Vascular Pattern of a Metastatic Liver Tumor in a Dog: A Scanning Electron Microscopic Study of Resin Casts—

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ABSTRACT. Metastasis of a malignant mixed tumor occurring in the abdominal wall was found in the liver of a 15-year-old dog male. The vascular system of the metastatic lesion was examined by scanning electron microscopy using the resin cast technique. The existence of arterio-portal shunts was confirmed. The shunts arose from branches of the hepatic artery in retrograde or vertical direction and merged into the capillary plexus replacing the branches of the portal vein, forming the so-called thread and streaks vessel in the field of hepatic angiography. Vessels with the thread and streaks appearance histologically represented tumor emboli growing in the lumen of a large branch of the portal vein. There were capillaries running inside along the portal vein and forming a longitudinal dense network in the vein. Branches of the hepatic artery feeding the metastatic lesion were well developed and formed a coarse arterial network in their course. Tributaries of the hepatic vein from the lesion were also well developed.—KEY WORDS: hepatic metastatic tumor, SEM, shunt, thread and streaks vessel, vasculature.


Hepatic angiography by selective catheterization of the celiac or hepatic artery is a useful procedure for the diagnosis of liver carcinoma. Regional chemotherapy by perfusion of a hepatic vascular bed has also come into use for patients with hepatic neoplasms. This diagnostic method and therapy could perhaps be made even more effective if the blood supply to the developing liver cancer is understood in greater detail.

Many clinicians have suggested possible existence of arterio-portal shunts as indicated chiefly by opacification of portal branches during or following injection of contrast medium from the hepatic artery [2, 10–12]. “Thread and streaks vessel” representing capillary plexuses nourishing tumor emboli in intrahepatic portal veins have been observed clinically in hepatic angiography [10–12]. However, neither the path way of contrast medium from arteries to portal branches nor the characteristics of the thread and streaks vessel has been described in detail. The present dog studies were designed to clarify the topographical relationship between the hepatic artery and portal vein systems and to evaluate the contribution of each of these vessels to the blood supply in tumor tissues. For this purpose, scanning electron microscopy of resin casts of vessels was used.

MATERIALS AND METHODS

The dog was a 15-year-old male Miniature Pinscher. Post-operatively, its clinical condition had declined despite anticancer drug therapy, and the dog was euthanatized and necropsied. The tumor was first noted at 13 years of age as a small, firm swelling in the subcutis around the inguinal region. When the animal died, the mass extended from the inguinal to the thoracic regions. At necropsy the tumor was found as a large mass located in the subcutis. A soft, cream-colored, multilobular mass, approximately 8 cm in diameter, was also found in the anterior mediastinum. A large metastatic tumor mass, approximately 7 cm in diameter, was present on the dorsal border of the right lobe of the liver (Fig. 1). This mass was soft, grayish-pink and had hemorrhagic necrotic areas with hemorrhages.

Small pieces of the primary and metastatic tumors were sampled from the liver and fixed in 10% formalin. Paraffin sections were prepared and stained with hematoxylin-eosin (HE) using routine methods.

The liver was perfused with Ringer’s solution at 37°C. Minimal volume of a mixture of methyl methacrylate monomer with 50% Mercox (Dainippon Ink Co., Ltd., Tokyo) was injected into the hepatic artery. Another acrylic resin with yellow-pigment was used for perfusing the portal vein. Perfusion was continued until the mixture was flowing out of the hepatic vein. Cast replicas were microdissected under a binocular microscope. Each piece of a cast was mounted on an aluminum stub and sputtered with gold for scanning electron microscopic observation.

RESULTS

Histology of the tumor: The primary tumor in the abdominal wall consisted of anaplastic epithelial cells, some of which were metastatic to squamous epithelium, and less differentiated osteocytes, and was diagnosed as a malignant mixed tumor. The metastatic tumor in the liver consisted of polygonal- or oval-shaped tumor cells possessing a large pleomorphic nucleus with prominent nucleoli and was adenocarcinomatous. No mesenchymal component was observed in the metastatic tumor. The vascular system of the lesion presented an irregular network of capillaries. Tumor cell emboli in the portal vein were arranged in clusters. These emboli occupied almost the whole lumen of the vessel and sometimes obliterated it.
trunks which anastomosed each other to form a coarse arterial network in its course to the metastatic tumor. It was significantly thick, 216–254 μm in diameter, at the site prior to entering the metastatic tumor. The artery diverged into several smaller arteries at this site. Shunts, 257–486 μm long and 27–74 μm in diameter to tributaries of the portal vein were arranged in vertical or retrograde direction to the blood flow and they merged into the thread and streaks vessel of the portal vein (Figs. 5 and 6). After entering the tumor the small arteries diverged into numerous capillaries. There was no regularity in the branching pattern or distribution of small arteries and capillaries (Fig. 7). Capillaries with spike-like protrusions representing neovascularization were frequently observed. In some areas many resin masses representing hemorrhage were also found. The venous system began from the capillaries, merged into small veins and drained into a major trunk of the hepatic vein. The major tributaries of the hepatic vein ran straight and parallel to the hepatic artery towards the hilus.

Casts of the portal vein showed the most drastic disorganization. Capillaries nourishing neoplastic emboli in the portal vein ran longitudinally along the vein and anastomosed each other, forming a dense network. They are called angiographically “thread and streaks vessel” (Figs. 5 and 6). They were 13–28 μm in diameter and had an undulating feature. The capillary network was directly connected with shunts arising from the hepatic artery. The thread and streaks vessel and shunts were frequently observed at the sites adjacent to the hilus and around the metastatic tumor.

DISCUSSION

Vascular injection of resin combined with scanning
electron microscopic observation of the casts allowed easy
detection and detailed view of even rare arterio-portal
shunts. A clear demonstration of thread and streaks
vessels, which are frequently found in intrahepatic portal
branches, was also provided by this technique. These
findings confirm the previous clinical studies by angiogra-
phy in human hepatoma [2, 10–12].

Arterio-portal shunts in hepatocellular carcinoma have
been reported using hepatic angiography in man [2, 12].
The exact trails of contrast medium from arteries to portal
branches, however, could not be described despite close
examination of the films. The present scanning electron
microscopic study of resin casts has clearly shown the
shunts between hepatic artery and capillaries in the portal
vein. Okuda et al. [10] emphasized that retrograde portal
flow of contrast medium might occur due to forceful
injection. Contrary to their opinion, retrograde flow may
occur easily even under low blood pressure, because in the
present case the shunt arose retrogradely or vertically
from the hepatic artery. Thus, arterial blood may easily
flow retrogradely through the shunts into the portal vein.

Although it is generally believed that primary or
metastatic hepatic tumors derive their main blood supply
from the hepatic artery [1], the tumor vessels can also be
Fig. 5. Scanning electron micrograph showing an arterio-portal shunt (S) between the hepatic artery (A) and portal vein (V). Note that the portal vein is replaced by a capillary plexus nourishing the embolus in the portal vein. The vessel is called "thread and streaks vessel" in the field of hepatic angiography. Note that the shunt branches off in retrograde direction to the blood flow (arrow) and merges into capillaries. × 70.

Fig. 6. Scanning electron micrograph of another arterio-portal shunts. The shunts are thicker than those in Fig. 5 and branch off in the vertical direction. × 70.
drained via the portal vein after hepatic artery ligation [8]. This fact can also be explained by the shunt formation. The direction of blood flow may be important in the use of radiotherapeutic and chemotherapeutic agents by this route.

The present study of resin casts has shown that arterio-portal shunts merge into capillaries feeding the tumor emboli in the portal vein. It is known that metastatic intravascular tumor cells reach the liver through the portal vein, lymphatic vessels or hepatic arterial vessels and rarely through peritoneal fluid. After they proliferate in the liver new vessels develop [5]. In the earlier stage when metastatic emboli are small, they are nourished by the portal venous blood. However, as the metastatic emboli grow, they stimulate new arterial supply to nourish themselves [5]. Although more direct evidence is required to prove the real mechanism of shunt formation, it is conceivable that growing tumor emboli stimulate neovascularization and induce capillaries from the neighboring hepatic artery as indicated in the present and other studies [3, 4]. As the induced capillaries develop they may form shunts to connect the hepatic artery and the portal vein to nourish the metastatic emboli in the vein.

When the liver was injected with minimal volume of the resin through the hepatic artery, the arterial branches were filled only partially, despite complete filling of tumor capillary network. This pattern of resin flow may explain the physiological characteristics of the tumor arterial system, as reported by Jirtile et al. [7] and other investigators [6, 9], that the supply of blood to the tumor exceeded that to the surrounding normal tissue.

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REFERENCES
