A study on histology of fetal liver

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Abstract

Background and aims: The liver during fetogenesis does not follow classical lobular pattern. Normal histology of the fetal liver at various stages of development was studied to get insight into the morphology of fetal liver and special function it performs in fetal life. Method: Dissection of 29 normal human fetuses was done and histological findings of liver were noted with respect to the age of fetus. The histology of fetal liver was studied using H & E stain and important features of fetal liver were studied. Result: Fetal liver histology is different from adult liver. Unlike adult liver, fetal liver shows hepatocytes arranged in sheets predominantly with cord-like pattern at places. The sinusoids are dilated and filled with hemopoietic cells, which could be appreciated at different stages of fetal development. The Kupffer cells were also noticed in fetal liver. Conclusion: The present study will be helpful in understanding the normal histology of fetal liver and add to the existing knowledge regarding development of fetal liver.

Key words: fetal hepatocytes, hematopoiesis, acinus, portal, sinusoid

Introduction

Fetal liver is one of the most primitive embryonic organs developed from endodermal evagination of foregut and septum transversum mesenchyme. The fetal hepatocytes were formed from endodermal cells of hepatic diverticulum. The portal veins develop from vitelline veins. The hepatoblast adjacent to mesenchyme differentiate in to future biliary tubular structures which mature from the hilum to outward, begin around the 11th week of gestation and continue past birth. The fetal liver is also center of hematopoiesis in fetus.

The aim of the present study is to find out the histological structure of fetal liver and to contribute to available literature in understanding the liver histology during gestational period including liver architecture, hepatocyte, Kupffer cells, sinusoid and hemopoietic nature of the liver during the fetal life.

Materials and methods

This prospective study was conducted at the Department of Anatomy, Government Medical College, Haldwani. The fetuses were obtained from Obstetrics and Gynecology Department, Dr Sushila Tiwari Hospital over a period of two years (period commencing from 2011 to 2013), with due regards on ethical ground. The fetuses were preserved in formalin.

The crown rump lengths (CRLs) of fetuses were recorded and histological features were studied in relation to CRL of the fetuses. In the fetus, the liver was observed for any gross and congenital anomalies. Its weight and size were recorded before embalming. The liver was removed by dissecting inferior vena cava and excising ligaments of the liver, and after that its weight was recorded. The liver tissue was taken for histological processing. Five µm-thick fetal liver sections were stained with hematoxylin-eosin stain and were studied by light microscopy.

Observations and results

Observations on the light microscopic structure of liver during fetal development: The hepatic lobular pattern was not defined up to CRL of 8.5 cm. The liver architecture showed ill-defined lobular pattern of fetal hepatocytes from CRL of 10.4 cm with a well-defined pattern noticed only in late gestation with CRL of 28 cm (Table 1). The fetal hepatocytes were appreciated from
CRL of 6.5 cm. They were arranged in anastomosing cord-like pattern which were one to two cell thick in all parts of gestation (Fig 1). The fetal hepatocytes were large oval to polygonal with abundant granular eosinophilic cytoplasm; the nucleus were large, round to oval with diffuse chromatin. The hepatocytes arranged in cords were seen to be separated by sinusoids which were thin endothelial cell lined spaces appreciated from the smallest CRL of 6.5 cm in our study. Late in gestation the sinusoids were found to be dilated along with the central vein and portal radical (Fig 2). The hemopoietic cells were found in the dilated sinusoids indicating that liver in fetal period is engaged in performing hemopoietic function (Table 2). Sinusoid were dilated and seen to be opening in to central vein and filled with hemopoietic cells. (Fig 3). The nucleated red blood cells were seen in the sinusoids suggesting of hemopoietic activity.

The fibrous tissue is seen extensively surrounding the portal triad and its radicle especially while entering in the liver (Fig 3). We have also noticed the presence of Kupffer cells at places from CRL 6.5 cm however in late fetuses more increase in number of Kupffer cells were noticeable. No apoptotic activity was noticed in our histological study.

Discussion

The present study has been done keeping in view the development of liver and its histological changes during fetal period. Liver is involved in metabolic, exocrine and endocrine functions. It is unique in its status that it acts as a hematopoietic organ. Septum transversum provides aggressive support in vascular organization inside the liver.

Unlike adult liver, the hepatic lobular, portal lobular and acinus pattern were not much recognizable except an ill-defined pattern of hepatic lobule noticed in some areas. These findings are supported by study by Notenboom who also found that lobular pattern is not well defined with cells arranged in anastomosing cell pattern with single cell thick cord-like pattern. They stated that fetal period is crucial for normal liver development.
development with differentiation in to adult phenotype from embryonic foregut being a multistep process.

Fibrous tissue along the central vein and portal triad was noticed. The hepatic artery and portal vein were found to be surrounded by fibrous connective tissue. Payushina found in their study that fibroblast and myofibroblast were present around portal triad and confirmed immuno histochemically.

Early work on histology of fetal liver was done by Lipp who described the embryology of the liver and stated that hepatic parenchymal plates develop from the cell cord organized along their nutrient vessel. The authors also noticed the cells of liver parenchymal cord and were uniform throughout the liver and also demonstrated anastomosing cord like pattern at places as described by Severn.

Villeneuve et al described that fetal hepatocytes were arranged in anastomosing sheets separated by capillaries. Hemopoiesis was evident in capillary lumen and space of Disse after 12 weeks of development. The portal tract was seen to be developed centrifugaly from hilum to the periphery of the liver. Initially sinusoids were dilated along with the central vein and portal radical indicating that liver in fetal period is engaged in performing hemopoietic function. Several workers also described the hemopoietic function of liver. Emura et al noticed the different erythrocytes series in hemopoietic system during early stage of hepatic hemopoiesis. We did not noticed any different series because our study ranges from 6.5 cm to 28 cm CRL, which might have crossed the period of differentiation for the formation of various series of erythropoiesis.

The authors also noticed the presence of Kupffer cells at places from 6.5 cm CRL. However, in late fetuses, increase in number of Kupffer cells was noticed. Presence of Kupffer cells has also been described by Naito et al who found that macrophage develops in yolk sac and migrates to fetus liver. During histogenesis.

<table>
<thead>
<tr>
<th>CRL (cm)</th>
<th>Portal triad</th>
<th>Lobular pattern</th>
<th>Central vein</th>
<th>Hepatocyte arrangement</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>Not specific</td>
<td>Under organization</td>
<td>Under organization</td>
<td>Present, no well defined cord pattern</td>
</tr>
<tr>
<td>10-15</td>
<td>Present</td>
<td>Ill defined</td>
<td>Present and dilated</td>
<td>Present in one to two cord</td>
</tr>
<tr>
<td>15-20</td>
<td>Present</td>
<td>Ill defined</td>
<td>Present</td>
<td>Present in one to two cord</td>
</tr>
<tr>
<td>20-25</td>
<td>Present</td>
<td>Ill defined</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>&gt;25</td>
<td>Present</td>
<td>Ill defined</td>
<td>Present</td>
<td>Present</td>
</tr>
</tbody>
</table>

Table 2: Sinusoidal pattern, hematopoietic cells and Kupffer cells of fetal liver for different crown rump length (CRL).

<table>
<thead>
<tr>
<th>CRL (cm)</th>
<th>Sinusoids</th>
<th>Hemopoietic Cells</th>
<th>Kupffer Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10</td>
<td>Present</td>
<td>Identified</td>
<td>Occasional</td>
</tr>
<tr>
<td>10-15</td>
<td>Dilated</td>
<td>Extensive</td>
<td>Present</td>
</tr>
<tr>
<td>15-20</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>20-25</td>
<td>Present</td>
<td>Present</td>
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<tr>
<td>&gt;25</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
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</table>
the role of apoptosis has been also described in development of liver\textsuperscript{16}. In our study we did not notice the activity of apoptosis because our field of study was limited from CRL 6.5 cm to 28 cm of the human fetuses. The role of apoptosis plays is seen in early stages of fetal development.

**Conclusion**

The histology of liver was studied in 29 human fetuses of either sex from CRL 6.5 cm to 28 cm, in other words 2.5 month to 5.6 month. Hepatic lobule, portal lobule and acinus pattern were not much evident except ill-defined pattern at places. The liver during fetogenesis does not follow classical lobular pattern. Fetal liver is primarily designed for hemopoiesis there for shows prominent erythropoietic activity. The vessels (portal vein, central vein and sinusoid) were extremely dilated; perhaps they were in way of organizational changes to achieve the adult morphological feature.

**References**
