

EMBRYOLOGIC PRECONDITIONS OF SOME CONGENITAL MALFORMATIONS OF COMMON BILE DUCT

ЕМБРІОЛОГІЧНІ ПЕРЕДУМОВИ ДЕЯКИХ ПРИРОДЖЕНИХ ВАД СПІЛЬНОЇ ЖОВЧНОЇ ПРОТОКИ

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Abstract. In order to identify the morphological preconditions of some congenital malformations of the biliary system, the research of the peculiarities of prenatal morphogenesis of the common bile duct (CBD) has been performed on 72 series of sequential histologic sections of human embryos and fetuses, also on 50 cadavers of human fetuses by means of the methods of microscopy, morphometry, macroscopic and microscopic preparation, graphic reconstruction. Statistical analysis of the results of research was carried out with calculation t-test. It has been established that the stage of embryonal occlusion of CBD from the 6th till the 8th weeks in the embryos 8,5-24 mm in in parietal-coccygeal length is a morphologic substrate for congenital biliary atresia. Deceleration of CBD growth and the diverticulum-like dilatation of last one at the beginning of the 4th month and during the 8th month of the human intrauterine development can become the morphologic predictors for the formation of congenital dilatation and cysts of this anatomic structure.

Key words: common bile duct, morphogenesis, congenital defects.

Резюме. З метою виявлення морфологічних передумов деяких природжених вад біліарної системи проведено дослідження особливостей пренатального морфогенезу спільної жовчної протоки та суміжних структур на 72 серіях послідовних гістологічних зрізів зародків і передплідів та 50 трупах плодів людини за допомогою методів мікроскопії, морфометрії, макро- і мікропрепарування, графічного реконструювання. Статистична аналіз результатів дослідження проведений з врахуванням t-критерію Ст'юдента. Встановлено, що стадія ембріональної оклюзії спільної жовчної протоки з 6-го по 8-й тижні внутрішньоутробного розвитку (у зародків 8,5-24,0 мм тім'янокуприкової довжини) є морфологічним субстратом для виникнення природженої атрезії жовчних проток. Уповільнення росту та дивертикулоподібна дилатація останньої упродовж 4-го й 8-го місяців внутрішньоутробного розвитку людини можуть стати морфологічними предикторами виникнення природженої дилатації та кіст у цій анатомічній ділянці.

Ключові слова: спільна жовчна протока, морфогенез, природжені вади.

Introduction. Congenital defects of bile ducts make up about 6-8% of all malformations [2, 6]. The greatest number of defects is found in the anatomical area of common bile duct (CBD). The main types of congenital defects of CBD are: congenital absence (agenesis, aplasia), absence of its lumen (atresia), dilatation of some its part (cystic dilatation) etc. [3] At present there is no consentient opinion about the mechanisms of the formation of bile ducts defects. A some of theories (disturbances of recanalization, intrauterine inflammation, "vascular catastrophe") are known, trying to explain the appearance of embryonal disorders of biliary system in humans [1, 5]. To this time there are no clear critical ontogenetic periods and morphological peculiarities of development of CBD as the main bile collector in the different age intervals of prenatal ontogenesis. In view of the above, the research of the peculiarities of prenatal morphogenesis of CBD in humans is actual to the detection of morphological preconditions for the possible occurrence of its congenital malformations.

The aim of research: to find out the morphological preconditions of possible occurrence of common bile duct congenital defects.

Material and methods. The investigation has been performed on 72 series of consistent histologic sections of embryos from 8,0 mm to 79,0 mm in parietal-coccygeal length (PCL) and 50 corpses of human fetuses and newborns by using methods of microscopy, macro- and microscopic preparation, graphic reconstruction, morphometry. Objects age defined using tables by B.M. Patten (1959), B.P. Hvatova, J.N. Shapovalov (1969). Statistical analysis of the results of research was carried out with calculation t-test. Research has been conducted according to "Following the Ethical and Legal Standards and requirements during carrying out scientific morphological research" and the main theses of Helsinki Declaration of the World Medical Association on ethical principles of scientific and medical research involving human subjects (1964-2000) as part of the National Project "New Life - a new quality of maternity and childhood" and the State Program of transition of Ukraine from 01.01.2007 to the International System of Accounting and Statistics (Order of Ministry of Health of Ukraine №179 on 29.03.2006 "On approval the instruction on definition the criteria of perinatal period and live births and stillbirths, order registration of live births and stillbirths").

Results and its discussion. It was established that the embryonic development of CBD is characterized by the presence of a solid stage.

Acc to our investigation the last one occurs during the 6-7th weeks of human intrauterine development (HIUD), it corresponds with the known bibliographic data [3]. Thus, in embryos of 8,5-11,0 mm of PCL the walls of CBD are formed by two lines of high cylindrical epithelium 225,0-250,0 μm in length and 40,0-75,0 μm in width. The duct's lumen filled by the agglomeration of epithelial cells, which form like a plug directly in the area of connection with the pancreatic duct (fig. 1)

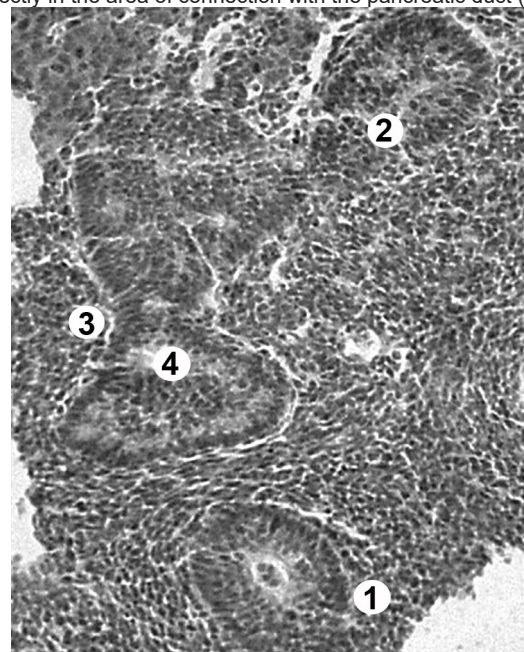


Fig. 1. Sagittal section of human embryo 8,5 mm of PCL. Microphoto. Magnification: ×280

1 – duodenum; 2 – primordium of gall bladder; 3 – pattern of common bile duct; 4 – epithelial agglomeration.

A recanalization of CBD lumen is completely finish at the end of the 8th week of HIUD. In particular, in prefetuses 21,0-24,0 mm of PCL



in the area of connection CBD with the ventral pancreatic duct we revealed a distinct enlargement of the duct's lumen which forms hepatic pancreatic ampule (HPA) connected to the duodenum (fig. 2).

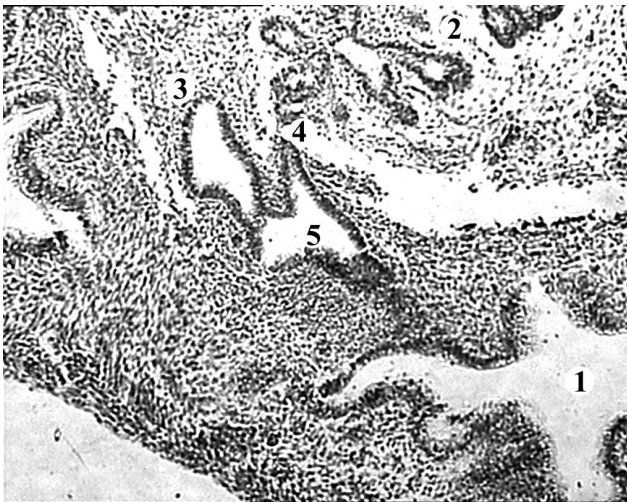


Fig. 2. Frontal section of human fetus 23,0 mm of PCL. Microphoto. Magnification $\times 80$
1 – duodenum; 2 – pancreas; 3 – common bile duct; 4 – pancreatic duct; 5 – hepatic pancreatic ampule.

As notes by a number of authors [4, 6], different disturbances of recanalization of its lumen, leads to the persistence of embryonal occlusion of the duct in postnatal period, which may becomes a morphological substrate for the formation of its congenital atresia.

At the beginning of 4th month of HIUD in CBD length topographically we can differentiate three parts: a retroduodenal, a pancreatic and an intraduodenal. The duct wall consists of a single line of prismatic epithelium, surrounded by longitudinal bundles of mesenchymal cells. In fetuses 82,0 mm of PCL in the pancreatic part of CBD we identified diverticula-like epithelial protrusions into the adjacent muscle layer of its wall. The last ones form specific oval pockets 40,0-100,0 μm in diameter (fig. 3).



Fig. 3. Frontal section of human fetus 82,0 mm of PCL. Microphoto. Magnification $\times 56$
1 – duodenum; 2 – pancreas; 3 – common bile duct; 4 – major duodenal papilla.

Such epithelial protrusions occur as a result of irregular growth of the duct wall and in case of disturbances of the differentiation of the mesenchymal elements of its muscular layer these can create morphological preconditions for cystic dilatation of CBD [5]. Occurrence of the last malformation is especially probable at the end of the 8th month of HIUD under the conditions of increased pressure in the duodenal-biliary system combined with various factors that don't let the normal outflow of bile in the duodenum (folds of the mucous membrane, valves) (fig. 4).

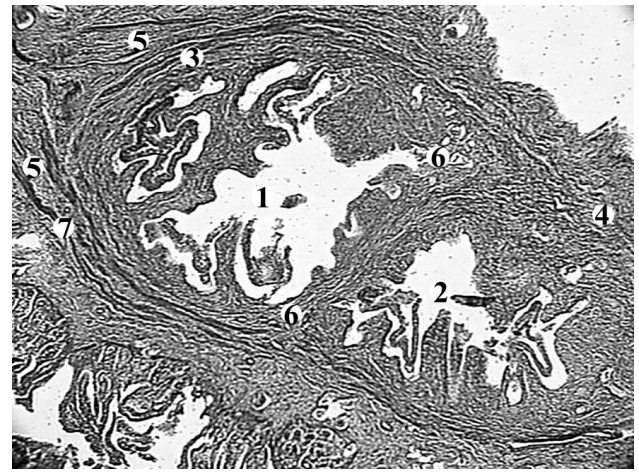


Fig. 4. Horizontal section of duodenum in human fetus 240,0 mm of PCL. Microphoto. Magnification $\times 35$
1 – common bile duct; 2 – pancreatic duct; 3 – sphincter of common bile duct; 4 – sphincter of pancreatic duct; 5 – sphincter of hepatic pancreatic ampule; 6 – valvular fold of mucosa; 7 – duodenum.

Comparative dynamics of increase the length of different parts of CBD has been analysed during the fetal period and in newborns. The greatest addition (in 6,4 times) was in the length of retroduodenal part of CBD ($p < 0,001$) which size is up to $7,00 \pm 0,090$ mm in newborns. The least addition (in 3,2 times) has been detected in the length of intramural part of CBD ($p < 0,001$) which size was $1,93 \pm 0,081$ mm in newborns. Increase the lengths of supraduodenal and pancreatic parts was 4,4 and 4,1 times accordingly ($p < 0,001$) and its indices in newborns were up to $4,69 \pm 0,13$ mm and $11,14 \pm 0,24$ mm proportionally. However, increasing of the length of individual parts of CBD characterized by the different rates. In particular the growth's character of pancreatic part of CBD corresponds to increase its total length. The growth of retroduodenal part of CBD accelerated from 4th till 7th months ($p < 0,001$) and it has period of deceleration in 8-9th months. A reliable increase of its length was again detected just before the birth ($p < 0,001$). The linear character of growth of supraduodenal part of CBD was detected from 6th till 10th months ($p < 0,001$) without the reliable changes of its length in newborns. Type of growth of intramural part of CBD was undulating with a slow increase its length during the 4th-7th months and a stabilization of its growth in the 8th month and the reliable acceleration of its growth during the 9th month ($p < 0,001$). Its length not reliable changed in newborns. The growth's rates of the diameters of supra- and retroduodenal parts of CBD were almost identical with the periods of acceleration until the 7th month and from 9th months till the birth ($p < 0,001$), and the period of deceleration during the 8th month ($p > 0,05$). Such dynamics of these changes of diameters of aforementioned parts of CBD may be conditioned by the asynchronous growth of different parts of the duodenum. Increase the diameter of the intramural part of CBD was slightly different from previous ones. The acceleration of the growth of its diameter was detected during the 5th month ($p < 0,001$) and 8th-10th months ($p < 0,01$), and deceleration – in fetuses 6-7th month aging and newborns, in last ones a tendency to reduce its diameter has been marked. According to obtained data, the indicated period of CBD growth deceleration combined with HPA enlargement caused by different temps of angiogenesis may be critical for the development of one of the types of congenital dilatation of CBD as the form of its distal (intraduodenal) dilatation – choledochocoele.

Thus, prenatal morphogenesis of CBD is a complex process of its spatial and chronological organization, it is implementing as wavelike one with alternating periods of accelerated and decelerated growth. The revealed structural transformations of CBD during prenatal ontogenesis allow to define several critical periods of its development. The term from the 6th to the 8th week of HIUD (stage of embryonic occlusion) we consider as a critical period for the possible formation of its congenital atresia. The beginning of the 4th month (the stage of diverticula-like dilatation) and the 8th month (stage of asynchronous growth of CBD and HPA) of prenatal development can be critical periods for the possible occurrence of congenital dilatation and cysts of CBD.

Conclusions. During human prenatal development the morphogenesis of the common bile duct implements asynchronously with alternating periods of accelerated and decelerated its growth. The stage of embryonic occlusion of the common bile duct during the 6th-8th weeks of prenatal ontogenesis is a morphological substrate for the occurrence of its congenital atresia. The revealed diverticula-like dilatation of the

duct at the beginning of the 4th month and the stage of its intraduodenal part extension during the 8th month of human intrauterine development may be morphological preconditions for the formation of congenital dilation and cyst of common bile duct.

Prospects of scientific research. We consider it expedient to continue research the peculiarities of morphogenesis and individual types of anatomical variability of the common bile duct in the human newborns.

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FIBRINOLYSIS SYSTEM PARAMETERS DYNAMICS IN PATIENTS WITH CHRONIC DIFFUSIVE LIVER DISEASES UNDER INFLUENCE OF SELEN SUPPLEMENTS APPLICATION

ДИНАМІКА ПОКАЗНИКІВ СИСТЕМИ ФІБРИНОЛІЗУ У ХВОРИХ НА ХРОНІЧНІ ДИФУЗНІ ЗАХВОРЮВАННЯ ПЕЧІНКИ НА ТЛІ ЗАСТОСУВАННЯ СЕЛЕНОВІСНИХ ПРЕПАРАТІВ

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Abstract. The dynamics of the indices of fibrinolysis and cellular adhesion in patients with chronic diffuse liver diseases against the ground of administration of "Triovit", a selenium-containing drug, has been studied. The administration of "Triovit" in a comprehensive therapy of patients with chronic diffuse liver diseases was found to improve the indices of the blood plasma fibrinolytic system, to reduce adhesive cellular properties and to increase total enzymatic activity of the blood plasma.

Keywords: the chronic diffuse liver diseases, cellular adhesion, fibrinolysis, Triovit

Анотація. Вивчено динаміку показників фібринолізу та клітинної адгезії у хворих на хронічні дифузні захворювання печінки на тлі використання селеновмісного препарату «Триовіт». Встановлено, що триовіт у комплексній терапії хворих на хронічні дифузні захворювання печінки сприяє оптимізації показників системи фібринолізу плазми крові, дозволяє істотно зменшити адгезивні властивості клітин та підвищити сумарну ферментативну активність плазми крові.

Ключові слова: хронічні дифузні захворювання печінки, тиреоїдний гомеостаз, клітинна адгезія, фібриноліз, триовіт.