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Fasciola hepatica Human Infection

Histopathological Study of Sixteen Cases

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Summary. Sixteen human cases of *Fasciola hepatica* infection are described. The liver was involved in 13 cases, the gall bladder in 9 cases and the stomach in 2 cases. Lesions containing parasitic remnants or fluke eggs were rarely seen. Surface scarring of the liver, scar tracks and granulomas within organs were the most characteristic changes seen and were the most useful for the histopathological diagnosis of the disease. The associated liver, bile and gastric lesions are briefly discussed.

Key words: *Fasciola hepatica* – Infection – Human – Histopathology.

Introduction

Human infection by *Fasciola hepatica* is a rare disease and affects mainly the liver and biliary ducts. The lesions caused in animals by the fluke were studied by Dow et al. (1967 and 1968) and Rahko (1969). Human lesions are rare and few histopathological studies have been reported. Sixteen human cases are described including the principal diagnostic features seen in this infection.

Materials and Methods

Surgical material received between 1953 and 1977 has been reviewed. Various clinical diagnoses were made but the true diagnosis was only revealed following surgical examination and biopsy. Material included 12 liver biopsies, 9 gall bladder and 2 partial gastrectomy specimens, 3 lymph nodes and an appendix obtained from a total of 15 cases. Material from the sixteenth patient was obtained at autopsy. The pertinent clinical and pathological data are presented in Table 1.

All the specimens were fixed in 10% neutral formalin. Serial sections at 5 µm were cut and 1 in 10 were stained with haemalum and eosin. Other stains employed on some cases included PAS method, Alcian Blue-PAS stain and Gomori's stain for reticulin.

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Table 1.

Case	Sex	Age	Clinical diagnosis	Surgical findings	Pathological findings
1953	M	43	Complicated hepatic hydatid cyst.	7 greyish-white scars in the left lobe of the liver. Biliary lithiasis. Cholecystectomy. Liver edge biopsy.	Granulomatous inflammatory process with Fh eggs in the gall bladder wall. Similar picture in the liver parenchyma, granuloma with Fh egg.
1955	M	44	Gall bladder and biliary lithiasis.	Splenomegaly. Fh in the cystic duct. Cholecystectomy.	Granulomatous inflammation and migratory tracks in the gall bladder wall.
1959	F	36	Gall bladder lithiasis.	Fh of the gall bladder. Cholecystectomy. 8 year follow-up.	Dense eosinophilic infiltrate of the gall bladder wall.
1959	M	37	Gall bladder lithiasis.	Multiple greyish-white 10 mm liver nodules, affecting predominantly right lobe of liver. Cholecystectomy. Liver edge biopsy.	Migratory tracks with granulomatous inflammation and necrotic cavities in the liver.
1965	F	50	Biliary lithiasis. Complicated liver hydatid cyst.	Nodule in the right lobe of the liver. Fh in bile ducts. Gall bladder lithiasis. Cholecystectomy. Liver biopsy of the nodule.	Dense eosinophilic infiltrates of the gall bladder wall. Granulomas in the liver parenchyma with migratory tracks.
1966	M	29	Sepsis. Complicated hydatid cyst of the liver.	3–4 mm multiple hepatic nodules. Liver biopsy. 7 year follow-up.	Migratory tracks with tuberculoid granulomas.
1971	M	30	Peptic ulcer of the stomach.	Gastric ulcer. Multiple yellowish-white hepatic nodules. Billroth I gastrectomy. Liver biopsy.	Peptic ulcer. Migratory tracks on the gastric wall and hepatic granulomas.
1975	F	63	Subacute cholecystitis.	Hepatomegaly. 10–20 mm multiple nodules. One was 60 mm diameter. Oedamatous gall bladder with fibrous adhesions. Cholecystostomy. Liver biopsy.	Migratory tracks in the liver, granulomas.
			Second operation.	Fh of common bile duct. Drainage of hepatic abscess. Cholecystectomy.	Chronic cholecystitis.
1975	F	44	Hepatic abscess. Postoperative findings, – Fh eggs in faeces. – Immunology for Fh+.	Hepatosplenomegaly. Multiple hepatic microabscesses. Cystic lymph node biopsy. Liver biopsy.	Granulomas with migratory tracks in the liver parenchyma.

Table 1 (continued).

Case	Sex	Age	Clinical diagnosis	Surgical Findings	Pathological findings
1975	F	35	Complicated hydatid cyst of the liver. Postoperative findings, – Fh eggs in bile.	Hepatomegaly. Multiple 5 mm nodules in right lobe of the liver. Liver biopsies.	Granulomas and Fh with calcification.
1975	F	29	Obstructive jaundice.	Gall bladder lithiasis. Cholecystectomy. Fh of the common bile duct.	Chronic cholecystitis.
1976	F	65	Gall bladder lithiasis. Hydatid cyst in the right hepatic lobe. Postoperative findings, – Immunology for Fh+.	Biliary lithiasis. Hepatomegaly with multiple yellowish nodules. Cystic tumour in the right liver. Cholecystostomy. Liver biopsy.	Granulomatous inflammation and migratory tracks in the liver. Chronic cholecystitis. Simple hepatic cyst of the liver.
1976	F	55	Acute cholecystitis. Postoperative findings, – Immunology for Fh+.	Prepyloric gastric ulcer. Gall bladder lithiasis. Yellowish subserous nodules in the stomach, gall bladder and left lobe of the liver. Billroth I subtotal gastrectomy. Cholecystectomy. Liver biopsy.	Migratory tracks and granulomas in the gastric wall. Similar picture in the hepatic parenchyma and gall bladder.
1976	M	65	Liver abscess.	Hepatomegaly. Nodules. Liver biopsy. Died 6 months later, no necropsy has been performed.	Granulomatous inflammation of liver parenchyma with migratory tracks.
1977	M	35	Acute cholecystitis.	30 mm diameter nodule in the right hepatic lobe and enlargement of hilar lymph nodes. 2 lymph node biopsies. Appendicectomy. Liver node biopsies.	Granulomatous inflammatory process in the liver. Migratory tracks. Lymph sinus histiocytosis. Normal appendix.
Necropsy 1953	M	37	Subarachnoidal haemorrhage.	Aneurysm of Circle of Willis. Multiple hepatic nodules. Calcified hydatid cyst in the right lobe. 7 adult flukes in the hepatic ducts.	Migratory tracks, granulomatous inflammation of the liver.

Results

Both acute and chronic lesions were seen though both forms were often present in the same patient.

Liver Lesions. The post mortem specimen showed some perihepatitis and multiple surface nodules mainly in the right lobe. The nodules varied from 5 to 15 mm in diameter and were yellowish or greyish-white in colour. On slicing the liver there were dilated intrahepatic bile ducts which contained 7 adult flukes (Figs. 1 and 2). Multiple subcapsular cavities filled with necrotic material, 5 to 10 mm in diameter lay below the surface nodules. Several reddish-purple tracks radiated from the nodules, while other tracks were greyish-white and fibrous. Most of the lesions were confined to a depth of less than 20 mm beneath the capsule. A calcified hydatid cyst was also found on the posterior surface of the right lobe.

In a further 8 cases the liver showed a similar gross appearance and the nodules were mistaken for metastatic growth and some were taken for biopsy. In 2 cases isolated nodules 10 and 20 mm in diameter were the sole lesions, and in a third case there were multiple nodules measuring from 2–30 mm across. Greyish-white scars were found in another patient.

Microscopic Appearances. These included both acute and chronic changes. The liver capsule showed focal depressions covered with fibrino-purulent material (Fig. 6). Adjacent intact peritoneal cells showed some proliferation, and oedema and congestion were prominent in the damaged zone. Migration tracks formed by the parasite commenced beneath these capsular lesions and penetrated 10 to 20 mm into the underlying parenchyma. The tracks contained a necrotic centre filled with cellular debris, fibrin and red cells and there was a considerable surrounding eosinophilic reaction. Occasional liver cells were found in the tracks. Necrotic areas formed by confluent parasitic tracks occurred and were surrounded by an eosinophil exudate. The liver cells bordering these lesions were hypereosinophilic, showed pyknotic nuclei and in some places fatty change was prominent and caused fat filled cysts. Occasional long parasitic tracks crossed several hepatic lobules (Fig. 7) but parasites were usually absent in these lesions.

In older lesions numerous phagocytic cells, lymphocytes, focal collections of eosinophils and increasing fibrosis were found. Some of the tracks were filled with eosinophilic necrotic tissue containing nuclear debris and were surrounded by a palisade of histiocytic cells (Fig. 4). Finally the tracks underwent fibrosis and ended in subcapsular cavities filled with necrotic, eosinophilic debris bounded by fibrin, granulation and fibrous tissue (Fig. 8). Charcot-Leyden crystals and eosinophilic granules were also found in the contents. Foci of calcification were sometimes present in the marginal zone of the necrotic material (Fig. 5), and in one lesion the calcific deposits formed the outline of a dead fluke. In one case also a spheroidal 75 mμ eosinophilic structure was seen within a foreign body type granuloma (Fig. 3). Widened portal tracts containing an abundance of lymphocytes and eosinophils surrounded the lesions and in

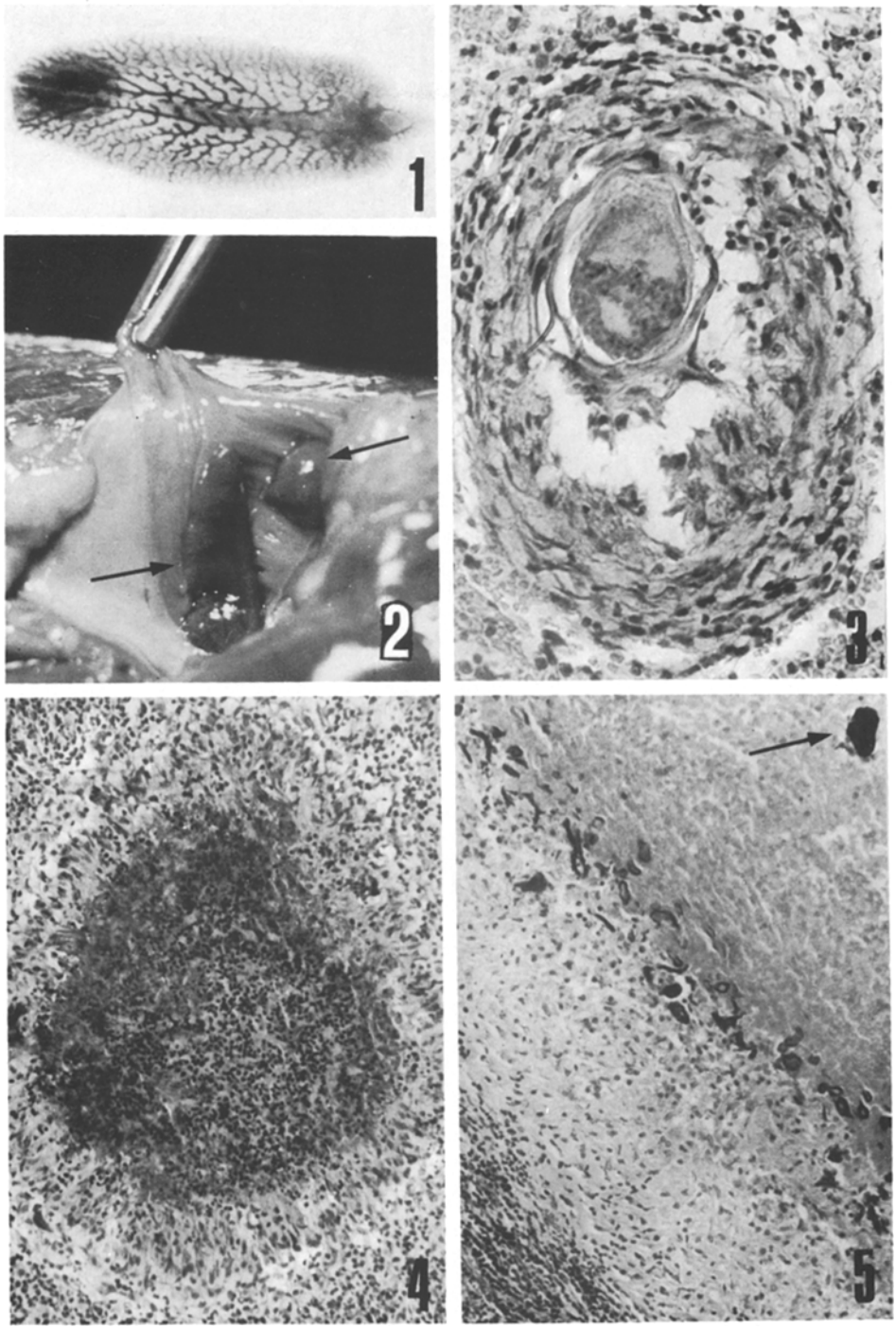

Fig. 1. Adult fluke. ×2

Fig. 2. Two adult flukes in the common hepatic duct (arrows). ×1

Fig. 3. Fh egg in the centre of a foreign body type granuloma. H & E. ×300

Fig. 4. Granuloma with hypereosinophilic centre and palisading of peripheral histiocytes. H & E. ×250

Fig. 5. Margin of a cavity showing peripheral calcification. Gross calcification is seen surrounded by necrotic rests (arrow). H & E. ×250

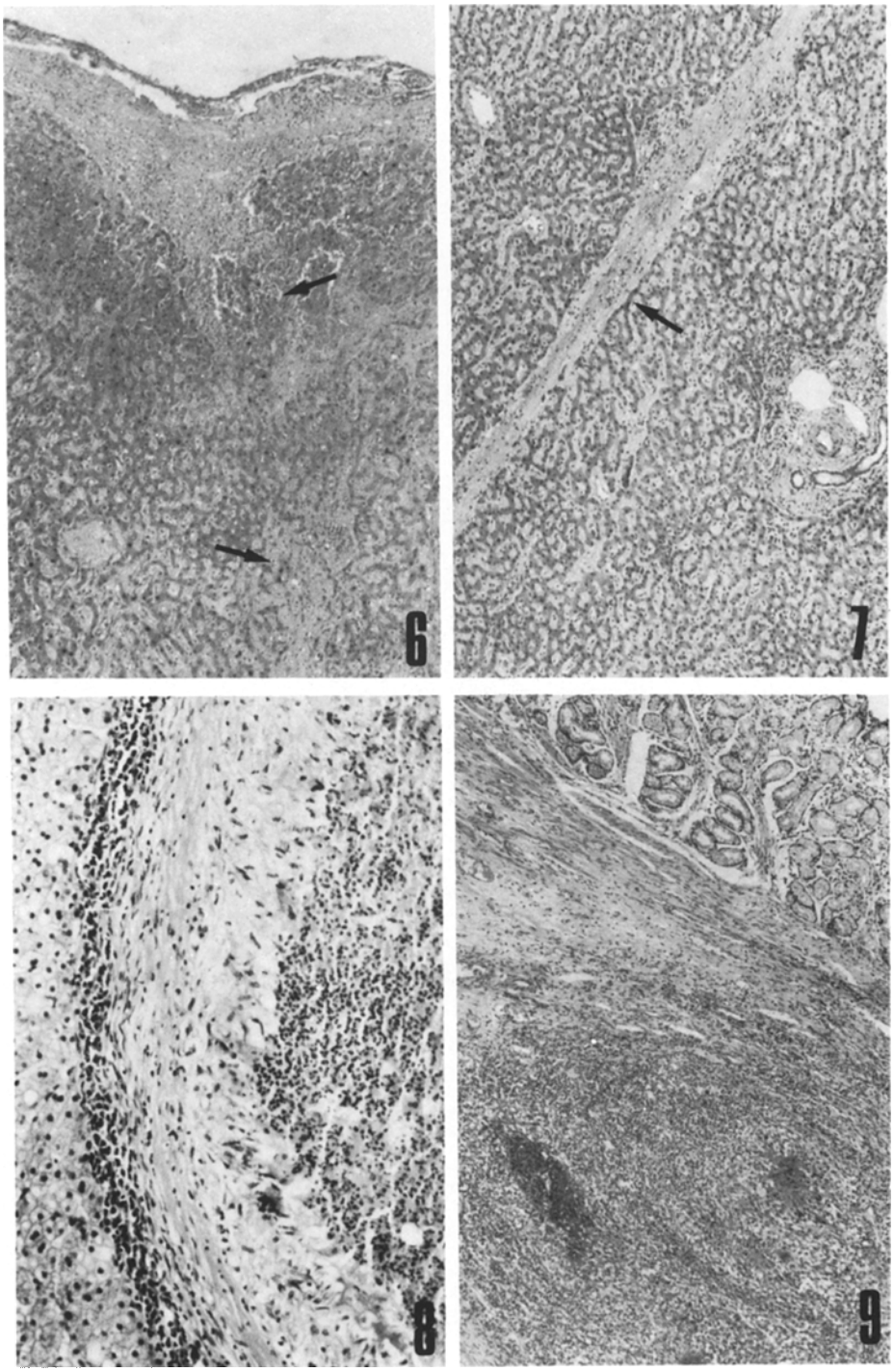

Fig. 6. Surface wound of the liver with a fibrino-purulent exudate covering it. Arrows show the commencement of the migratory track. H & E. ×100

Fig. 7. Long migratory track (*arrow*) crossing through several hepatic lobules. H & E. ×100

Fig. 8. The wall of a cavity with necrotic centre and nuclear debris; some multinucleated giant cells and a collection of lymphocytes are observed at its periphery. H & E. ×250

Fig. 9. Migratory tracks in the pyloric zone of the stomach. H & E. ×100

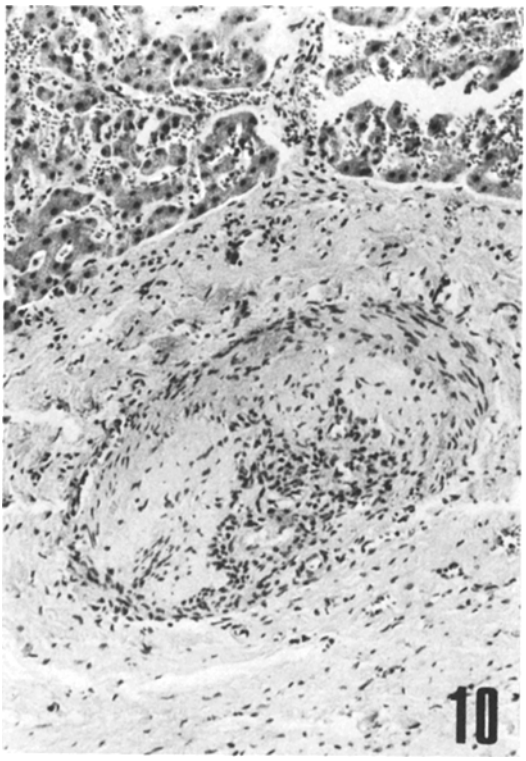

Fig. 10. Arterial wall in a portal space. Recanalised thrombus with residual lymphocytic exudate. H & E. ×250

some cases fused with the walls of the cavities. The portal tracts showed bile duct proliferation, fibrinoid changes in the hepatic arteries and recanalised thrombi within these arteries and the portal veins (Fig. 10).

The gall bladder lesions presented as greyish-white, multiple, subserous nodules and there were adhesions of the gall bladder to adjacent structures. In 5 cases there was biliary lithiasis. The parasitic migration tracks presented the same microscopic features as those described above within the liver. The gastric lesions presented as yellowish-white subserosal nodules 3–5 mms in diameter. Microscopically they showed the same features already described for the liver lesions (Fig. 9).

Discussion

Fasciola hepatica is the only parasite causing distomatosis in Uruguay (Geninazzi, 1978). Ingestion of the metacercariae is followed by their penetration of the intestinal wall and subsequent migration across the peritoneal cavity and they then most frequently enter the peritoneal surface of the liver and penetrate into its substance (Faust et al., 1970).

Multiple nodules on the surface of the liver are the most common macroscopic lesions (Sagar, 1962; Nicholas, 1970). The microscopic changes may

be of a specific or non-specific character. The presence of an identifiable parasite or parasitic remains confirms the diagnosis but was present only in one case in the present series. Foreign body granulomas containing rounded eosinophilic structures considered to be eggs of the fluke were seen in two cases (liver and gall bladder) and have been described by Cassinelli (1965) and Jones et al. (1977).

Histological identification of parasitic remains in the lesions though almost diagnostic is uncommon. More commonly parasite migration tracks are found in the liver and other organs. The tracks extend from the liver capsule and often terminate in subcapsular cavities filled with necrotic material, and such lesions were found in the livers studied in the present series. The walls of the cavities often contain Charcot-Leyden crystals, eosinophils and may show multiple calcific foci but contain very few giant cells. The migration of the parasite within the liver is considered to take place in two phases, first a migratory phase and a second in which it localises. This has been shown to occur in animals (Dow et al., 1968). Only specimens of liver obtained by surgery show lesions resulting from both phases. Liver needle biopsy specimens only show such non-specific features as eosinophil infiltration and the presence of Charcot-Leyden crystals both of which though suggestive are not diagnostic (Schusselé and Laperrouza, 1971).

Although multiple lesions were found on the surfaces of the livers, in only 5 cases were adult flukes identified i.e. in 31.25%. The majority of immature migrating flukes become trapped in the immediate subcapsular tissues where they die leaving a cavity filled with necrotic debris. Similar changes were described by Ross et al. (1967) who regarded such lesions as evidence of resistance by the host to the infection.

Parasitic tracks within the liver may be of the acute and chronic types as in animals (Rahko, 1969) with some intermediate stages. The chronic granulomatous lesions consist of necrotic hypereosinophilic debris surrounded by a palisade of macrophage cells. Eosinophils are numerous but both lymphocytes and giant cells are scanty and the lesions bear no resemblance to those found in tuberculosis or sarcoidosis. Extra-hepatic localisation of flukes has been reported (Neghme and Ossandon, 1943) and in 5 of the present series invasion of the stomach and gall bladder had occurred, and in two eggs were observed in the granulomas. Granulomatous lesions in the stomach due to *Fasciola hepatica* can be distinguished from lesions caused by allergic granulomatosis (Ming, 1973) by the absence of migration tracks in the latter.

Necrotising vasculitis affecting arterial vessels and thrombosis of veins were found in most cases and similar lesions have been found in animals which have been attributed to mechanical and toxoallergic mechanisms (Dow et al., 1967). The latter may be due to antigens of parasitic origin (Alarcón-Segovia, 1977).

Hyperplasia of the biliary duct epithelium is frequently seen and may result from the high proline excretion by the parasite (Isseroff, 1977). Other associated lesions include gall bladder lithiasis (Faiguenbaum, 1958; Roux et al., 1973) which was present in five of the present series. In 2 cases with gastric involvement peptic ulcers were found, but no cirrhotic or neoplastic changes were en-

countered. Other parasitic diseases including hydatid disease may be present in the liver in regions where there is a high incidence in the population.

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