Rev. Inst. Med. trop. São Paulo
32 (2): 91-95, março-abril, 1990

HEPATOBILIARY ALTERATIONS IN MASSIVE BILIARY ASCARIASIS. HISTOPATHOLOGICAL ASPECTS OF AN AUTOPSY CASE

Luiz Carlos da Costa GAYOTTO (1), Regina Maria Leitão MUSZKAT (2) & Irene Vieira SOUZA (3)

SUMMARY

Hepatobiliary alterations found in an autopsy case of massive Biliary Ascariasis, are reported on histological grounds. Severe cholangitis was the main finding, but other changes were also detected, such as pyloric and intestinal metaplasia, hyperplasia of the epithelial lining, with intraductal papillomas and adenomatous proliferation. Remnants of the worm were observed tightly adhered to the epithelium, forming microscopic intrahepatic calculi. Mucopolysaccharides, especially acid, showed to be strongly positive on the luminal border, and in proliferated glands around the ducts.

The authors discuss the similarity between such findings and Oriental Cholangiohepatitis, and suggest that inflammation and the presence of the parasitic remnants are responsible for the hyperplastic and metaplastic changes, similarly with what occurs in chlonorchiasis, fascioliasis and schistosomiasis.

KEY WORDS: Ascariasis, Recurrent Pyogenic Cholangitis; Bile Ducts; Helminthic Infection.

INTRODUCTION

Ascariasis is a helminthic infection of the small bowell caused by a roundworm **Ascaris lumbricoides**, whose distribution is worldwide, but more frequent in tropical countries. It is estimated that one in four inhabitants of our planet is infected, mainly during childhood and in rural areas[2].

Ascaris lumbricoides can be a major aetiologic factor of biliary and pancreatic disease, as it has been demonstrated prospectively in Índia[9]. Obstruction of the biliary tree by adult worms can lead to cholangitis, liver abscess and formation of calculi around remnants of the body of the helminth.

The penetration of the biliary tree can be asymptomatic and when present, the symptoms vary depending upon the number of migrated parasites. After reaching the common duct, the worms can go further to thinner branches of the biliary tree, pervade the liver parenchyma, perforate the Glisson's capsule, and get into the subdiaphragmatic space.

(1) Divisão de Anatomia Patológica do Hospital das Clínicas, e Departamento de Patologia da Faculdade de Medicina da Universidade de São Paulo.
(2) Unidade de Fígado da Faculdade de Medicina da Universidade de São Paulo.
(3) Departamento de Patologia do Centro de Ciências da Saúde da Universidade Federal de Santa Catarina.
Address for correspondence: Prof. Dr. Luiz Carlos da Costa Gayotto. Departamento de Patologia, Faculdade de Medicina da Universidade de São Paulo. Av. Dr. Arnaldo, 455. CEP 01246 São Paulo, SP, Brasil.

The macroscopic lesions include enlargement of the liver, mainly of the portal tracts, thickeness of the common duct and irregular dilatation of the branches of the biliary tree.

When the worm is trapped in the intrahepatic bile ducts, desintegration of its body and release of a large amount of eggs, can produce cholangitis, pylephlebitis and erosion of the surrounding parenchyma that can lead to hepatic abscesses with rests of bodies of the worms or their ova. In the pus aspirated from liver abscesses, **E. coli** can often be grown.

A granulomatous response to the dead worms or the eggs sometimes can be seen[11]. Although it is widely accepted that maturation of the eggs occurs only after they leave the body, segmented ova are seen within the granulomata.

To our knowledge, the microscopic aspects of the liver and the biliary tree in cholangitis due to biliary ascariasis (BA) has not deserved detailed attention from pathologists.

This study aims at analysing the histopathological and histochemical aspects of hepatobiliary alterations found in an autopsy case of massive BA.

CASE REPORT

A 47 years old caucasian female from Florianópolis, Santa Catarina, Brazil, was found dead without any report of previous illness. There was no jaundice or any other relevant autopsy findings, besides pulmonary oedema and liver alterations. Macroscopically the liver was enlarged and budding in the outer surface, liver abscess were seen, as well as several adult **Ascaris** perforating the liver capsule. The cut surface confirmed these aspects, and showed dilatation of the biliary tree and irregulary distributed fibrous scars (Figure 1). Within the dilated ducts and abscesses, bodies of adult **Ascaris** or their remnants could be found (Figure 2).

Microscopically, all portal tracts, even in the absence of the worm, showed oedema, marginal bile duct proliferation, and a mixed inflammatory infiltrate composed mainly of polimorphonuclear neutrophils, that pervaded the epithelial lining of bile ducts and occasionally clumped within their lumina.

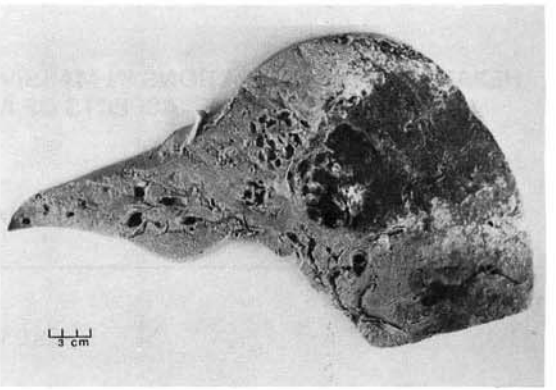

Fig. 1 — Cut surface of the liver: the bile ducts are dilated and several confluent abscesses are seen at the centre of the picture.

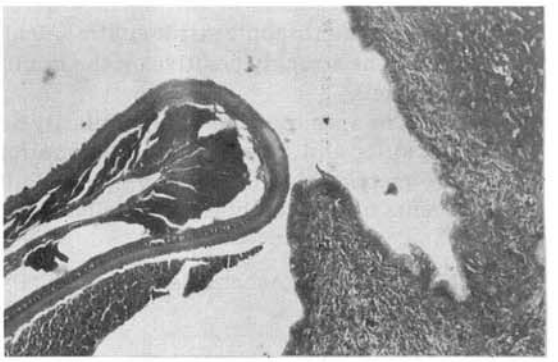

Fig. 2 — In a large duct a fragment of the body of the worm is seen partially surrounded by pus and close to a intraductal papilloma (HE, 40X).

In portal tracts with severe duct damage and dense scarring, the mononuclear component predominated, and occasionally lymphoid folicles were seen.

Bile ducts, irrespective of their size, showed marked periductal fibrosis but the most outstanding features involved the biliary epithelium, that showed areas of atrophy and ulceration, alternating with pronounced hyperplasia. These aspects included intense pseudoestratification, with an occasional adenomatous pattern, numerous mitoses and formation of intraduct papillomas (Figures 2 and 3). In larger bile ducts, fragments of dead worms could be clearly identified, whereas amorphous rests were found adhered to the epithelial lining of ducts of various sizes including interlobular bile ducts (Figure 4). In dilated septal and segmental bile ducts, there

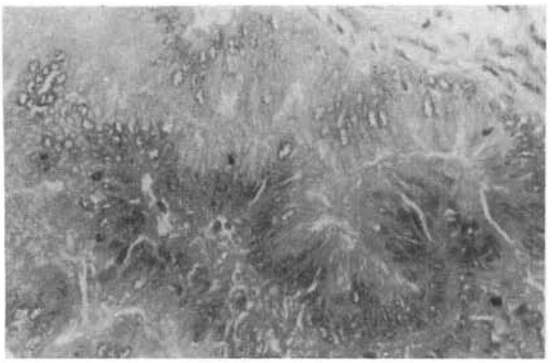

Fig. 3 — In a damaged bile duct the epithelium undergoes an adenomatous hyperplasia. Several mitotic figures are seen. (HE, 400X).

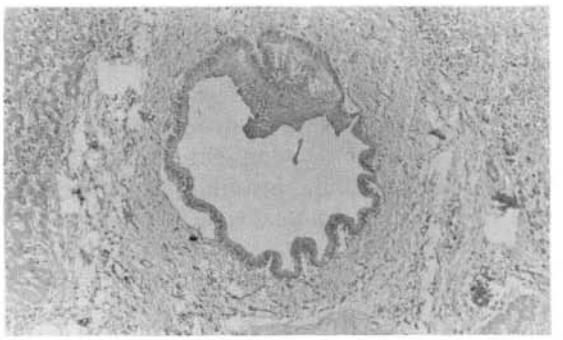

Fig. 4 — Remnants of a dead worm mixed with cellular debris are tightly attached to the hyperplastic epithelial lining. The portal tract shows inflammation and severe erosion of the limiting plate. (HE, 40X).

was pyloric and intestinal metaplasia, and also epithelial budding with formation of sattelite glands (Figure 5). Histochemical procedures showed strong production of mucin, mainly acid, within the lumen, along the luminal border of the epithelium, in vacuoles of goblet cells, and a weaker reaction around remnants of the worm (Figure 6).

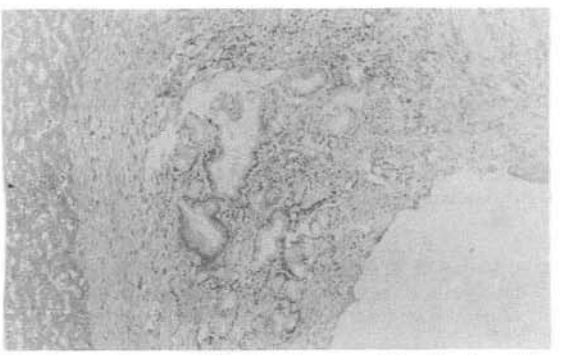

Fig. 5 — A damaged bile duct is seen with widening of its lumen, ulceration of the epithelium line, pyloric metaplasia and epithelial budding with surrounding glandular proliferation. (HE, 40X).

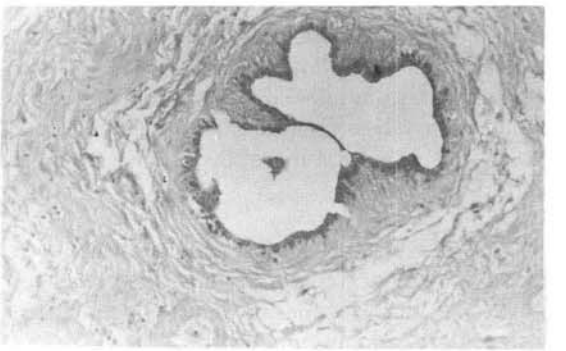

Fig. 6 — In the luminal border the secretion of acid mucopolysaccharides is increased. There are a few goblet cells (PAS diastase/alcian blue, 100X).

The hepatic artery branches showed arterioloesclerosis and there was pylephlebitis near the abscesses and in the neighbourhood of severely damaged bile ducts. In these areas, the limiting plate was eroded and liver cells trapped by the mesenchymal proliferation that raised from expanded portal tracts.

DISCUSSION

The absence of cholestasis in this case of severe biliary ascariasis and cholangitis is in keeping with other reports in literature, in which jaundice is reported in less than 20% of the cases[4, 8]. Jaundice appears usually when there are intrahepatic stones and especially when calculi are formed around the remnants of the worm.

In a series of 15 patients with intrahepatic stones described in South Africa, in 14 the cause of the calculi was probably **Ascaris lumbricoides**[12].

The histopathological features in biliary ascariasis are similar to those of oriental cholangiohepatitis (OCH), a form of recurrent pyogenic cholangitis described in the Far East. This is the most common cause of surgical emergencies in Asia and its precise aetiology is unknown.

Besides the histological picture, biliary ascariasis and oriental cholangiohepatitis have in common, the predominance of patients up to

the third decade of life, the incidence in a low socioeconomic class and intrahepatic calculi, often without gallbladder involvement[15].

Although of unclear aetiology, oriental cholangiohepatitis is, especially in Taiwan, often associated with infection by **Chlonorchis sinensis**, whose deleterious effect on the lining epithelium of the biliary tree include adenomatous hyperplasia and intestinal metaplasia, both found in the present case[16].

The presence of ova of **Ascaris** and/or remnants of degenerated worms has been reported by TEOH[13] in the stones of 16 out of 42 patients with oriental cholangiohepatitis.

Although no stones were identified at macroscopy, several PAS diastase/alcian blue positive concretions were found adhered to the epithelial lining and around fragments of dead worms, forming what seems to be microscopic counterparts of intrahepatic calculi (Figure 4).

Parasites such as **C. sinensis** and **F. hepatica** can produce severe alterations in the biliary tree involving the epithelial lining with subsequent appearance of proliferated glandular spaces around the ducts. They live, as **A. lumbricoides** in biliary ascariasis, within the biliary lumen and the damage caused to bile ducts can be attributed to substances produced by the living parasites or by products of degradation of dead bodies[1, 3, 6].

Recently, similar alterations had been reported in mansonic schistosomiasis where the worm, not living within the biliary tree, would produce biliary damage through the dissemination of products of the parasites through the intrahepatic peribiliary vascular plexus[14]. It is likely that in biliary ascariasis the first mechanism predominates but the pathogenic role of products released by dead worms or eggs in the interstitium should be also considered.

Finally, adenomatous hyperplasia of the biliary epithelium, as well as intestinal metaplasia and mucous gland hyperplasia are regarded by some[7, 10] as pre-neoplastic conditions. The development of cholangiocarcinoma in humans and experimental animals infected by various species of **Chlonorchis** in Asia and Europe[5] supports these assumptions. Such alterations are found also in biliary ascariasis, in which bile duct neoplasia has not been described so far. It can be speculated however that in longstanding untreated cases of massive biliary ascariasis, this tumour could eventually arise or if in areas of high prevalence of the infection, biliary ascariasis would represent an aetiologic step towards the cancer of the biliary tree.

RESUMO

Lesões hepatobiliares em ascaridíase biliar maciça. Aspectos histopatológicos em um caso de autópsia.

Os autores apresentam os aspectos histopatológicos encontrados no fígado de um caso de autópsia de Ascaridíase Biliar maciça. A intensa colangite foi o aspecto predominante, mas outras lesões também foram encontradas, tais como metaplasia pilórica e intestinal, hiperplasia epitelial com papilomas intraductais, e por vezes padrão adenomatoso. Restos do helminto foram encontrados fortemente aderidos ao epitélio, sendo intensa a positividade de mucopolissacárides, principalmente ácidos, na borda luminal do epitélio ductal e em glândulas proliferadas ao redor dos ductos.

Os autores discutem a semelhança da Ascaridíase Biliar com a Colangio Hepatite Oriental, e sugerem que o processo inflamatório e a presença de restos do verme são responsáveis pelas alterações hiperplásicas e metaplásicas, analogamente ao que ocorre na clonorquíase, fasciolíase e esquistossomose.

REFERENCES

1. ACOSTA-FERREIRA, W.; VERCELLI RELTA, J. & FALCONI, L. M. — **Fasciola hepatica** human infection. Histopathological study of sixteen cases. **Virchows Arch, Abt. A. path. Anat., 383:** 319-327, 1979.

2. BENENSON, A. S. — **El control de las enfermedades transmisibles en el hombre.** Washington, PAHO; WHO, 1983.

3. CHOU, S. T. & GIBSON, J. B. — The histochemistry of biliary mucins and the changes caused by infestation with clonorchis sinensis. **J. Path., 101:** 185-197, 1970.

4. DEMERAU, E. F. — **Tratamento da ascaridíase das vias biliares: contribuição ao seu estudo.** Santa Catarina, 1974. (Tese de Livre Docência — Universidade Federal de Santa Catarina).

5. EVANS, H.; BURGEOIS, C. H.; COMER, D. S. & KESCHAMARAS, N. — Biliary changes in opisthorchiasis. **Amer. J. trop. Med. Hyg., 20:** 667-671, 1971.

6. HOU, P. C. — The pathology of **Chlonorchis sinensis** infestation of the liver. **J. Path. Bact., 70:** 53-64, 1955.

7. HOU, P. C. — The relationship between primary carcinoma of the liver and infestation with **Chlonorchis sinensis. J. Path. Bact., 72:** 239-246, 1956.

8. HSU, F. H. — Clinical observation on 110 cases of Ascaris invasion into the biliary tract. **Nagoya J. med. Sci., 24:** 215-233, 1962.

9. KHUROO, M. S. & ZARGAR, S. A. — Biliary Ascariasis. A common cause of biliary and pancreatic disease in an endemic area. **Gastroenterology, 88:** 418-423, 1985.

10. KOSUKA, S.; KURASHIVA, M.; TSUTONE, M.; HACHISUKA, K. & YASUI, A. — Significance of intestinal metaplasia for the evolution of cancer in the biliary tract. **Cancer, 54:** 2277-2285, 1984.

11. MARCIAL, M. A. & MARCIAL-ROJAS, R. A. — Parasitic diseases of the liver. In: SCHIFF, L. & SCHIFF, E. R., ed. **Diseases of the liver.** Philadelphia, J. B. Lippincott, 1987. p. 1171-1196.

12. SCHULMAN, A. — Non-western patterns of biliary stones and the role of Ascariasis. **Radiology, 162:** 425-430, 1987.

13. TEOH, T. B. — A study of gall-stones and included worms in recurrent pyogenic cholangitis. **J. Path. Bact., 86:** 123-130, 1963.

14. VIANNA, M. R.; GAYOTTO, L. C. G.; SANTOS, R. T. M.; ALVES, V. A. F.; FUKUSHIMA, J. & BRITO, T. de — Intrahepatic bile duct changes in human hepatosplenic schistosomiasis mansoni. **Liver, 9:** 100-109, 1989.

15. WEN, C. & LEE, H. — Intrahepatic stones: a clinical study. **Ann. Surg., 175:** 166-177, 1972.

16. YELLIN, A. G. & DONOVAN, A. — Biliary lithiasis and helminthiasis. **Amer. J. Surg., 142:** 128-136, 1981.

Recebido para publicação em 02/8/1989.