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EARLY STAGES OF THE DEVELOPMENT OF THE EXTRAHEPATIC BILE DUCTS

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РАННІ СТАДІЇ РОЗВИТКУ ПОЗАПЕЧІНКОВИХ ЖОВЧНИХ ПРОТОК

Резюме. В результаті дослідження 12 серійних гістологічних зрізів препаратів зародків 4,0-13,0 мм тім'яно-п'яткової довжини вивчені джерела закладки, критичні періоди розвитку та динаміка просторово-часових перетворень позапечінкових жовчних проток. Встановлено, що позапечінкові та внутрішньопечінкові жовчні протоки з моменту їх закладки розрізнені, але наприкінці зародкового періоду простежується тенденція до їх сполучення. Ключові слова: позапечінкові жовчні протоки, розвиток, людина.

The development of diagnostic methods and new non-invasive technologies in biliary surgery is impossible without exhaustive information concerning the embryogenesis and anatomy of the extrahepatic bile ducts [1], including variants of the blood supply and myeloarchitectonics of their sphincter apparatus [2, 3]. Understanding the etiopathogenesis of congenital malformations of the system of the pancreatic and bile ducts requires ascertaining their embryonal development [4-6]. Meanwhile the findings of modern scientific literature are fragmentary and controversial. A comprehensive study of the prenatal development of the sphincter apparatus of the extrahepatic bile ducts in the light of modern demands of practical medicine is a highly important, timely and topical task of the morphological science [6-8].

The object of the research – to establish the sources of the anlage and the dynamics of spatio-temporal transformations of the extrahepatic bile ducts at an early stage of human prenatal ontogenesis.

Material and methods of the research. The study was carried out by means of light microscopy of 12 series of histologic sections of embryonal specimens, measuring 4.0-13.0 mm of the parietocalcaneal length (PCL) from the embryologic collection of Bukovinian State Medical University. The obtained digital images of histologic specimens were studied be means of three-dimensional and graphic reconstruction based on the computer program "Virtual Anatomist" (Kharkiv). In cases when more than one embryo represented an identical age period, the specimens were compared as to their similarity or distinction within the range of their age and were compared with the previous and the next ones according to an age-related scale. This made it possible to refer embryos to a certain chronological group. The study was started with a 4 mm embryo of the PCL whose anlage of the liver and extrahepatic bile ducts was clearly identified. The morphologic development was traced in chronologic order of serial sections of histologic specimens of embryos of 4 to 6 weeks of gestation.

The results of the research and their discussion. It has been established that the anlage of the bile ducts and liver is a hepatic diverticulum which is clearly traced in a 4.0 mm PCL embryo. This hepatic bud is a diverticulum of the endoblastic epithelium of the ventral wall of the upper portion of the foregut (the future duodenum) into the transverse septum that is a mesodermal lamina between the pericardial cavity and the peduncle of the yolk sac. The cells of the bud rapidly proliferate and grow into the caudal portion of the mesoderm of the transverse membrane between the right and left cardinal veins, into the so-called hepatic mesoderm. The hepatic diverticulum, spreading out, in broad cellular layers, is rapidly divided into the cranial and caudal portions, in its turn. At the end of the 4th week the form of the liver bud gradually transforms and one can discern a head (in the cranial larger portion) and a neck (in the caudal lesser portion) in the liver diverticulum. The cranial part has the dimensions $500x315 \mu m$ and is a liver anlage, whereas the caudal one reaches $250 \times 125 \ \mu m$.

Starting from the end of the 4th – the beginning of the 5th weeks of the intrauterine development, the extrahepatic portion of the bile duct is formed owing to the elongation of the caudal part of the liver diverticulum. The caudal portion of the liver diverticulum (the cystic diverticulum, transforms into the gallbladder and its "neck" forms the cystic duct. It has been traced that the cells, forming the gallbladder and the cystic duct originate from a histologically distinct population of cells of the entoderm. The stalk of the hepatic diverticulum between the primitive gut, which is differentiated into the duodenum and the cystic diverticulum, transforms into the common bile duct. Thus, during the 4th week there occur intensive processes of a transformation of the liver diverticulum and the form-building of the human biliary system, therefore any unfavourable factors of the internal or external environment may bring about the appearance of structural variants or congenital malformations

of the gallbladder and extrahepatic bile ducts [5, 7]

Throughout the 5th week an intensive proliferation of the hepatic cells and an elongation of the extrahepatic bile ducts occur. The intestinal tube starts closing, forming the duodenum. At the end of the 5th week the lumen of these tubular structures is filled in and closed by epithelial cells. During this period the cystic diverticulum is well traced, its measurement makes up 250x130 µm. The anlage of the gallbladder is surrounded by a mesenchymal layer from which its muscular and connective tissue membrane are formed, and by the hepatic tissue. The dorsal pancreatic diverticulum is formed from the dorsal wall of the duodenum opposite the place of the origination of the liver diverticulum and shortly the ventral pancreatic diverticulum arises from the anlage of the bile duct, more caudally from the primordium of the gallbladder. Although the hepatic diverticulum arose from the ventral wall of the foregut, the processes of the growth and rotation of the duodenum lead to a shift of the place of the confluence of the bile duct and the ventral pancreatic primordium on the dorsal wall of the intestine and their location within the bounds of the dorsal mesentery.

At the beginning of the 6th week of the intrauterine development the sizes of the hepatic anlage continue to grow intensively (the transverse size $-900 \mu m$, the dorsoventral size $-400 \mu m$, the craniocaudal one is 455 μm), it occupies the cranioventral section of the abdominal cavity, its right segment exceeds in size its left one, reaching the posterior wall of the abdominal cavity. The anlage of the organ separates itself gradually more distinctly from the diaphragmatic part of the transversal septum and becomes a true abdominal structure between the leaves of the ventral mesentary which were formed owing to the closure of the gut and the abdominal wall. The hepatic ligaments, the lesser omentum, in particular, are formed from the remnants of the transversal and the ventral mesentery. The ventral mesentary provides a peculiar framework to the ducts

and vessels which go to the porta hepatis, but it degenerates in a caudal direction from them. The lesser omentum, in particular, the hepatoduodenal ligament, passes the portal vein, the hepatic artery and the common bile duct (the portal triad). A formation of topographic variants and malformations of the hepatic vessels during this period is possible, for example, the origination of an accessory (displaced) left hepatic artery from the left gastric (in case when it passes in the cranial portion of the hepatogastric ligament), or an accessory (displaced) right hepatic artery, when the latter is a branch of the superior mesenteric artery, located in this ligament.

Throughout the 6th week of the development there occurs vacuolization and recanalization of the lumen of the tubular structures, this process being initiated in the duodenal end of the intestinal tube. A disturbance of the processes of recanalization (incomplete recanalization) may induce the appearance of the membranous common bile duct with further atresia at this stage of the development, for example, due to viral inflammatory infections, resulting in sclerotic changes of the ducts. At the beginning of the 6th week of the development, the ventral and dorsal pancreatic anlages become contiguous between themselves within the bounds of the dorsal mesentery and at the end of the week their complete fusion takes place with the formation of the definitive pancreas.

It has been traced that the hepatic duct de-

velops from the superior cranial portion of the hepatic diverticulum. The caudal parts of the right and left hepatic ducts arise from the extrahepatic ducts and are well-defined at the end of the 6th week of the development. A reconstruction of the extrahepatic bile ducts has demonstrated their independent development from the intrahepatic ductal system as well as that both bile systems are separate since the time of their anlage, but at the end of the embryonal period a tendency towards their union is traced.

Conclusions: 1. Intensive processes of a transformation of the hepatic diverticulum and form-building of the bile system throughout the 4th week of the development may be regarded as a critical period. 2. The extrahepatic bile ducts are traced in the form of a well-defined tubular structure, starting from the 6th month of the development, whereas the intrahepatic bile ducts are represented by a primitive tubular plate. 3. The extrahepatic and intrahepatic bile ducts are isolated, but at the end of the embryonal period a tendency towards their fusion is traced.

Outlooks of a scientific inquiry. A promising trend of a scientific research of the extrahepatic bile ducts at an early stage of human ontogenesis of man is a study of the characteristics of the forming of their microsurgical anatomy, the sources of the blood supply and innervation that will make it possible to determine the structural components of their apparatus.

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РАННИЕ СТАДИИ РАЗВИТИЯ ВНЕПЕ-ЧЕНОЧНЫХ ЖЕЛЧНЫХ ПРОТОКОВ

Резюме. В результате исследования 12 серий гистологических срезов препаратов зародышей 4,0-13,0 мм теменно-пяточной длины изученны источники закладки, критические периоды развития и динамика пространственно-временных преобразований внепеченочных желчных протоков. Установлено, что внепеченочные и внутрипеченочные желчные протоки с момента их закладки разобщены, но в конце зародышевого периода прослеживается тенденция к их соединению.

Ключевые слова: внепеченочные желчные протоки, развитие, человек.

EARLY STAGES OF THE DEVELOP-MENT OF THE EXTRAHEPATIC BILE DUCTS

Abstract. As a result of a study of 12 serial histologic sections of embryonal specimens, measuring 4.0-13.0 mm of the parieto-coccygeal length the sources of anlage, the critical periods of the development and the dynamics of spatio-temporal transformations of the extrahepatic bile ducts have been studied. It has been established that the extrahepatic and intrahepatic bile ducts are separated since the moment of their anlage, but at the end of the embryonal period a tendency towards their union is traced.

Key words: extrahepatic bile ducts, development, human.

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