Hepatic Veno-Occlusive Disease in A Wild Boar (*Sus scrofa*)

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Hepatic veno-occlusive disease (VOD) is defined as an obliteration of small intrahepatic veins, resulting from subendothelial fibrosis. VOD in humans is an uncommon disease described as a hepatotoxicity, but has recently been particularly noted in patients who received chemoradiation therapy for bone marrow transplantation [5, 6, 8]. Experimentally induced VOD as the model of human disease has been reported in some species of animals [1, 2, 4, 9, 10]. Although VOD is considered as a venous lesion arising from endothelial injury, the pathogenesis remains obscure. There have been a few reports of spontaneous VOD in felidae [3, 7], but not in the other species of animals. The present note describes the pathological findings of spontaneous VOD in a wild boar (*Sus scrofa*).

A juvenile male animal weighing 3.3 kg, housed for one month after trapping was admitted to the Veterinary Hospital, Faculty of Agriculture, the Yamaguchi University. He showed anorexia and weight loss. At necropsy, there was slight ascites. The liver was large, firm and discolored. Tiny nodules were diffusely dispersed in the liver. Pneumonia and focal lesions of gastric ulceration were found.

Tissues from the main visceral organs and central nervous system were fixed in 10% buffered formalin and processed routinely. They were stained with hematoxylin and eosin and Masson's trichrome methods. For electron microscopy, formalin-fixed hepatic tissues were post-fixed in 2% osmium tetroxide and embedded in epoxy resin. Ultra-thin sections were stained with uranyl acetate and lead citrate.

On histopathologic examination of the liver, the central veins showed intimal thickening, resulting from a proliferation of spindle cells and an increase in loosely arranged fibrous connective tissue (Fig. 1). The majority of the central veins showed concentric narrowing and occlusion of the lumens. This vascular lesion was widely dispersed in the liver. Severe fibrosis showed bridging between the central vein and portal area. The sinusoids were dilated and congested. Degenerated hepatocytes were diffusely scattered. Foci of hepatocellular necrosis were often found in the centrilobular region. Fat-storing cells with large lipid vacuoles were frequently seen. No vascular lesion was found in either the hepatic arteries or the veins of the other organs. Focal necrotic lesions and fresh ulcers were found in the mucosa of the stomach and duodenum. In the lungs, there was bronchopneumonia. No significant changes were seen in the other visceral organs and central nervous system.

On electron microscopic examination of the liver, subendothelial proliferation of spindle cells was noted in the wall of the central veins (Fig. 2). Bundles of collagen fibrils were widely dispersed among the spindle cells. They had elongated and invaginated nuclei and the cytoplasm containing abundant filaments with a basal lamina around the cell surface, showing the characteristics of a relatively mature smooth muscle cell (Fig. 3). There were frequently degeneration and loss of the endothelial cells in the central veins. Hypertrophic fat-storing cells with large lipid vacuoles were often seen. However, an increase in collagen fibrils was not prominent in the space of Disse.

VOD in humans after bone marrow transplantation is thought to be caused by a wide variety of therapeutic drugs [5, 6, 8]. Various antimetabolites and alkylating agents have been associated with VOD. Experimentally induced VOD by the treatment of alkylating agents and irradiation has been reported in the dog [4, 9], rat [2], golden hamster [10] and monkey [1]. The vascular lesion of the liver is characterized by subendothelial fibrosis of the small intrahepatic veins. However, arteries of the liver are not involved. Endothelial injury is considered to be a primary event in the pathogenesis of VOD. It has been

Fig. 1. Intimal thickening and partial occlusion of central veins in the liver, resulting from proliferation of spindle cells. Hematoxylin and eosin stain, $\times 33$.

Fig. 2. Vascular wall of a central vein, showing proliferation of spindle cells with dispersed collagen fibrils. $\times 4,800$.

Fig. 3. A spindle cell has characteristics of the smooth muscle cell: The cytoplasm contains abundant filaments and a basal lamina is noted around the cell surface. $\times 10,000$.

suggested that the coagulation cascade is triggered within the walls of the central veins [8].

Recently, a high incidence of VOD in the cheetah and snow leopard has been reported [3, 7]. In the cheetah, the hepatic lesion was characterized by subendothelial fibrosis

and proliferation of smooth muscle-like cells in the central veins. Hyperplasia of the fat-storing cells and perisinusoidal fibrosis were also found. Vitamin A excess in the diet was considered to be an important factor in the development of VOD in the cheetah [3].

The main lesion of the liver in the present case was subendothelial fibrosis of the intrahepatic veins, resulting from an increase in collagen fibrils and proliferation of smooth muscle cells. This resembled the vascular lesions of VOD in the cheetah [3], and progressed to centrilobular fibrosis and liver cirrhosis. However, hyperplasia of fat-storing cells and perisinusoidal fibrosis were not prominent. Although endothelial injury of the hepatic veins is considered to be a primary event for VOD, the specific cause cannot be determined in the present case.

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