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PATHOLOGICAL STUDIES ON FASCIOLIASIS
I. A Caprine Case of Long-Term Infection with Fasciola sp.

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(Received for Publication on August 11, 1975)

Abstract
A goat suffering from long-term infection with liver fluke was examined pathologically. A characteristic histological change of the liver was an increase in connective tissue around necrotic foci and bile ducts. Cell infiltration, chiefly by eosinophil leukocytes and lymphocytes, appeared in some hepatic lobules and around the bile ducts. Fibroblasts, most of which were arranged concentrically, were seen in the periphery of the lesion. The inflammation of the bile ducts was characterized by complicated formation of crypts from the epithelium and adenomatous proliferation of the mucosa. Epithelial cells grew so actively at times that papillomatous structures were produced on the mucosa. Arteritis was most prominent in areas where increased fibrous tissue surrounded the bile ducts.

The life cycle of Fasciola hepatica was clarified in detail many years ago. There is now an extensive literature on the epizootiology, symptoms and treatment of fascioliasis. Relatively little, however, has been written about pathological changes of the liver in ruminant animals infected with liver flukes.

This paper deals with the results of observation on the pathological changes of the liver of a goat in long-term infection with Fasciola sp. Furthermore, discussion is made on the tissue reaction to the adult liver fluke in the goat, in comparison with that in any other host.

Materials and Methods
The goat studied was a 4-year-old Saanen raised on a farm in Awaji Island. It was observed for three years after it was naturally infested with liver flukes in order to examine clinical symptoms and hematological changes in the disease. The clinical symptoms detected were anemia of the conjunctiva, hepatalgia on palpation, cardiac dysfunction, and rough hair coat. Mild eosinophilia was recognized in the white blood cell count.

After macroscopical examination, the liver was collected from this goat and fixed in 10% formalin solution. Fixed materials were embedded in paraffin. Sections were stained with hematoxylin and eosin. Some of them were subjected to the VAN GIESON staining method.

Results
Macroscopic findings
Thirty-two liver flukes were found in the bile ducts of the liver, which was atrophic. Induration was present in some part of the left lobe of the liver. The larger biliary passages were considerably dilated, with thickened walls. The biliary passages contained viscid greenish-brown bile and sometime masses of pus mixed with numerous flukes. These changes were also seen on the posterior surface of the right lobe, showing white nodular cords. When sectioned, the liver was generally rich in fibers; the intrahepatic bile ducts were distended with their walls thickened and their lumina sometimes containing flukes. Focal necrosis and cloudy swelling were found in the parenchyma of the liver (Fig. 1).

Histological findings
Older tracks were composed largely of granulation tissue infiltrated by a mixture of
eosinophils and lymphocytes. They passed through a number of lobules, linking up several areas. Necrotic foci completely surrounded by connective tissue were scattered in the liver parenchyma (Fig. 2). Cellular infiltration, chiefly by lymphocytes and eosinophiles, appeared around the bile ducts and blood vessels (Fig. 3). Some fibroblasts and hepatic cells in the cords immediately adjacent to the necrotic foci were atrophied, their nuclei being pyknotic.

Connective tissue had increased around the bile ducts (Fig. 4). Edema was marked in the lamina propria of smaller sublobular bile ducts and induced a wide separation of peri-ductal collagen fibres. The duct epithelium had become columnar. Focal hyperplasia had produced numerous small epithelial intraductal papillomata (Fig. 5). This type of hyperplasia was more pronounced in the larger bile ducts and gave rise to numerous small crypts and acini lined with very tall columnar cells. Moderate edema, necrosis, desquamation of the epithelium and cellular infiltration were seen in the inner layer of the lamina propria of the larger ducts, and more changes in the outer layer. A few flukes contain in the ducts were inducing desquamation of the superficial epithelium, but no hemorrhage was apparent. In some bile ducts, the wall was divided almost equally into two layers, an outer fibromuscular and an inner mucosal layer. The inner half of the wall consisted of villi and crypts, which led to the formation of irregular branching acini in the basal half. Peculiar cells containing eosinophilic granules in the cytoplasm were often seen among epithelial cells and inside the epithelial layers (Fig. 6). Pseudo-lymph follicular structures were frequently observed around the foci of cholangitis in the liver. They consisted of lymphocytes and lymphoblasts (Fig. 7).

Larger sublobular branches of the hepatic artery were affected severely with arteritis and their walls thickened. The intima was edematous and swollen to form irregular projections, which almost occluded the lumen. The internal elastic lamina was broken into fragments. The smooth muscle of the media was hypertrophic. The adventitia was fibrous, containing few or no infiltrating cells (Fig. 8). Thrombosis was not observed in any affected artery.

**Discussion**

Many of the lesions observed in the goat in the present experiment were similar to those previously reported in experimental and natural fascioliasis in ruminant animals 1-4,6-8,10. A review of these reports has revealed that damage caused by flukes in the liver is the result of a rather simple mode of invasion, and that damage of the bile ducts is accompanied by the tissue and cellular reaction of fibroblasts, eosinophiles and lymphocytes, as well as by the proliferation of ductules due to the mechanical effect. In the present case examined, cross-sections showed that the liver was fibrotic, and that the intrahepatic bile ducts were distended with thickened walls. These ducts were often hyperplastic. Many of them were lacking in epithelium, with only fibrous tissue remaining in the wall.

DAWES 5) observed the development of hyperplasia of the bile duct in the mouse and sheep. When adult flukes entered the bile duct in these animals, the epithelium became folded into numerous crypt-like invaginations with crowded nuclei. In many cases mild damage was caused to the surface of the epithelium by the spines of the flukes. The subepithelial tissue was fibrous and densely crowded with nuclei of cells derived from the local tissue reaction of the host. The crypt-like invaginations extended deep into the subepithelial tissue, which was in an intense fibrotic condition. So that the flukes inhabited the duct snugly far from vascular or hepatic tissue.

Spines, eggs and suckers of the flukes clearly inflict much damage upon the hyperplastic epithelium, which is sometimes completely denuded in some portions. This damage may be severe or induce gradual attrition. Even when the entire superficial epithelium is removed, the invaginations may remain intact. Superficial debris produced clearly due to abrasion caused by spines can be seen in the bile ducts and in the vicinity
of fluke drifts. It is evident that regenerative processes are at work, for old cells are broken and fresh cells increase in the depth of the epithelium. In some instances, remarkable adenomatous thickening occurs in great depth. In such processes, there is a copious secretion of a mucus-like substance from the free surfaces of the cells. The simple epithelium of the bile duct is transformed into a thick, glandular structure.

A very striking vascular lesion became apparent in the liver. It was nearly confined to arteries. There was diffuse edema of the arterial wall with swelling of the intima. Progressive hypertrophy of the media and edema or fibrosis of the adventitia were observed. Arteritis was most prominent in areas where increased fibrous tissue surrounded the bile ducts. It did not appear to have been induced by direct traumatic damage of the arterial wall. ASHIZAWA\(^1\) reported the presence of changes of the liver in goats infected with *Fasciola* sp., but mentioned nothing about arterial lesions. In the present study, the veins were affected much less frequently than the arteries. There is no reference to a specific arteritis in any previous paper dealing with chronic fascioliasis in laboratory animals.

In rabbits, fluke egg granuloma and chronic cholangitis associated with the presence of flukes in the larger bile ducts were held to be significant in the evolution of comparable cirrhosis of the liver\(^{11}\). In goat, fluke egg granuloma was not found and *Fasciola* eggs were rarely detected from the lumen of small intrahepatic bile ducts.

**References**


Explanation of Plate

All the histological sections were stained with hematoxylin and eosin.

Fig. 1. Cut surface of the liver infested with Fasciola sp. The wall of the bile duct are thickened in the left lobe. The ducts were filled with adult worms.

Fig. 2. Transverse section of old fluke tract, showing necrotic debris in center surrounded by lymphocytes, eosinophil leukocytes, and young connective tissue. × 48.

Fig. 3. Infiltration of lymphocytes and eosinophil leukocytes around the bile duct. × 120.

Fig. 4. Increase of connective tissue around the bile duct. × 48.

Fig. 5. Glandular hyperplasia of the lining epithelium of a large intrahepatic bile duct. × 120.

Fig. 6. Peculiar cells containing eosinophilic granules in the ductal epithelium. × 48.

Fig. 7. Lympho-follicular tissue in the increased fibrous tissue around the bile duct. × 48.

Fig. 8. Hypertrophy of the hepatic artery in the increased fibrous tissue around the bile duct. × 48.