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Histopathological Study of Liver Lesions in Medicolegal Cases

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Abstract

Background: Autopsy study of liver aids in the knowledge of pathology by revealing lesions that were asymptomatic during life. Due to enormous functional reserve, many liver lesions are silent till late in the course of disease. Hence histopathological study of all liver specimens is necessary. *Material and methods:* The present study included 260 liver specimens from medicolegal autopsies received over a period of two years from August 2014 to July 2016. Thorough gross examination was done followed by microscopy. *Result:* The most common lesion was steatosis, accounting for 78 (30%) out of 260 liver specimens. There were 43 (16.5%) cases of congestion, 20 (7.8%) cases of hepatitis and 17 (6.5%) cases of steatohepatitis. Ten (4%) cases of cirrhosis were noted. Other lesions included microabscesses 7 (2.6%), granulomas 6 (2.3%), and one case (0.3%) each of bile duct hamartoma, sickle cell anemia, disseminated intravascular coagulation, extramedullary hematopoiesis, disseminated cryptococcosis and microfilarial infection. *Conclusion:* The present study showed that fatty change was the most common lesion encountered in liver specimens from medicolegal cases, followed by congestion and hepatitis. Hence histopathology of every liver specimen is must.

Keywords: Medicolegal autopsy; Fatty change; Cirrhosis.

Introduction

The liver is the largest organ of human body.[1] On the basis of blood flow, the functional hepatic acinus has three zones, peripheral zone one, perivenular zone three and intermediate zone two.[2] The hepatocytes perform numerous and vital functions like synthesis of serum proteins, production of bile, regulation of nutrients and metabolism of drugs.[1] Diseases affecting the liver are infectious diseases like viral hepatitis, tuberculosis, malaria, metabolic diseases like nonalcoholic fatty liver disease, Wilson, disease, cirrhosis and neoplasms. Cirrhosis is a progressive disease characterized histopathologically by diffuse fibrosis leading to formation of regenerative nodules. Etiologies of cirrhosis include alcoholism, chronic viral hepatitis, metabolic diseases, etc.

Primary benign neoplasms of liver include hemangioma, hepatic adenoma, hamartoma and others while primary malignant tumors include hepatocellular carcinoma, cholangiocarcinoma, angiosarcoma, hepatoblastoma, etc. Metastatic malignancy is more common than primary hepatic neoplasms. Common primary sources include colon, breast, lung and pancreas.[2] Hence a study was undertaken on liver specimens received from medicolegal autopsies to estimate the frequency and analyze the histopathological features of various liver diseases.

Materials and Methods

Total 294 liver specimens from medicolegal autopsies were received over a period of two years

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from August 2014 to July 2016. Thirty-four specimens were excluded on account of extensive autolysis. Hence the study included 260 cases. Tissue was fixed in 10% formalin. Representative tissue bits were submitted for paraffin embedding. Sections were routinely stained by hematoxyline and eosin. Special stains were used wherever necessary. Sections were studied under light microscope and findings of the examination were recorded and analyzed.

Results

The age ranged from less than 1 year to 90 years. As depicted in (Fig. 1), majority of the cases were seen in the age group 21–30 years (80 cases, i.e. 28.6%). Number of males was 168 (64.6%) much higher than females (92 cases, 35.4%) with male : female ratio of 1.8 : 1. Various lesions encountered in the study and their prevalence is presented in Table 1. The most common lesion was steatosis (fatty change) seen in 78 (30%) cases affecting 61 males and 17 females. All cases showed macrovesicular steatosis. History of alcohol consumption was available in 17 males. Congestion was seen in 43 (16.5%) cases affecting 23 males and 20 females. We had total 20 (7.8%) cases of hepatitis, including 13 cases of nonspecific reactive hepatitis, five cases of ischemic hepatitis and two cases of acute hepatitis. There were 17 (6.5%) cases of steatohepatitis characterized by ballooning degeneration of hepatocytes, pericellular

Table 1: Showing histopathological findings of liver and their prevalence

Histopathological findings	Cases	Percentage
Steatosis	78	30%
Congestion	43	16.5%
Hepatitis	20	7.8%
Acute hepatitis	2	0.7%
Ischaemic hepatitis	5	1.9%
Nonspecific reactive hepatitis	13	5.2%
Steatohepatitis	17	6.5%
Cirrhosis	10	4.0%
Microabscesses	7	2.6%
Hepatic granulomas	6	2.33%
DIC	1	0.33%
Disseminated cryptococcosis	1	0.33%
Disseminated microfilarial infection	1	0.33%
Bile duct hamartoama	1	0.33%
Sickle cell anaemia	1	0.33%
Extramedullary hematopoiesis	1	0.33%
No specific lesion	73	28.0%
Total	260	100

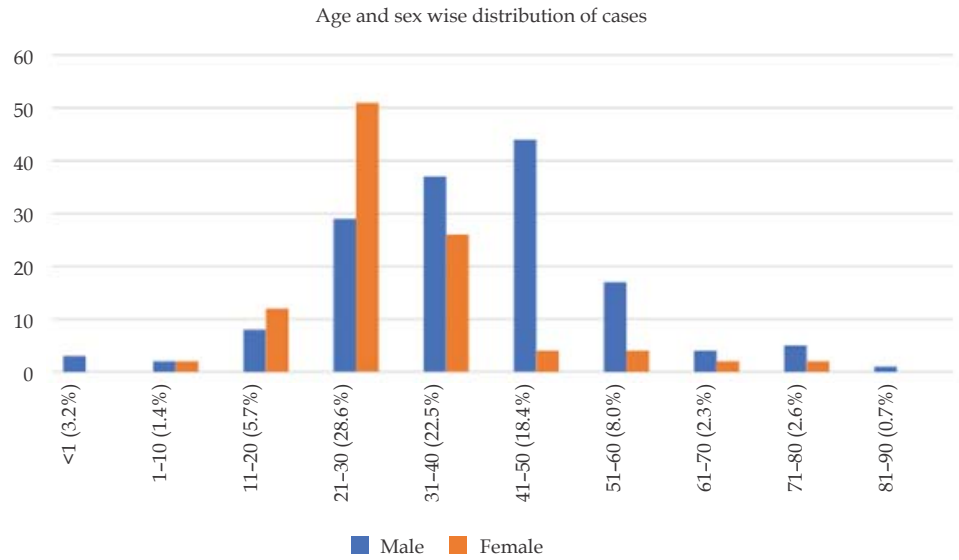

Fig. 1: Showing age and sex distribution of medicolegal cases in the present study.

polymorphonuclear infiltrate and chickenwire fibrosis. Only two males with steatohepatitis had history of chronic alcoholism. Ten (4%) cases of cirrhosis were seen affecting 7 males and 3 females. History of alcohol consumption was present in two males. We had 7 (2.6%) cases of microabscesses and 6 (2.33%) cases of hepatic granulomas. There was one case each of disseminated intravascular coagulation, disseminated cryptococcosis, microfilarial infection, bile duct hamartoma, sickle cell anemia and extramedullary hematopoiesis.

Discussion

Liver diseases are an important cause of morbidity and mortality in both developed and developing countries. The incidence as well as pattern of liver disease varies from one region to another depending on the various etiological factors. Thus, a study of liver specimens from medicolegal autopsies was undertaken to evaluate the prevalence and relative frequency of various types of liver diseases. Excluding 34 specimens with extensive autolysis, 260 specimens were included in the study.

Steatosis (Fatty change) refers to accumulation of triglycerides in the cytoplasm of hepatocytes. Microvesicular steatosis is characterized by very small, fine fat globules that do not displace the nucleus and is a result of mitochondrial injury [3] . In macrovesicular steatosis the nucleus is displaced to the periphery. The degree of fat accumulation is variable. In the present study, 78 out of 260 medicolegal cases showed macrovesicular fatty change. Comparison of our findings with other authors is shown in Table 2.

In the study done by Selvi et al., 29 out of 108 (26.9%) cases showed fatty liver. Alagarsamy et al. reported 10 out of 50 cases (20%) while Umesh reported 24 out of 105 (22.8%) cases of steatosis. Patel et al. observed 146 (35.69%) cases of steatosis out of total 450 cases. In the study conducted by Bal et al., steatosis was seen in 39 (46.9%) cases.[4–8]

Right sided cardiac decompensation leads to passive congestion of the liver. The liver is slightly enlarged, tense and cyanotic, with roughened edges.[9] Microscopically there is congestion of centrilobular sinusoids. In the present study 43 (16.5%) cases showed congestion. In the study done by Selvi et al., there were 18 out of 108 (16.7%) cases of congestion while Alagarsamy et al. observed congestion in 13 out of 50 cases (26%).[4,5]

We had total 20 cases of hepatitis, including 13 cases of nonspecific reactive hepatitis, five cases of ischaemic hepatitis and two cases of acute hepatitis. In nonspecific reactive hepatitis there is no uniform zonal distribution of the parenchymal changes and only some portal tracts are involved. The involved portal tracts contain variable chronic inflammatory cell infiltrate with predominance of lymphocytes. The limiting plate is intact. Parenchymal changes include foci of liver cell necrosis, which may involve only few hepatocytes or several liver cell plates. Surrounding these foci, there is accumulation of lymphocytes and macrophages.[10] We had 13 cases of nonspecific reactive hepatitis.

Ischemic hepatitis or shock liver is a manifestation of liver injury due to reduced blood flow. It is seen in acute myocardial infarction, circulatory shock due to sepsis, burns, severe trauma, vascular obstruction and other causes. We observed five cases of ischemic hepatitis characterized histologically by coagulative hepatocytic necrosis and marked perivenular sinusoidal congestion (Fig. 2.).

Table 2: Showing the comparison of liver diseases by various authors.

Pathology	R.Thamil Selvi et al.[4] (2011)	Alagarsamy J et al.[5] (2012)	Umesh BR et al.[6] (2015)	Patel PR et al.[7] (2016)	Present Study (2016)
Total cases	108	50	105	450	260
Fatty change	29 (26.9)	10 (20%)	24 (22.8%)	146 (35.69)	78 (30.0%)
Congestion	18 (16.7%)	13 (26%)	10 (9.52%)	5 (1.22%)	43(16.5%)
Hepatitis Nonspecific reactive Ischaemic Acute	15 (13.9%)	5 (10%)	22 (20.9%)	4 (0.98)	20 (7.8%)
Steatohepatitis	–	–	37 (32.2%)	–	17 (6.5%)
Cirrhosis	8 (7.4%)	8 (16%)	2 (1.9%)	10 (2.44%)	10 (4.0%)
Microabscesses	8 (7.4%)	–	–	–	7 (2.6%)
Hepatic granulomas	–	–	4 (3.8%)	2 (0.49%)	6 (2.3%)
Others	–	–	–	–	6 (2.3%)
No specific lesion	28 (25.9%)	3 (6%)	5 (4.76%)	233 (56.97%)	73 (28.0%)

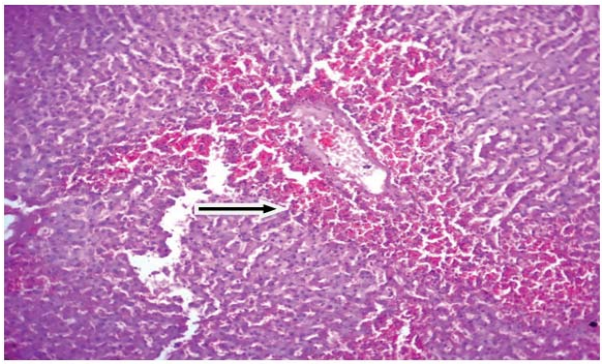

Fig. 2: Photomicrograph showing ischaemic hepatitis with centrilobular hemorrhagic necrosis of liver (H &E, x100)

Acute hepatitis is an inflammation of liver caused by infectious agents including hepatotropic viruses, certain medications or autoimmune etiology. We had two cases of acute hepatitis showing lobular disarray, ballooning of hepatocytes and mononuclear cell infiltrate in portal tracts and periportal parenchyma.[3] Prevalence of hepatitis in various studies ranged from 0.98% to 20.9%.[4–7] Selvi et al. reported 15 out of 108 (13.9%) cases, Algarsamy et al. reported 5 out of 50 (10%) cases, Umesh reported 22 out of 105 (20.9%) cases and Patel PR et al. reported only 4 (0.98%) out of 450 cases of hepatitis.

The essential features of steatohepatitis, i.e. ballooning degeneration of hepatocytes, inflammatory infiltrate and pericellular fibrosis were seen in 17 (6.5%) cases. Mallory–Denk bodies were however not seen in any of the cases. Common causes of steatohepatitis are alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD).[3,10] There is a significant difference in the prevalence of steatohepatitis in different studies. Selvi et al., Alagarsamy et al. and Patel et al. did not come across a single case of steatohepatitis in their study.[4,5,7] In the present study 17 (6.5%) cases of steatohepatitis were observed, while Umesh BR et al. reported steatohepatitis in 37 (32.2%) out of 105 cases.

Liver cirrhosis is a common end-stage liver disease characterized by diffuse hepatic fibrosis with replacement of normal lobular architecture by parenchymal nodules separated by bands of fibrous tissue. Morphologically liver cirrhosis is classified as Micronodular cirrhosis (nodules less than 3 mm), Macronodular cirrhosis (nodules more than 3 mm) and mixed cirrhosis.[3,11,10] In our study 10 cases of cirrhosis were observed out of which 7 were males and 3 were females. History of alcohol consumption was present in 2 males showing mixed nodular cirrhosis. Remaining eight cases showed micronodular cirrhosis. However no specific cause could be identified in these cases. Selvi et al. and Algarsamy et al. observed cirrhosis in 8 cases each accounting for (7.4%) and (16%) cases respectively.[4,5] Umesh et al. reported 2 out of total 105 (1.9%) cases and Patel et al reported 10 out of 450 (2.2%) cases of cirrhosis.[4–7]

A multitude of organisms can infect the liver and biliary tree including bacteria, fungi, helminths and protozoa. In many cases of pyemic abscesses, the origin of the infection is not obvious.[10] We had 7 cases of microabscesses affecting one male and six females. There were multiple scattered 1–2 cm sized microabscesses in the liver along with mild to moderate cholestasis.All the females were postpartum with evidence of acute deciduitis and myometritis along with microabscesses in the spleen, kidney and lung in addition to liver suggesting puerperal sepsis. The single male patient had bronchopneumonia with microabscesses in liver, spleen and heart indicating sepsis. Selvi et al. observed microabscesses in 8 out of 108 cases (7.4%)[4]. Other studies have not reported microabscesses.

Hepatic granulomas may occur secondary to infections like tuberculosis or fungal infections, drugs, foreign bodies or immunologic, neoplastic and idiopathic causes.[12] We had 6 (2.3%) cases of hepatic granulomas. Microscopy showed numerous randomly distributed granulomas composed of occasional Langhan's type giant cells, epithelioid cells and lymphocytes. In 3 cases there was central caseous necrosis indicating tuberculosis as the most likely cause (Fig. 3).

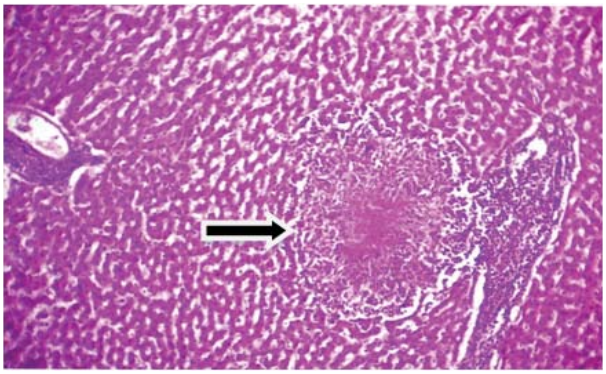

Fig. 3: Photomicrograph showing hepatic granuloma with central caseation suggestive of tuberculosis (H &E, x100)

However Ziehl Neelsen staining was negative for acid–fast bacilli. Liver may be involved in primary or reactivation tuberculosis, either alone or as a part of multiorgan involvement.[13] In remaining 3 cases definite cause of granuloma could not be identified. Patel et al. reported 2 cases of granulomas out of

total 450 cases (0.49%), while Umesh et al. observed 4 cases of granuloma out of 105 cases (3.8%).[6,7]

DIC is an acute, subacute or chronic thrombohemorrhagic disorder characterized by excessive activation of coagulation, which leads to the formation of thrombi in the microvasculature of the body. DIC is not a primary disease but occurs as a secondary complication of a variety of disorders such as septicemia, allergic reactions, liver cirrhosis, acute fatty liver, vasculitis, polytrauma, aortic aneurysm and obstetric complications.[2] In our study, we had a single case of DIC affecting a 25-year-old primigravida with history of nine months amenorrhea. Patient was admitted with shock, severe hypotension, and thrombocytopenia following cesarean section. Grossly, the external surface and cut surface of liver showed few blackish areas. On microscopy, there was subcapsular hemorrhage along with sinusoidal fibrin deposition in periportal areas. Capillary thrombi were seen in the lungs and kidney. Microhemorrhages were evident in the epicardium, myocardium and lung, features suggestive of DIC.

We came across a single case of disseminated cryptococcosis in a 42-year-old HIV positive male. Cryptococcosis more frequently presents as an opportunistic infection in immunocompromised people.[13,11] Grossly, the external and cut surface of liver was unremarkable. Microscopically, sections showed disseminated cryptococcal infection involving liver (Fig. 4.) and other organs like meninges, lung, spleen and kidney.

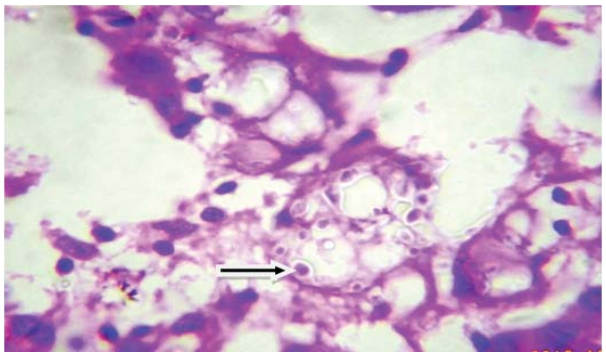

Fig. 4: Photomicrograph showing yeast forms of cryptococcus (H &E, x1000)

Nematode *W. Bancrofti* is a cause of lymphatic filariasis in tropics and subtropics. It is an adult worm which inhabits the lymphatics and produces lymphangitis and lymphadenitis. The best known clinical manifestation is tropical pulmonary eosinophilia.[11] We had a rare case of disseminated microfilarial infection. Patient was a 30-year-unknown male. Hence detailed history was not available. Grossly, all the organs were unremarkable. Microscopically, there were eosinophilic microabscesses and fibrin- rich inflammatory exudate containing microfilariae in the liver, spleen and kidneys.

Bile duct hamartomas also known as Von Meyenberg complexes or biliary microhamartomas are multiple biliary channels lined by bile duct epithelium set in a dense fibrous stroma. The lumen often contains inspissated bile. They are usually found incidentally and do not give rise to symptoms or abnormalities of liver function[3,13]. In the present study, we found a single case of biliary microhamartoma incidentally in a 70-years-old male (Fig. 5).

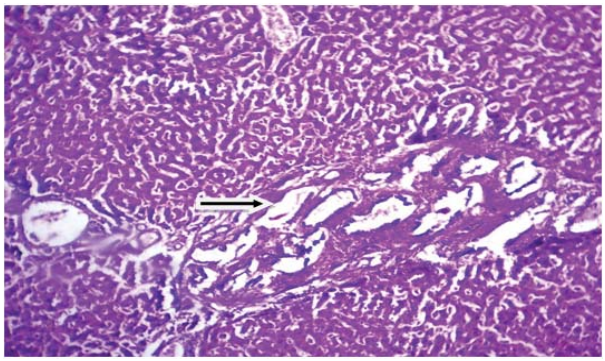

Fig. 5: Photomicrograph showing biliary microhamartoma of liver (H &E, x100)

We encountered a single case of sickle cell anemia in a 25-year-old pregnant lady with 32–33 week gestation with eclampsia and severely deranged liver function tests. Patient delivered a fresh still born female baby and died on the next day. Grossly, liver was dark brown to blackish in appearance. Microscopically, blood vessels of all organs as well as liver sinusoids revealed sickled RBCs.

Extramedullary hematopoiesis refers to hematopoiesis that occurs in organs other than bone marrow. Normal erythropoiesis occurs in fetal yolk sac, liver and spleen. We came across a single case of extramedullary hematopoiesis in the liver in a 3-day-old neonate.

Conclusion

Autopsy based studies are useful in estimating the prevalence of liver diseases which are often asymptomatic till late in the course of disease. Histopathological study of liver specimens enables to diagnose primary liver diseases like hepatitis,

steatohepatitis and cirrhosis as well as systemic diseases like DIC. Macrovesicular steatosis was the most frequently encountered lesion in this study.

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