Case report

Neonatal fatty liver: An autopsy case report

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Abstract:
Neonatal fatty liver is an important morphological finding associated with sudden infant death. We report one such case of a 5-day-old female neonate with an uneventful birth history. Two previous siblings of the present case had succumbed in early neonatal period similarly after an uneventful birth. There was no history of salicylate 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. 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. Furthermore, one need to be aware and should consider such a possibility beforehand so that appropriate samples can be collected immediately after the death. However, some of such defects may have characteristic histological and electron microscopic appearance or abnormal storage products that can be detected. All the same recognition of the nature of disease allows precise diagnosis in subsequent pregnancies. 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 normal 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 jaundice. The neonate was breast-fed. Maternal history revealed mother to be third gravida and second para. The first delivery was full term normal and the second delivery was full term and by LSCS done for transverse lie. Both these neonates died on the first day of birth. The present neonate weighed 2.26 Kilograms. Anthropometrical examination revealed: Height – 55 cm, Head circumference – 32 cm, Chest circumference – 30 cm, Mid arm circumference – 9 cm, Mid thigh circumference – 14 cm. Nothing abnormal was
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
paracetamol, 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](image1)

![Fig. 2: High power view (40x) showing fatty change in liver](image2)

**Discussions:**
The finding of fatty liver by itself is quite
nonspecific. 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
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. 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 characterised by cholestasis. In galactose intolerance hepatocytes show fatty droplets around central nucleus rather than macrovesicular form of fatty liver. 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 paracetamol for last two days. Wigglesworth 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 et al has suggested a novel approach which involves biochemical estimation of certain metabolites in constantly available autopsy samples like liver. 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 et al in all cases of non Medium chain acyl COA dehydrogenase deficiency.

Thanka 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. Considering this clinical information it seems probable that the fatal event in present case was intractable undetected hypoglycemia.
References:


