Research Article

Morphopathological aspects of uncomplicated omphalocele in new-borns

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Abstract

Aspecte morfopatologice în omfalocelul necomplicat la nou-născuți

Scopul studiului constă în elucidarea particularităților morfostructurale și morfofuncționale ale peretelui și zonei regionale a omfalocelului necomplicat în estimarea prognosticului evoluției complicațiilor locale și alegerea tacticii de tratament.
În lotul de studiu au fost incluși 18 nou-născuți din nașteri la termen de gestație de 37-40 săptămâni, cu masa ponderală la naștere 2850-3780 g, dintre care 4 (22,2 %) cu omfalocel major și 14 (77,8 %) cu omfalocel minor și mediu necomplicat, predominând formele de dimensiuni medii. Examinării morfologice au fost supuse regiunea limitrofă la nivelul peretelui abdominal, peretele și regiunea bolții omfalocelului și sectoarele din cordonul ombilical adiacent. Material pentru examinările histomorfologice au servit probele tisulare (1,0×1,0×0,5 cm) prelevate intraoperator și din piesele anatomo-chirurgicale din zonele menționare ale omfalocelului, în medie 6-7 probe. La etapa de colorare s-au utilizat metodele: *hematoxilină-eozină* (H&E) şi selectiv *Van Gieson* (VG), pentru evidenţierea țesutului conjunctiv, și *Azur-Eozină* (A&E), pentru testarea prezenţei florei micotico-bacteriene.
În funcție de zonele cercetate ale omfalocelului și țesuturile din zona limitrofă, inclusiv în bioptatele musculaturii abdominale, a fost observată o variație structurală a componentei tisulare și vascularizării. În probele prelevate din vecinătatea zonei omfalo-abdominală, începând cu regiunea limitrofă cu structurile tisulare abdominale (nivelul de rezecţie), în peretele omfalocelului în limitele a 1,5 -2 cm, pe unele arii până la 3 cm, spre bolta sau zona apicală a omfalocelului au fost depistate structuri mozaice asemănătoare arhitectural cu cele abdominale, zona internă *muco-conjunctiv-vascularizată* fiind bogată în fibre și dotată cu o rețea vasculară mult mai dezvoltată.
Rezultatele studiului a permis de a conchide că structura morfologică a omfalocelului reprezintă o membrană muco-conjunctiv-epitelială dimorfă, determinată de componenta mezotelio-fibro-epidermală, cu prezența țesuturilor predecesorii fibro-musculare și vasculare mixte sanguino-limfatice și folicular limfoide protectoare locale, care în perioada extrauterină au un impact semnificativ în evoluția proceselor reparative. În omfalocelul necomplicat există unii factori de risc major în evoluția rupturilor spontane, proceselor inflamatorii prin contaminarea complexului placentar, riscul sindromului tromboembolic placento-fetal și în peretele omfalocelului în perioada intranatală cu repercusiuni evidente hemoragice, neonatal precoce, la nivel de omfalocel. Au fost identificate unele particularități etiopatogenetice ce confirmă parțial ipoteza înaintată de unii autori că omfalocelul se dezvoltă secundar unor dereglări de migrare și de maturizare a mioblastelor în peretele abdominal.
CONCLUZII. În omfalocelul de dimensiuni majore necomplicat, cu disproporție viscero-abdominală semnificativă, ținând cont de structura arhitecturală a sacului, există condiții favorabile pentru procesele reparative, cu epitelizarea treptată a sacului și transformarea lui în hernie ventrală. Rata scăzută a letalității în lotul studiat justifică conduita conservativă în formele date ale malformației. În afectarea intraamnională există riscul de penetrare a componentului infecțios-inflamator a omfalocelului, îndeosebi în cazurile rezolvate cu întârziere, cu o posibilă contaminare postnatală.

Cuvinte cheie: omfalocel, disproporție viscero-abdominală, hernie ventrală, investigații morfologice

Abstract

The purpose of the study was to elucidate the morphostructural and morphofunctional features of the wall and regional area of uncomplicated omphalocele in estimating the prognosis of evolution of local complications and the choice of treatment tactics.

The study group included 18 new-born babies, 37- 40 weeks of gestation, with birth weight 2850-3780 g, of which 4 (22.2%) with major omphalocele and 14 (77, 8%) with minor and medium uncomplicated omphalocele, predominantly medium-sized one.

The morphological examination was performed on the adjacent region of the abdominal wall, the omphalocele domewall and the adjacent umbilical cord areas.Tissue samples (1.0×1.0×0.5 cm) of anatomical-surgical specimens taken intraoperatively from the mentioned omphalocele areas, on average 6-7 samples, were used as material for histomorphological examinations.

At the staining stage the following methods were used: *hematoxylin-eosin* (H & E) and selectively *Van Gieson* (VG) to highlight the connective tissue, and *Azur-Eosin* (A & E) to test the presence of mycotic-bacterial flora.

Depending on the investigated areas of the omphalocele and the tissues in the adjacent area, including abdominal muscle biopsy, a structural variation of the tissue and vascularization component was observed. In the samples taken nearby the omphalo-abdominal region, starting with the region adjacent to the abdominal tissue structures (resection level), in the omphalocele wall within 1.5-2 cm, in some areas up to 3 cm, towards the domor apical area of omphalocele, mosaic structures similar architecturally to the abdominal ones were found, the internal muco-connective-vascularized area being rich in fiber and supplied with a much more developed vascular network.

The results of the study allowed to conclude that the morphological structure of omphalocele represents a dimorphic muco-connective-epithelial membrane determined by a mesothelial-fibro-epidermal component has been established, with the presence of the predecessor fibro-muscular tissue and mixed vascular blood-lymphatic and protective local follicular-lymphoid, tissues which during the extrauterine period have a significant impact on the evolution of reparative processes.In the uncomplicated omphalocele there are some major risk factors in the development of spontaneous ruptures, inflammatory processes by placental complex contamination, the risk of thromboembolic placental-fetal syndrome during the intranatal period with obvious hemorrhagic and early neonatal repercussions on the omphalocele level.Some etiopathogenetic features have been identified which partially confirm the hypothesis advanced by some authors that omphalocele develops secondary to migration and maturation disorders of myoblasts in the abdominal wall.

Thus, in the uncomplicated major omphalocel, with significant viscero-abdominal disproportion, taking into account the architectural structure of the sac, there are favorable conditions for reparative processes, with the gradual epithelization of the sac and its transformation into ventral hernia. The low rate of lethality in the studied group justifies conservative behavior in the given form of malformation. In intra-amnional involvement there is a risk of penetration of the infectious-inflammatory component of the omphalocele, especially in delayed cases, with possible postnatal contamination.

Keywords: omphalocele, viscero-abdominal disproportion, ventral hernia, morphological examination

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Introduction

Omphalocele (*exomphalos*) represents a medial defect of the anterior abdominal wall at the base of the umbilical cord, covered by an amnio-peritoneal membranous sac, through which the abdominal organs are extruded [1, 23]. The omphalocele dimensions and location have important implications in the therapeutic conduct of this malformation. The defect size ranges from 2 cm to 12 cm, and the location can be centered on the upper, middle or lower abdomen [13, 17]. The membranous sac, on which the umbilical cord is implanted, consists of the amnion, Wharton`s jelly and peritoneum [16, 27]. The omphalocele contents include: intestinal loops, often liver portion and occasionally other organs, such as the spleen [18].

The type of omphalocele is determined by the embryonic fold involved in the pathological process. Thus, epigastric omphalocele resulting from the cephalic envelope defects, was found in the pentalogy of Cantrell (epigastric omphalocele, anterior diaphragmatic defect, sternal defect, pericardial defect, and associated intracardiac defects). The lateral fold defects cause the development of the *"classic"*omphalocele, while the caudal fold defects cause hypogastric omphalocele, bladder and cloacal exstrophy.

Omphalocele may be a part of various genetic syndromes, indicating that this malformation does not have a specific etiology [8, 9, 17]. Animal studies, as well as human gene research, have highlighted several genes incriminated in the development of this defect, including:Rock-1, Pitx2, IGFR-1, FGFR1 and FGFR2, FOXA2 and Hoxb4, Alx-4, MSX1 etc. [19]. Familial cases of omphalocele have also been described [21].

The management of omphalocele, which aims at closing the defect, depends mainly on its dimensions [2, 7], the reduction of abdominal viscera, the presence of complications, the degree of pulmonary and cardiovascular insufficiency, associated anomalies [10,20].

Practice has shown that only in 30% -50% of cases the defect can be primarily closed, in most cases alternative correction strategies being needed [5].

In the literature special attention is paid to surgical techniques based on the macroanatomic peculiarities of omphalocele and less on the structural and morpho-functional ones, including the adjacent umbilical-abdominal area, being important in the medical-surgical management of this condition, which justifies the approach of this issue in the present study.

The purpose of the study was to elucidate the morphostructural and morphofunctional features of the wall and regional area of uncomplicated omphalocele in estimating the prognosis of evolution of local complications and the choice of treatment tactics.

Material and Methods

The study group included 18 new-born babies, 37-40 weeks of gestation, with birth weight 2850-3780 g, of which 4 (22.2%) with major omphalocele and 14 (77, 8%) with minor and medium uncomplicated omphalocele, predominantly medium-sized one.

The morphological examination was performed on the adjacent region of the abdominal wall, theomphalocele domewall and the adjacent umbilical cord areas (fig. 1). In 5 (27.8%) cases,the placental complexes were examined morphoanatomically. Tissue samples (1.0×1.0×0.5 cm) of anatomical-surgical specimens taken intraoperatively from the mentioned omphalocele areas, on average 6-7 samples,were used as material for histomorphological examinations.In 7 (38.9%) cases, the intraoperative abdominal muscle biopsy (0.3x0.6 cm) was taken. There were taken 5-6 samples from the placental complexes, including annexes.

The tissue samples were preserved in Formol 10% for 6-12 hours, then processed according to the standard protocol for histological investigations with the automatic histoprocessor (Diapath) and the staining network (Raffaello) of the histomorphological tests. At the staining stage the following methods were used: *hematoxylin-eosin* (H & E) and selectively *Van Gieson* (VG) to highlight the connective tissue, and *Azur-Eosin* (A & E) to test the presence of mycotic-bacterial flora. The histological examination was performed using the following microscopes: Nikon Labophot-2 and Carl Zeiss with *oculars× 10, lenses × 2.5; × 10; × 20; × 40.*

Results and Discussions

The omphalocele diameter varied between 3.5 cm and 12 cm, having a non-uniform translucent wall (fig. 1). In 11 (61.1%) cases, the presence of the vascular network, radially or spirally traced in the wall area was confirmed, more frequently at the domeand adjacent to the proximal cutaneous resection area. In 7 (38.9%) cases, the vascular network was more compact, embedded in a gelatinous cord (proper umbilical cord), with increased density, with or without vascular varicosities, passing continuously into the umbilical cord. In the basal area, the omphalocele wall is unevenly thickened, matte or whitish. Some vessels, along the trajectory, have a purple shade of varying intensity due to the gelatinous tissue, including the umbilical cord in the omphalocele area.

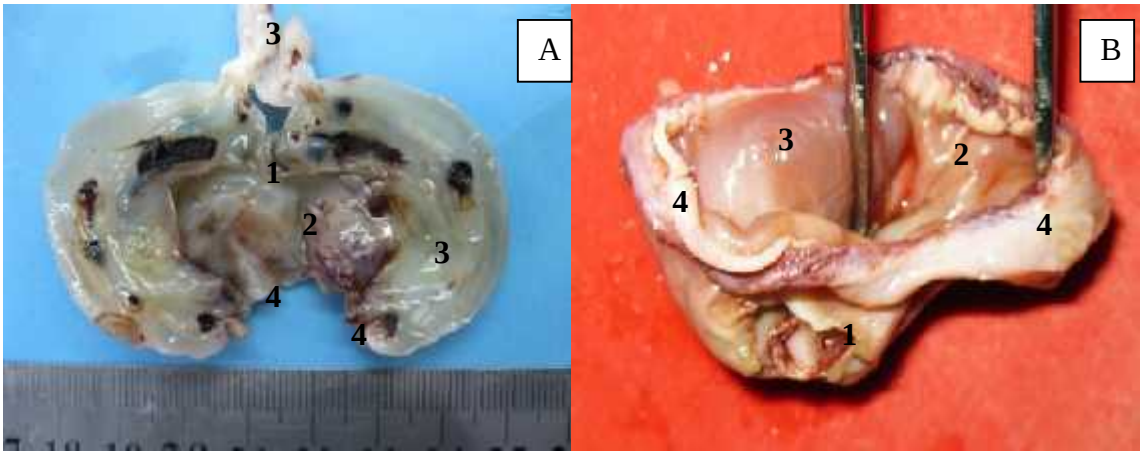

Fig. 1. Anatomo-surgical specimens.Excisionedomphalocele.Hernialsac - omphalocele: 1 - apical-umbilical area; 2 - gelatinous membranous wall; 3 - umbilical cord in the hernial wall area; 4 – adjacent cutaneous area

Another characteristic of omphalocele, found in 4 (22.2%) cases, was the presence of adhesion structures. In one case, a partial herniation of an intestinal segment through the double orifice was determined through the adhesion. This phenomenon, in our opinion, deserves attention because it reflects the pathogenesis of omphalocele and indicates the preexistence of a major risk of strangulation of the mentioned intestinal segment.

The membraneous wall of omphalocele had a gelatinous consistency due to the predominance of the fundamental extracellular substance compared to the cellular one, the fibrillary component being less present. From the outside, omphalocele was circumscribed by amniotic or pavemental epithelium, andunistratified directed to the adjacent area. The inner omphalocele surface, in all cases and throughout the whole area, is represented by mesothelium. Thus, there are two layers in the omphalocele structure: *external muco-connective*, avascular, lax, where the fundamental extracellular substance prevails, and *internal muco-connective-vascularized*, much more compact and hypercellularized, with pseudofibrillary aspect and the presence of the vascular component (fig. 2A). In the umbilical cord only the muco-connective tissue is present with a dispersed discrete cellular component (fig. 2B). In the samples taken from the omphaloceledome, the internal area is much more diminished, sometimes merging with the epithelial structures of the mesothelium and amnion, determining itsdimorphic muco-connective-epithelial membranous structure. Depending on the investigated areas of the omphalocele and the tissues in the adjacent area, including abdominal muscle biopsy, a structural variation of the tissue and vascularization component was observed. In the samples taken from the omphalo-abdominal proximal region, starting with the region adjacent to the abdominal tissue structures (resection level), in the omphalocele wall within 1.5-2 cm, in some areas up to 3 cm, towards the domeor apical area of omphalocele, mosaic structures architecturally similar to the abdominal ones were found, the internal muco-connective-vascularized area being rich in fiber and supplied with a much more developed vascular network.

Microarhitecturally, closely to the defect, between the muco-fibro-vascular and muco-connective components myocytic and fibrotic elements were found, being dispersed chaotically and ordered in bundles, forming a lax fibro-muscular layer to the omphalocele dome. At the median level, the fibrillary-myocytic component was more orderly, on some areas with fascicular appearance. Later on, the presence of a comparatively dense fibromuscular fascicular layer, predominantly of connective-fibrillary or fascicular origin, was found. Throughout the internal area, mesothelium, regardless of its volume, was present.A lax connective tissue layer supplied with an abundant vascular network was present towards the periphery (fig. 3A). The gelatinous component was circumscribed towards the periphery, in different proportions, by fibrocytic-fibroblastic cellular elements, among which small capillaries and angioblasts could be found. Externally, a squamous pavemental epithelial layer was found, which, towards the omphaloceleapex, transformed into a pluristratified or unistratified layer of amniocytes.

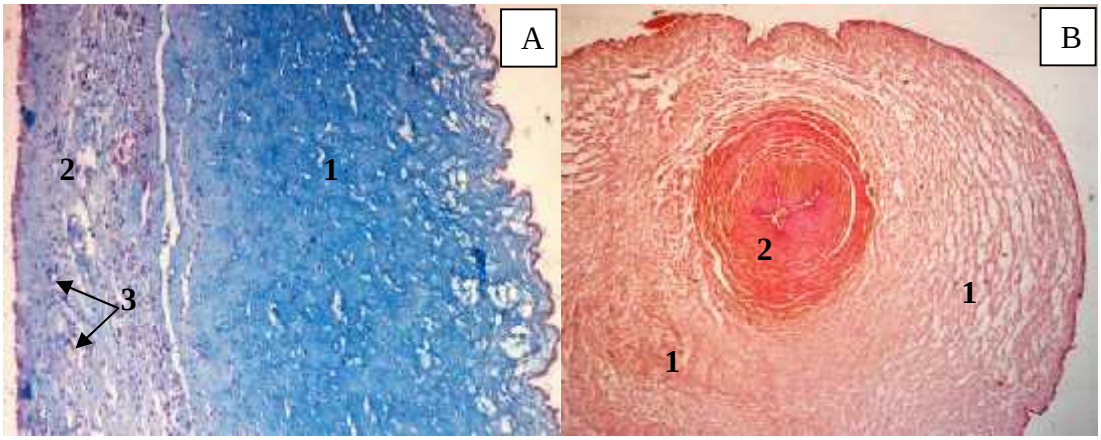

Fig. 2. Muco-connective component in omphalocele and umbilical cord. A-omphalocele: 1-external muco-connective area; 2 - internal muco-connective-vascular area; 3 - venous capillaries × 75. *Alcian blue staining*; B - umbilical cord: 1- muco-connective component; 2 - umbilical artery × 25. *Hematoxylin-Eosin Staining*

Vascular structures, especially those in the umbilical cord, exhibited dysplastic processes of the vascular tunica muscularis. The musculo-fibro-vascular component sometimes had a chaotic fibro-cellular appearance, consisting of fibrocytes, myocytes, and mucocytes with small gelatinous accumulations, including the area adjacent to the omphalo-abdominal aperture (fig. 3B).

In other areas,the deficiency of fibro-cellular and fibrocytic-muscular components with ordered or lax aspect, especially at the apical level of the omphalocelewas observed, as well asaltered and hydropic degenerations, with the formation of serous accumulations(fig. 3C). In 8 (44.4%) cases, nodular and follicular lymphoid structures (fig. 3D) were found in the orifice of the hernial sac (omphalocele), arranged in chain on the perimeter of the orifice, sometimes in the gelatinous area, in the form of lymphocyte depletion of sinusoid type. Lymphoid structures could also be observed throughout the vascular network, with a varied depletion of the lymphocyte component.

In some cases the presence of amniotic adhesions was found in omphalocele on the internal surface, with connective-vascular mesothelium-coated cords and supplied with small and medium capillary and vascular network, sometimes with small lymphocytic pseudo-follicular structures (fig. 4A). In 2 cases, solitary myocytes were detected. Adhesion changes point to another omphalocele genesis, which differentiates it ontogenetically from the umbilical hernia itself. The presence of lymphoid structures at this level may, in our opinion, can be the consequence of the amnio-liquid content action that can penetrate the gelatinous layer, as well as the lymphoid-cellular barrier function of protecting the eventrated intestinal loops or the abdominal cavity.

In the exploration of the abdominal muscle area in the immediate vicinity of the omphalocelic orifice, an obvious disruption of the muscular connective and cellular-adipose tissue components manifested by an amorphous and irregularly structured appearance was confirmed (fig. 4B, C, D). Muscle tissue is composed of bundles of hypoplastic and hypertrophied muscle fibers that are oriented disorderly between themselves and in relation with cell-adipose tissue and fibrillary connective tissue (fig. 4B). In some samples, a correlation between identical tissues is preserved except for the hypotrophy of myocytes (fig. 4C), some areas being more hypotrophic or as myocyte islets, embedded in the connective tissue mass (fig. 4D).

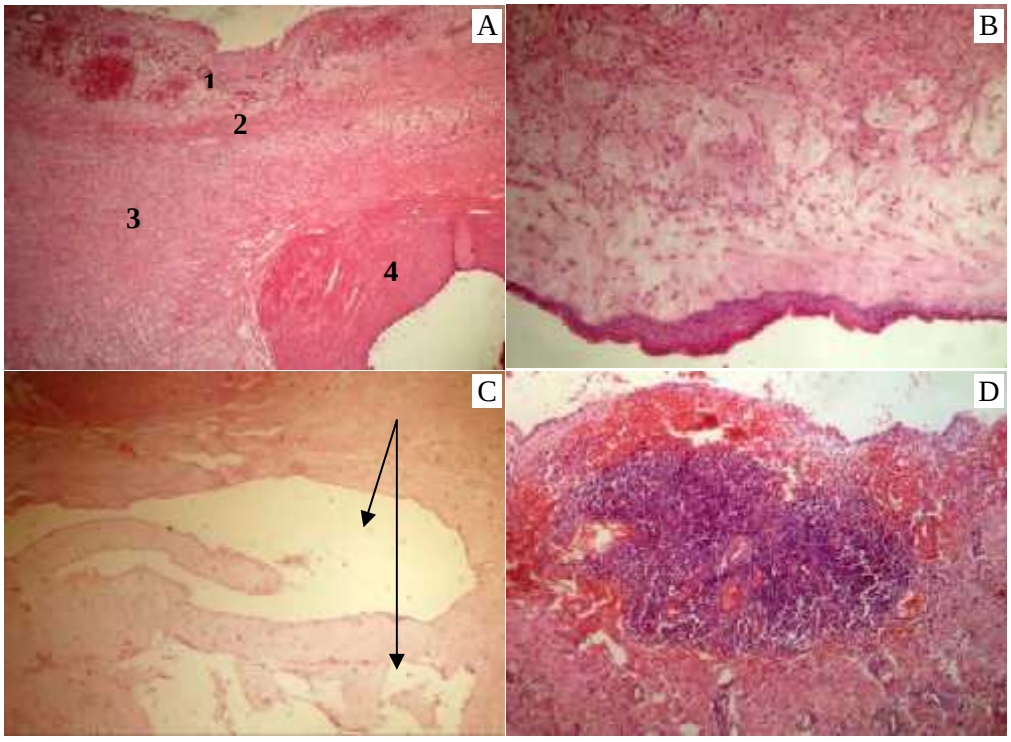

Fig. 3. The overall histopathological appearance of the omphalocele. A - internal structure of the omphalocele wall: 1 - vascular network; 2 - fibromuscular layer; 3 - gelatinous substance; 4 - umbilical vessel with the tunica muscularisdysplasia; B - Peripheral area of the omphalocelic wall: 1 cellularized gelatinous mass with fibrocytic-fibroblastic cells; 2 - multilayered squamous pavemental epithelium; C - gelatinous area with hydropic degeneration with serum fluid accumulation; D - follicular lymphocellular structures in the area adjacent to the resection.

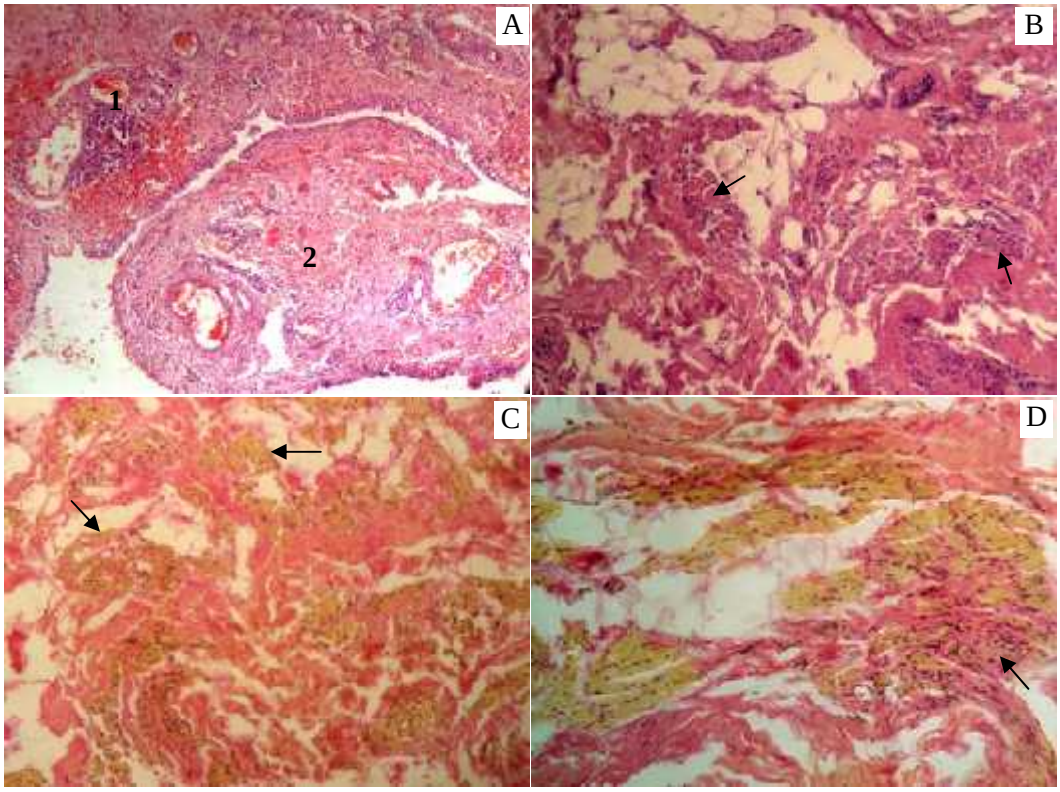

Fig. 4. Histopathological aspects of the abdominal muscle component A - internal structure of the omphalocele wall: 1 - fibro-vascular adhesion with vascular network coated with mesothelium; 2 - the perivascular lymphocytic pseudo-follicle in the omphalocele wall in the adjacent area × 25; B - disordered muscular bundles with a hypertrophic appearance in the fibrillar-connective and cellular-adipose tissue component. × 75; C - slightly ordered abdominal tissue plate with hypertrophied muscle fibers × 75; D - islets of muscle fibers and myocytes with intumescence aspectand atrophy of connective tissue masses. Colors H-E (A, B) and VG (C, D)

In 7 (38.9%) cases the presence of an inflammatory process in omphalocele structures was found (fig. 5A, B), especially in cases where the inflammatory processes involved the placental complex structures. The inflammatory process had different intensity, especially in the middle and apical areas of the omphalocele, being more pronounced in cases resolved surgically 3-5 days after birth. A pronounced inflammatory process was concomitantly detected on the internal side, being less pronounced in intermediate or superficial areas. In these cases, a visceral intestinal peritoneum reaction could also be observed.

At the same time, vascular dysplasia was confirmed both in the umbilical cord area included in omphalocele and in its branches. In 5,6% (1) of cases, vascular aneurysm was detected, which ruptured during the first hours after birth (fig. 5C), the muco-fibrillary component being invaded with red blood cells masses, resembling hemorrhagic accumulations (fig. 5D).

Histological examinations of placental complexes in neonates with omphalocele (10 cases) allowed changes to be observed in both the villous chorion and the amniotic membranes.

In 27.8% (5) of cases there were maturation changes of the villous chorion corresponding to the term of gestation, minimal adaptive compensatory processes, predominantly in the presence of nonspecific inflammatory lesions, confirmed in 16.7% (2) of the cases. Calcification foci, marked fibrosis and dilated-varicose angiopathy characterized by small and large varicosities, especially of venous vessels, including truncal villosities (fig. 6A, B), have been reported. Some aneurysms of impressive size, compared to villosity, and very thin walls, advocate for vascular dysplasia that occurs at the embryonic or embryonic-fetal stage (fig. 6B).

In placental angiopathies there was found the presence of thromboembolism in the lumen of venous vessels, indicating the risk of a placento-fetal thromboembolic syndrome and the evolution of vascular thromboembolic lesions in the omphalocele (fig. 6B). Following the exploration of the vascular network of omphalocele and the placental complexes, there was found an omphalo-umbilical and villous chorion vascular dysplasia, i.e. the fetal vascular network. Therefore, its evolution begins at the stage of the fetal concept and continues until the first 3-5 weeks of intrauterine development, which corresponds to the embryonic period when the blood circulation installs with repercussions, especially on the placental-allantoid one.

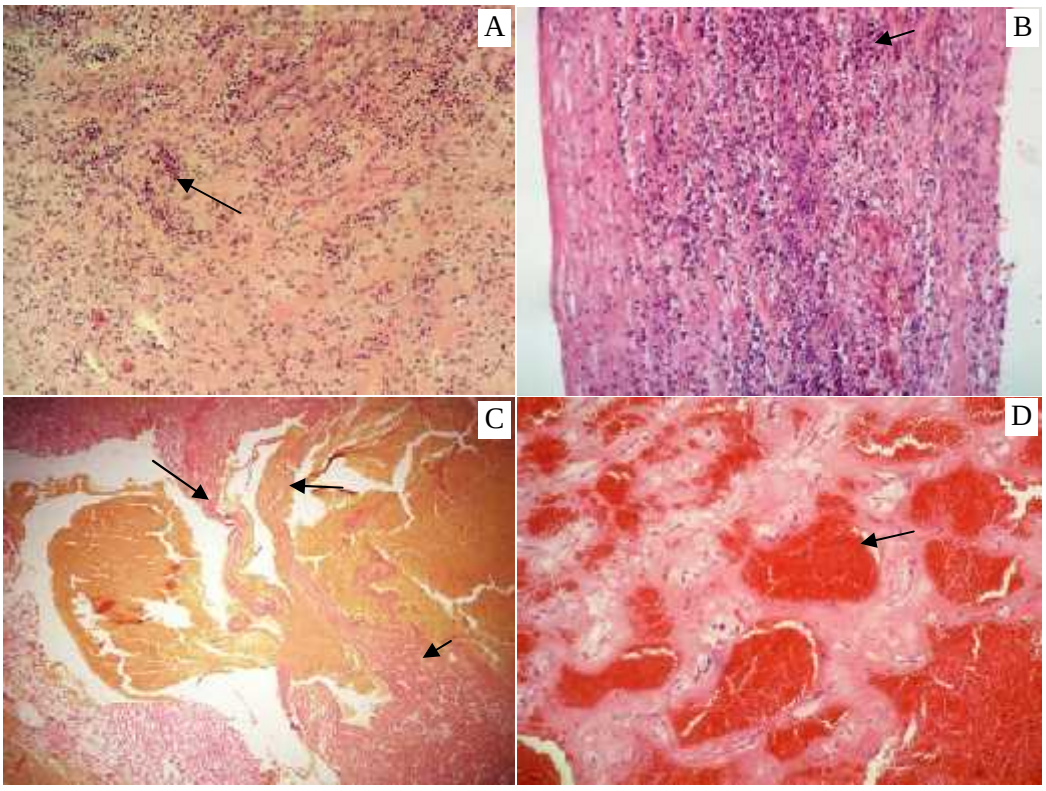

Fig. 5. The appearance of pre-existing lesions, accidentally evolving in omphalocele. A - microfocal and dispersed lympho-leukocytic inflammatory process in the proximal area of the resection × 50; B - micro-abscessed leukocytic inflammatory process in the middle area of the omphalocele wall × 75; C - ruptured aneurysm with the invasion of the musculo-fibrillary component of omphalocele. D - blood accumulations in the muco-fibrillary tissue of the omphalocelic umbilical segment. × 75. H-E staining (A, B, D); VG (C)

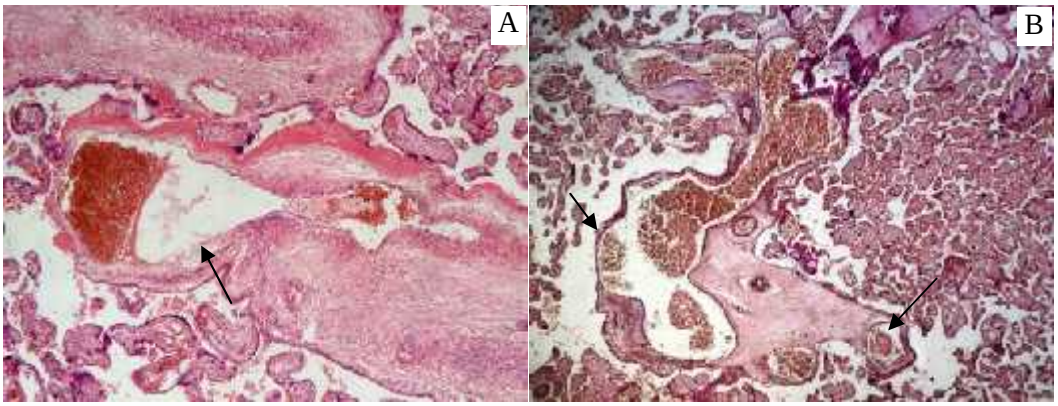

Fig. 6. Histopathological aspects of placental villous chorion vascularization in omphalocele. A - varicose dysplasia of the venous villous truncal vessel × 25; B - Varicose veins of a villous chorion tree with the presence of thromboembolus in the lumen × 25. *H-E staining.*

At the level of the villous chorion, a delayed discronism was identified with aspects of deficiency of the stromal connective component of the intermediate and terminal villosities, which determined their moderate monstrous appearance (fig. 7B). At this level, the syncytial epithelium was attenuated, poorly differentiated and with less proliferation in the form of buds. This could suggest a correlation between reduced cellular-syncytial activity and deficiency of connective density of the villosity stroma.

In some areas, varicose ectasia (fig. 7C) involved the entire venous vascular network of terminal, intermediate and truncal villosities. This phenomenon could be the consequence of hypertension in the venous trajectory, possibly, also at the level of the great vessels of the placental chorio-amnional plaque and umbilical cord.

In 8 cases there were some changes in the villous chorion arterial network, manifested by hypertrophic-stenotic arterial angiopathies in the truncal and intermediate villosities, unevenly zonally or segmentally distributed (fig. 7D). At the level of the basal decidua membrane, lymphocyte infiltration, more frequently focal one, of variable intensity, was determined, ranging from discrete to moderate. Concomitantly with the inflammatory process, significant fibrinoid deposition was detected at this level in the inter-villous spaces (fig. 7A). The morphopathological changes of the membranes comprised discrete and moderate micro-macrofocal leukocyte infiltration, in some areas associated with edema and amnion dystrophy (fig. 7B).

In the case of an amniotic adhesion, the amniotic epithelium manifested an active proliferation of the amniocytes, more pronounced in the membranes and at the level of the amniotic adhesion (fig. 7C).

On the basis of the revealed findings, we can conclude that, in the case of omphalocele, in the placental complexes there is a dysplasia of the villous chorion associated with varicose arterio-venous angiopathy and hypertrophic-stenotic arterial angiopathy. Vascular alterations found at this level, in our opinion, may be present from the very beginning along with the deficiency of the stromal connective component, or may be a consequence of omphalocele. Depending on the size, it may induce the hypertensive phenomenon in the umbilical vein with reflection on the chorionic vascularization, causing the hypertrophic spasm of the arterial network.

At present, according to histomorphological features and etiopathogenesis, omphalocele is a hernial sac in the omphalo-umbilical abdominal segment. However, over time, this malformation has been treated as an umbilical cord hernia in the structure of umbilical cord malformations or the abdominal supra-umbilical region caused by lack of aponeurosis and herniation of the peritoneal membrane at the umbilical fossa level.

The earliest description of omphalocele belongs to Ambroise Parè [15] and the first success in its surgical treatment were recorded by Hey (1803) and Hamilton (1806). Scarpa (1812) drew attention to the association of omphalocele with other malformations, which determines the fatal prognosis of omphalocele. Ahlfeld (1899), applying alcohol dressings on the hernial sac, was the first to treat omphalocele without surgery [15, 24]. At the moment, theetiopathogenesis of omphalocele is not fully elucidated [14].

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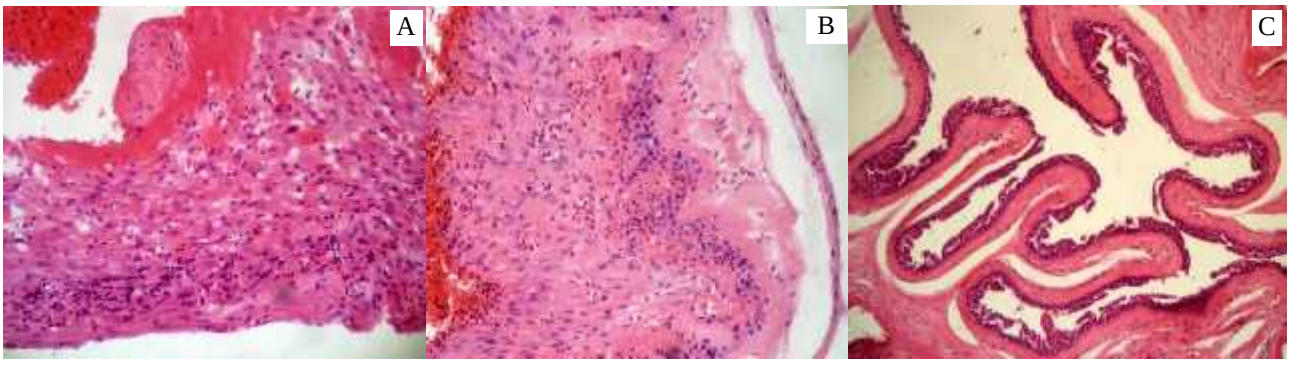

Fig. 7. A - moderate lymphocyte basal deciduitis in the focus. B – amniotic membrane, focal serous- leukocyte membranitis× 25. C - Papillary proliferation of amniocytes at membrane level. × 100. H & E staining

According to the study results, omphalocele is a vicious defect, triggered in the embryonic period in the abdominal wall, especially the omphalo-umbilical region. The deficiency and structural disturbances of the abdominal wall muscles in the areas underlying the omphalo-umbilical orifice as well as functional muscular dischronism serve as evidence. The latter is characterized by muscle fiber atrophy and hypertrophy, muscle fragmentation and disordered muscle fiber orientation in relation to fibrillar-connective tissue and cellular-adipose tissue, which causes a considerable muscle deficiency at this level.

Determination of the muscular, fibrillar-connective and epidermal-epithelial elements in omphalocele contradicts the assertions that omphalocele includes only the peritoneum elements and the amniotic membrane of the umbilical cord. The presence of epidermal fibro-muscular elements and vascularization may accelerate reparative and epithelialization processes of the muco-fibro-epithelial sac of omphalocele

Based on the results obtained, we can conclude that omphalocele is not a simple umbilical hernia, which is not a serious problem for pediatric surgery, but a defect of the abdominal muscles separation in the omphalo-umbilical region. The insignificant visual defects in the orifice are associated with major regional abdominal disturbances of the rectilinear musculature, being a problem in the medical-surgical management of this malformation and in the application of the umbilical cord ligature.

In this regard, some researchers believe that the midgut disturbances of return into the abdominal cavity underlie the malformation development during the embryonic period, after the normal embryonic herniation in the umbilical cord in the 6th-12th week of the intrauterine development, and the central migration of the mesodermal fold [12, 25, 26]. The liver does not migrate out of the abdominal cavity and, therefore will not be present in the physiological hernia contents. However, some authors state that if the lateral folds do not close, then there is a major defectof the abdominal wall, through which the abdominal cavity contents, including the liver, will herniate [11].

According to some studies, the differentiation of the abdominal wall muscles simultaneously occurs with the process of intestine rotation and return of the intestinal loops into the abdominal cavity. The above mentioned plays a central role in the development of omphalocele [6]. The primary abdominal wall is made up of ectoderm and the lateral mesodermal plate(somatopleura) which extends laterally and coalesces along the ventral medial line around the navel, forming the abdominal cavity. Myoblasts, migrating from the myotome to the primary wall, form secondary structures such as muscles and connective tissues. Thus, when the secondary abdominal development is completed, the abdominal wall is composed of four pairs of muscles (*oblique externe, oblique interne, transvesus abdominae and rectus abdominae*), surrounding connective tissues and skin. The orientation of the myofibrils in a particular muscle is unidirectional and distinct from the adjacent ipsilateral muscles and symmetrical to the muscle pair on the contralateral side [19, 22]. Omphalocele results from staged developmental disturbances of the secondary abdominal wall, caused by the failure of the migration process of myoblasts to thedestination point, with the alteration of spatial relations between the oblique and transverse muscles [19]. In giant omphalocele there are two distinct correction strategies, including surgical closure of the abdominal defect after multiple operations and delayed nonoperative closure by measures that contribute to the sac epithelialization [4, 5].

Soave F. (1963) considered that prognosis in omphalocele, especially in giant forms, could be improved if the conservative treatment were considered by surgeons with more confidence [24]. Currently, this strategy remains a safe and effective alternative to the treatment of omphalocele [3].

Conclusions

1. The morphological structure of omphalocele as a dimorphic muco-connective-epithelial membrane determined by the mesothelial-fibro-epidermal component has been established, with the presence of the predecessor fibro-muscular tissue and mixed vascular blood-lymphatic and protective local follicular-lymphoid, which during the extrauterine period have a significant impact on the evolution of reparative processes.
2. The presence of major risk factors of uncomplicated omphalocelein the evolution of spontaneous rupture, inflammatory processes by placental complex contamination, the risk of thromboembolic placental-fetal syndrome and in the omphalocele wall during the intranatal period with obvious hemorrhagicand early neonatal repercussions at the omphalocele level.
3. In 22.2% of cases, anatomic abnormalities of omphalocele, determined by adhesion aspects and adhesions, have been found, which can contribute to the strangulation of loops, herniated organs with irreversible complications, especially the intestinal segments.
4. Some etiopathogenetic features have been identified which partially confirm the hypothesis advanced by some authors [19] that omphalocele develops secondary to migration and maturation disorders of myoblastsin the abdominal wall.
5. In major uncomplicated omphalocele, with significant viscero-abdominal disproportion,

taking into account the architectural structure of the sac, there are favorable conditions for reparative processes, with gradual epithelization of the sac and its transformation into ventral hernia. The low lethality rate in the studied group justifies the conservative behavior in the given forms of malformation.

6. In intra-amnional involvement, there is a risk of the infectious-inflammatory component to penetrate omphalocele, especially in cases that are resolved with delay, with a possible postnatal contamination.

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