis, *peliosis hepatis*, and *spongiosis hepatis* can each be confused with early neoplastic lesions of vascular origin (see pp. 111, 116). In areas of telangiectasis the vessels undergo dilatation without proliferation of the endothelium or hepatocytes, and both elements are morphologically normal except for dilatation of sinusoids. Peliosis hepatis is characterized by blood-filled cystic spaces bounded by hepatocytes and having no endothelium, and in spongiosis hepatis, a lesion described by Bannasch et al. (1981) (see p. 116) in which there is an extracellular accumulation of mucopolysaccharides and/or protein, no proliferation of endothelial cells is seen, although there may be proliferation of surrounding hepatocytes.

The morphologic features of the malignant endothelial cells observed in hemangiosarcoma are usually sufficient to delineate this from hemangioma. In general, malignant endothelial cells vary widely in size and shape and line irregular vascular spaces often to a depth of several cells. The cells have considerable nuclear polymorphism, a relatively high mitotic rate and invade adjacent tissues.

Biologic Features

The relatively low frequency with which hemangioma of the rat liver occurs makes comment on the behavior of such tumors difficult. There is, however, no evidence to suggest that hemangiomas progress to malignant forms in the rat.

Comparison with Other Species

Hemangioma of the liver is rare in most species. The neoplasm does occur in mice (Frith and Ward 1980) and there are suggestions that in the mouse the development of hemangiosarcoma is a progression from hemangioma. In man, cavernous hemangiomas of the liver are not uncommon.

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Kupffer's Cell Sarcoma, Liver, Rat

James A. Popp

Synonym Hepatic reticulum cell sarcoma.

Gross Appearance

Kupffer's cell sarcoma usually consists of numerous small nodules (1–5 mm) randomly distributed throughout the liver (Chopra et al. 1979; Ford and Becker 1982). The lesions usually are irregular in shape and frequently have indistinct borders. On cut surface the color is a homogeneous gray-white, although the tissue may be discolored by necrosis and hemorrhage in large lesions.

Microscopic Features

Neoplastic cells may form nodules or irregular sheets which arise in and infiltrate along the sinusoids throughout the lobule (Fig. 58). In the latter case, isolated hepatocytes or remnants of the lobular architecture may be evident (Chopra et al. 1979; Ford and Becker 1982). Individual neoplastic cells are usually round to oval with indistinct cytoplasmic borders. The cytoplasm is abundant, is frequently vacuolated, and may contain phagocytized necrotic debris or red blood cells. The nucleus is typically oval, pale, and often indented (Fig. 59). In some lesions, the cells are pleomorphic and assume a spindle shape with limited cyto-