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Original Article

Evaluation of Liver Biopsy in Pediatric Age Group Upto 12 Years

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Abstract

Paediatric Pathology has always been a challenge: an attractive and at the same time a menace for all the pathologists. Hepatomegaly is a common mode of presentation of disorders specific to childhood and common systemic diseases. Liver biopsies remains the procedure of choice for many hepatic disorders for both primary diagnosis and monitoring of the disease. In this study, aim was to document the patterns of liver disease in paediatric age group and study the role of histopathologist in identifying hepatic diseases in children.

Keywords: Hepatomegaly; Cell hepatitis; Tyrosinemia; Hepatobiliary disorders; Cholestasis.

Introduction

Pediatric pathology has always been a challenge: an attractive and at the same time a menace for most pathologists it all depends in that whatever appears on the pathologist microscope may never have been seen by anyone before. In liver disease, new paediatric entities regularly appear. Liver biopsy remains the procedure of choice for many hepatic disorders for both primary diagnosis and monitoring of disease. In paediatric age group, the liver biopsy is generally prompted by the presence of a discrete mass or hepatomegaly, cholestasis, abnormal serum transaminase levels, a concern that a metabolic disorder may be present, or concern that infection may be present. These categories may overlap. These require prompt recognition, quick investigational processes and targeted management. Estimation of the probable cause for neonatal cholestasis is also important from the perspective of prognosis.

In this study, we have endeavoured to document the pattern of liver diseases in paediatric age group as seen in liver biopsy and to study the role of histopathology in identifying hepatic diseases in children.

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Materials and Methods

The study material is a combination of an analysis of eight years of retrospective material and 2 years of prospective material undertaken at Department of Pathology, MSRMC, Bangalore.

Results

The study included 100 cases of liver biopsy samples. The commonest presentation was Jaundice, Fever,

Hepatomegaly, Ascites. The commonest pathology encountered were cholestatic disorders of infancy and childhood, storage disorders, neoplasm and non specific changes. Amongst cholestatic disorders, the neonatal cholestatic syndrome, biliary atresia, choledochal cyst and intrahepatic paucity of bile ducts were seen. Wide spectrum of histopathology with idiopathic giant cell hepatitis, cytomegalovirus infection, congenital rubella infection, lysosomal storage disease, neonatal sepsis to tyrosinemia were seen.

Materials and Methods

This is a combination of an analysis of eight years retrospective material and two years prospective material undertaken at the Department of Pathology, MSRMC, Bangalore. All paediatric liver biopsies sent to the department of Pathology during the period (1992-2002) were included in this study on satisfying the inclusion/exclusion criteria. Sample size was 100 cases. Liver biopsies with less than 3 portal triads were excluded.

Results

The present study deals with the evaluation of liver biopsies in the paediatric age group (upto 12 years). Salient observations made in this study are as follows.

Table 1: The following is the age distribution of the pts.

Age	No. of cases (n=100)
Neonates(0-28D)	8
Infants (28D-1 yr)	56
1 yr- 4 yr	18
>4 yr-8 yr	9
>8 yr-12 yr	9

Table 2: The following is the sex distribution of the patients.

Sex	No. of cases	%
Male	56	56
Female	44	44

Table 3: The clinical presentation of the cases was as follows.

Clinical features	No. of cases (n=100)
Jaundice	65
Fever	59
Hepatomegaly	92
Ascites	13
Vitamin A deficiency	10
Altered sensorium	4

Table 4: The following were the main indications of liver biopsy.

Indications	No. of cases
Jaundice for evaluation	23
Hepatomegaly for evaluation	14
To determine the aetiology of a systemic disease. Ex -PUO, miliary TB	29
Primary liver parenchymal injury assessment in liver disease	35

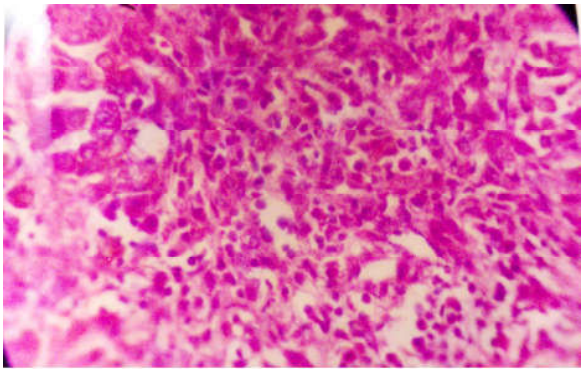

Fig. 1: Neonatal Hepatitis showing feathery degeneration and multinugiant cell transformation (H & E x 100).

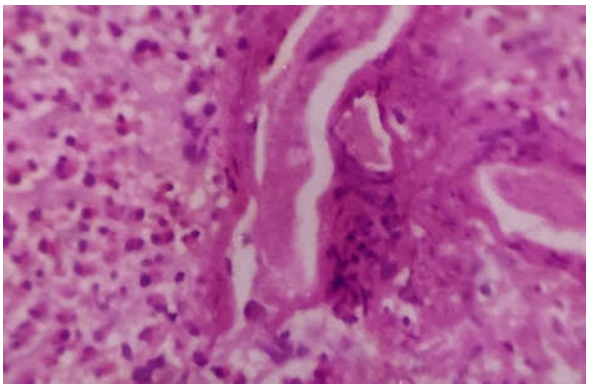

Fig. 2: Visceral larva migrans (H & E x 400).

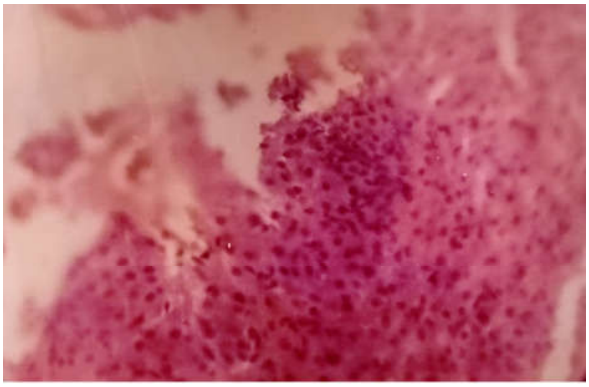

Fig. 3: Neonatal hepatitis showing lymphoid follicle formation (H & E).

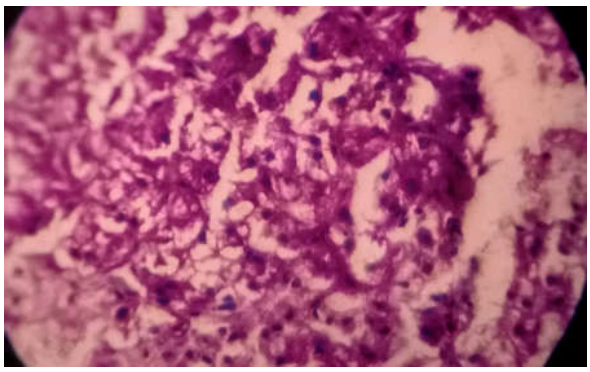

Fig. 4: Glycogen storage disease, hepatocytes showing PAs positivity (PAS x 400).

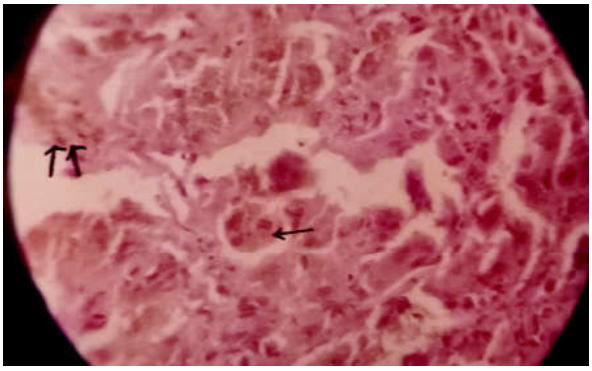

Fig. 5: Neonatal Cholestasis showing intracellular bile (←) and extra cellular bile (←←) (H & E x 400).

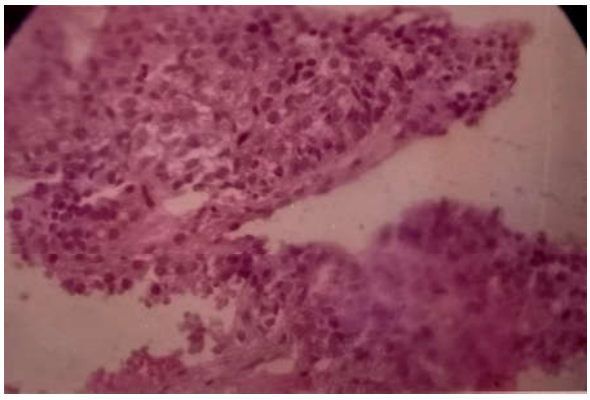

Fig. 6: Hepatoblastoma showing clusters of blastemal cells with nuclear pleomorphism and anisonucleosis (H & E x 100).

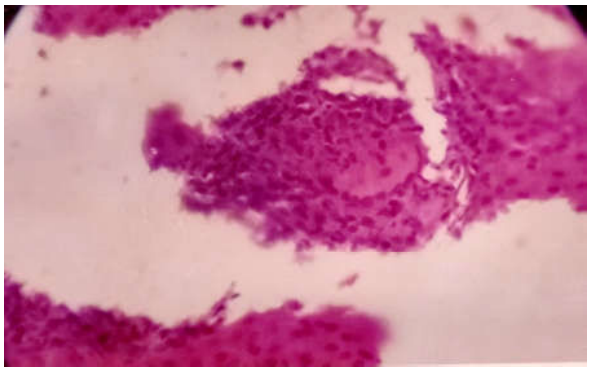

Fig. 7: Miliary tuberculosis showing granulomas (H & E x 100).

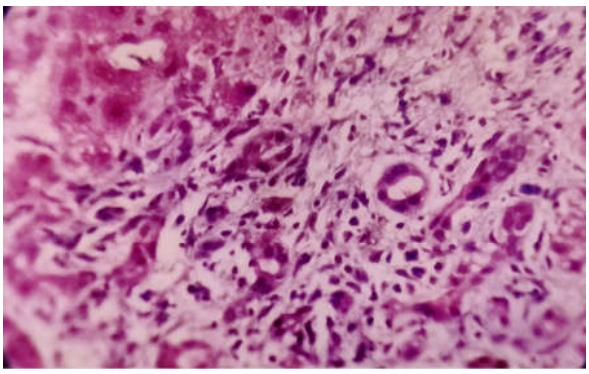

Fig. 8: Primary Biliary Cirrhosis showing bile duet proliferation (Masson's Trichome x 400).

Conclusion

Our study revealed neonatal cholestasis constitutes 47% of hepatobiliary disorders in pediatric age group in our hospital. Liver biopsy is highly accurate in differentiating EHBA and neonatal hepatitis. Persistence of neonatal jaundice beyond 2 weeks of age demands evaluation to differentiate 3 most common causes Hepatitis, Biliary atresia and choledochal cyst. Percutaneous liver biopsy is necessary to narrow down the differential diagnosis and to identify patients who require more invasive techniques. (Example-Intraoperative cholangiography).

Manuscript

Introduction

Cholestasis, an important manifestation of liver disease in infants, can be caused by wide spectrum of aetiological conditions. "Neonatal cholestasis" or 'cholestasis of infancy' is defined as prolonged elevation of serum conjugated bilirubin levels in infants beyond his/her 14 days of life. It requires prompt recognition, quick investigation and targeted management. The clinical, biochemical features of the patients provide very few clues towards underlying aetiology. Economic restraints of our Indian patient make TORCH and Radio Isotope Scan beyond the reach of most patients. Hence, liver biopsy remains the most appropriate, feasible and essential tool in elaborate work up.

Table 4: The patients were classified into the following broad categories.

Etiology	No. of cases (n=100)
Cholestatic disorders of infancy and childhood.	64
Storage disorders	5
Neoplasm	1
Non-specific changes	24
Others	6

Table 5: The following cholestatic disorders of infancy and childhood were encountered during the study period.

Etiology	No. of cases(n=48)	Percentage
Neonatal cholestasis syndrome	29	60.41%
Biliary atresia	15	31.25%
Choledochal cyst	3	6.25%
Intrahepatic paucity of bile ducts	1	2.08%

Table 6: The following are the causes of neonatal hepatitis syndrome encountered.

Etiology	No. of cases(n=27)
Idiopathic giant cell hepatitis	19
Cytomegalovirus infection	1
Congenital Rubella Infection	1
Lysosomal storage disease	1
Neonatal sepsis	4
Tyrosinemia Type 1	1

Table 7: Within non-specific changes, the following distribution was seen.

Morphology	No. of cases(n=24)	Percentage
Fatty change	10	41.66%
Cloudy change	6	25%
Hydropic change	7	29.16%
Reactive	1	4.16%

Table 8: Within the miscellaneous or other group, the following cases were encountered.

Etiology	No. of cases(n=6)	Percentage
Visceral larva migrans	1	1
Congenital hepatic fibrosis	1	1
Inborn errors of metabolism	2	2
Miliary tuberculosis	1	1
REYE's syndrome	1	1

Discussion

Neonatal cholestasis constitutes 30% of hepatobiliary disorders in India. In our series of 46 patients with infantile cholestasis in which a broad categorization could be done, 58.6% had neonatal hepatitis syndrome, 32.6% had EHBA, 6.5% had Choledochal cysts, 2.17% had intrahepatic paucity of bile ducts. Liver biopsy was found the most important and valuable investigation for distinguishing between EHBA and NH.

Histologically, considerable overlapping of patterns from disorder to disorder was seen.

Table 9: Histopathological Patterns in Neonatal Cholestasis

Histological features	Giant cell hepatitis	EHBA	Choledochal cyst	Intrahepatic paucity of bile ducts
Number	27	15	3	1
Giant cell transformation	27	3	0	0
Bile duct proliferation	1	15	1	0
Bile duct loss	0	0	0	1
Inflammatary cell infiltration	24	13	3	1
Portal expansion	20	10	1	1
Fibrosis	22	8	2	0
Cholestasis within the biliary canaliculi	7	10	2	0

Neo proliferation of interlobular bile ducts was noted to be an important histological finding and was seen in all the infants with EHBA. The sensitivity of this finding was 100% and specificity 92.8% for biliary atresia. The other histopathological finding include presence of portal expansion and presence of cholestasis within bile canaliculi, portal fibrosis which were contributory findings in infants with EHBA. Giant cell transformation was not found to be very helpful in distinguishing intra and extra hepatic causes of infantile cholestasis. The most valuable hepatic histopathological variable for distinction between intra and extra hepatic cholestasis in decreasing order of importance were periductular proliferation, portal duct proliferation, portal expansion, cholestasis in neoductules, foci of myeloid metaplasia and portal portal bridges. The only variable which pointed to the diagnosis of intra hepatic cholestasis was myeloid metaplasia.

Periportal ductal proliferation, portal ductal proliferation, portal portal bridges suggested extra hepatic obstruction.

Many a times clinical diagnosis was totally different and liver biopsy provided the diagnosis and the patient was treated as per the revised diagnosis and did well.

Table 10: Clinicopathological Spectrum of Pediatric liver lesions.

Clinical Impression	Histopathological impression
Massive hepatomegaly with anaemia and jaundice	Hepatoblastoma
Hepatosplenomegaly with fever and anaemia	Visceral larva migrans
Testicular swelling for evaluation	Lipid storage disorder consistent with Wolman's disease
Failure to thrive with visceromegaly	Glycogen storage disease
PUO for evaluation	Miliary tuberculosis
Disseminated tuberculosis	Glycogen storage disease
Collagen vascular disease	Viral hepatitis

But for liver biopsies, the identification of storage disorder clinically presenting as Cholestatic jaundice could not have been possible. Some reactions to injury largely peculiar to infancy were seen. Two important findings in infants with liver disease were giant cell change of hepatocyte and persistence of hematopoietic elements. Icterus, failure to gain weight, hepatomegaly, splenomegaly were commonly seen in infants with neonatal hepatitis syndrome and extra hepatic biliary atresia. As expected, fat soluble vitamin deficiencies were seen frequently in infants with cholestasis. Liver biopsy as a tool contributes to the diagnosis and outcome in patients with infantile cholestasis syndrome, storage disorders, infective (cytomegalovirus, congenital Rubella virus), surgical disorders (choledochal cyst, biliary atresia) by providing and confirming the diagnosis so as to enable to decrease the morbidity due to late presentation.

Conclusion

Liver disorders in childhood are mainly constituted by cholestatic, metabolic and infectious disorders. Neonatal cholestasis constitutes 47% of hepatobiliary disorders in pediatric age group. Liver biopsy is highly accurate in differentiating EHBA and neonatal hepatitis. Persistence of neonatal jaundice beyond two weeks of age demands evaluation to differentiate between three most common causes- hepatitis, biliary atresia and choledochal cyst. The most valuable histopathological variables for distinction between intra and extra hepatic cholestasis were periportal ductular proliferation, portal ductular proliferation, portal expansion, cholestasis in neoductules, foci of myeloid metaplasia, portal portal bridges.

Special stains were very helpful in diagnosis of storage disorders. Rarity of Indian childhood cirrhosis was observed in our study.

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