Case report

Neonatal fatty liver: An autopsy case report

[1]Dr. Kalpana K. Kulkarni, [1]Dr. Somnath S. Khedkar,[2]Dr. Meenal Jadhav

[1]Associate Professor,[2]Professor, B. J. Government Medical College, Pune-411001.Maharashtra, India.

Corresponding author: Dr. Kalpana K. Kulkarni

Abstract:

Neonatal fatty liver is an important morphological finding associated with sudden infant death. We report one such case of 5 days old female neonate with uneventful birth history. Two previous siblings of present case had succumbed in early neonatal period similarly after uneventful birth. There was no history of salicilate consumption, top feeding or fructose intake. On autopsy, liver showed macrovesicular fatty change and aqueous liver homogenates showed raised cholesterol, triglycerides and reduced glucose content. Though biochemical tests for pertinent enzyme deficiencies were not undertaken, based on morphological findings and clinicopathological correlation, we presume the case to be of fatty acid oxidation disorder.

Key words : Neonatal fatty liver, sudden infant death syndrome, fatty acid oxidation disorder.

Background:

Neonatal fatty liver is seen in acquired conditions like perinatal anoxic stress, Reye syndrome and variety of inborn errors of metabolism. It is an important morphological change associated with sudden and often unexplained neonatal death. It suggests possibility of poisoning or acute metabolic abnormality inherited or acquired.[1-3] It is rather difficult to make a firm autopsy diagnosis of inborn error of metabolism in perinatal period in a moderately equipped set up for want of facilities for specific enzyme assays needed for their confirmation.

Further more, one need to be aware and sho-uld consider such a possibility beforehand so th-at appropriate samples can be collected immedia-tely after the death. However, some of such defe-cts may have characteristic histological and elec-tron microscopic appearance or abnormal storage products that can be detected.All the same recog-nition of the nature of disease allows precise diagnosis in subsequent pregnancies.[1] Recently we have come across one such autopsy case with history of neonatal death in previous siblings, which we thought was worthy to report.

Clinical Summary:

A female neonate, product of full term nor-mal delivery succumbed on fifth day of life. APGAR score was 8 at zero minute and 9 at five and ten minutes. There was no history of jaun-dice. The neonate was breast-fed. Maternal his-tory revealed mother to be third gravida and sec-ond para. The first delivery was full term normal and the second delivery was full term and by LSCS done for transverse lie. Both these neona-tes died on the first day of birth. The present neo-nate weighed 2.26 Kilograms. Anthropometrical examination revealed: Height – 55 cm, Head cir-cumference – 32 cm, Chest circumference – 30 cm, Mid arm circumference – 9 cm, Mid thigh circumference – 14 cm. Nothing abnormal was

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detected on general and systemic examination. There was no icterus. On investigations, Hb was 17 gm%, peripheral blood smear done on the third day was within normal limits. Blood group was B positive. The neonate received syrup paracitamol, Injection Ampicilin and Gentamicin, third day onwards. Medico legal postmortem was performed and records of postmortem findings along with clinical notes and organs namely whole liver, lungs, heart, spleen, and kidneys were referred to us for histopathological examination.

Pathological findings:

On external examination, there was no evidence of icterus, oedema, cyanosis, lymphadenopathy, prematurity or external congenital anomalies. There was mild hepatomegaly with liver being two fingers below costal margins.On systemic examination, liver weighed 60 gms and was pale yellow in colour. Microscopy of liver revealed panlobular macrovesicular fatty change with hepatocytic nucleus pushed to periphery. There was no evidence of cholestasis. PAS with diastase stain done on section of liver was not contributing for glycogen storage disease. Frozen section of liver stained with Sudan III revealed fat droplets in hepatocytes.The extract of liver homogenate was grossly fatty and showed cholesterol and triglyceride content to be one and a half and two times more respectively and glucose content to half that of control neonatal liver.

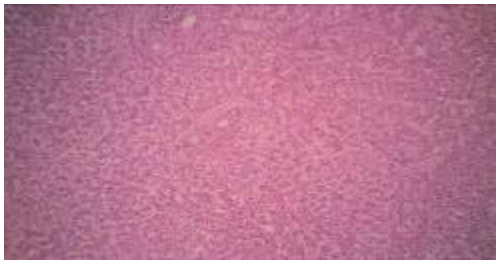

Fig. 1: low power view (10x) showing fatty change in liver

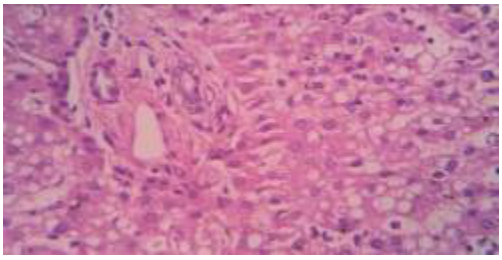

Fig. 2: High power view (40x) showing fatty change in liver

Discussions:

The finding of fatty liver by itself is quite nonspecific.[4] Perinatal anoxia and Rey's syndrome are some of the important acquired causes of neonatal fatty liver. These possibilities were ruled out on clinical and morphological grounds in present case. The birth was uneventful and APGAR score was within normal limits. There was no history of Salicylate consumption and unlike in Reye syndrome fatty change was macrovesicular rather than microvesicular.

The history of death in early neonatal period in previous two siblings in present study strongly suggested possibility of inborn error of metabolism. For want of facilities, precise diagnosis of it could not be substantiated with confirmatory biochemical tests to demonstrate enzyme deficiency. However, certain assumptions could be made with careful morphological study and a thorough clinicopathological correlation.Inborn errors of

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metabolism that can show fatty change include some form of glycogenosis, Refsums disease, Wolmans disease, familial hyperlipemia, tyrosinemia, galactosemia, fructose intolerance and fatty acid oxidation disorders.[1-3] Most of these possibilities could be ruled out on clinical and morphological grounds.Jaundice can be an important manifestation of tyrosinemia and galactose intolerance. Fatal forms of tyrosinemia are charecterised by cholestasis. In galactose intolerance hepatocytes show fatty droplets around central nucleus rather than macrovesicular form of fatty liver.[1] In absence of these findings, diagnosis of these conditions was disregarded.

Fructose intolerance and disorders of fatty acid oxidation are important differential diagnoses of neonatal fatty liver. Present neonate was not top fed and sugar syrup was not administered additionally except for syrup paracitamol for last two days. Wigglesworth[1] has described a case where failure to recognize fructose intolerance resulted in neonatal death which at autopsy showed diffuse fatty charge in liver. By taking due cognizance of this family history, tragedy was not repeated in subsequent child birth. The fructose was withdrawn after noting vomiting in neonate. This emphasizes importance of autopsy study of such cases, their notification and counseling for postnatal care to be taken in subsequent child births.

Evaluation of a possible inherited metabolic cause is of particular importance. Boles[4] et al has suggested a novel approach which involves biochemical estimation of certain metabolites in constantly available autopsy samples like liver.[4] Interestingly, in present case aqueous liver homogenates showed grossly fatty appearance and raised cholesterol and triglycerides as compared to control neonatal liver. Similarly glucose content was reduced. Similar findings are noted by Boles[4] et al in all cases of non Medium chain acyl COA dehydrogenase and 40% cases of Medium chain acyl COA dehydrogenese deficiency.

Thanka[5] et al have recently described one such case where despite of the absence of biochemical assay, presumptive diagnosis of fatty oxidation disorder was offered in a case of sudden infant death syndrome. With these considerations, we presume present case to be most probably of fatty acid oxidation disorder. According to Olpin SE, fatty acid oxidation disorders show considerable phenotypic diversity. There is seen a very wide spectrum of clinical presentations in neonatal period and infancy, adolescence and adulthood. The important manifestations in neonatal period and infancy are recurrent hypoketotic hypoglycemic encephalopathy, deranged hepatic function with hyperammonemia and cardiac dysfunction. In older children and adults there is seen exercise intolerance to aerobic type of exercise with episodic rhabdomyolysis. In some disorders toxic metabolites can be attributed to various central and peripheral nervous disorder including encephalopathy, axonopathy, polyneuropathy and also retinopathy. [6] Considering this clinical information It seems probable that the fatal event in present case was intractable undetected hypoglycemia.

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