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CYTOMORPHOLOGICAL STUDIES OF CELL COMPONENTS OF THE PERIPANCREATIC FLUID COLLECTIONS IN THE EVALUATION OF CLINICAL COURSE SEVERITY OF ACUTE COMPLICATED PANCREATITIS

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Abstract. Purpose. To study the character and peculiarities of cytomorphological changes of cellular sediment material of fluid collections (FC) as criterion for objective assessment of the clinical course severity in acute complicated pancreatitis (ACP).

Materials and methods. The results of cytological researches of peripancreatic sediments of FC obtained during interventional ultrasonography in 51 (88%) and videolaparoscopy in 7 (12%) observations in 58 patients on ACP were analysed.

Results. It was found that in intraabdominal FC (n=37) in 10 (27%) cases the dominating of proliferative mesothelium with its polymorphism was observed. In 15 cases (41%) degenerative-dystrophic changes of cytoplasm whippings with the appearance of large "ring-similar" cells were manifested. In 12 studies (32%), atypically altered mesothelium cells with anisocytosis and anisonucleosis, as well as cytomorphological changes similar to the neoplastic process were detected. In retroperitoneal localization of FC (n=21) more significant changes were observed in granulocyte-nuclei cells, in particular, in 9 cases (43%), irreversible violations of their structure were identified as phenomena of cariopicnosis, carioresix and cariolysis. Was established that depth of structural changes of mesotheliocyte cells and neutrophil granulocytes depended on degree of ACP severity.

Conclusions. Estimation of cytomorphological changes of the FC cell components can serve as objective criterion of the ACP severity.

Key words: *acute complicated pancreatitis, fluid collections, cytological research.*

Introduction. The updated classification of acute pancreatitis (AP) (Atlanta, 2012) provides an in-depth description of local disease complications and, first of all, pancreatic fluid collections (FC) [2; 4; 9]. Thus, the following FC types distinguished. 1. Acute peripancreatic FC with aseptic contents without signs of pancreas necrosis and parapancreatic fat, which are aseptic (Acute peripancreatic flud collection – APFC). 2. Acute necrotic FC with different amounts of both fluid and necrotic tissue fragments associated with the necrosis in pancreas parenchyma and/or parapancreatic tissue (Acute necrotic collection – ANC). 3. Post-necrotic infected pancreatic and/or parapancreatic FC with contents in the form of a fluid component/purulence and necrotic tissue/detritus predominantly infected (Post-necrotic pancreatic/retropancreatic flud collection – PNFC).

Remarks to this classification indicate that the operational tactical approaches in these complications have their own characteristics [9]. Is it possible to assess FC content in determining the severity of the clinical course of disease?

Purpose. To study the character and peculiarities of cytomorphological changes of cellular sediment material of fluid collections (FC) as criterion for objective assessment of the clinical course severity in acute complicated pancreatitis (ACP).

Materials and methods. Cytomorphological study of peripancreatic FC sediment produced during interventional ultrasonography in 51 (88%) and video-laparoscopy in 7 (12%) observations was performed in 58 patients who were under the inpatient treatment in the City Pancreatic Centre at the Academic Department of General Surgery of Danylo Halytsky Lviv National Medical University, with a confirmed ACP diagnosis (based on clinical, laboratory-biochemical, radiological and instrumental methods). The age of hospitalised patients ranged from 22 to 74 years. 36 female (33%), 73 male (67%). The cytological study of pancreatic and peripancreatal FC contents provided for the implementation of two stages – pre-analytical and analytical. The first one included qualified collec-

tion and transportation of study material, which was important for further result. The analytical stage provided for a cytological study of native and stained samples. Samples were Pappenheim-stained.

Fluid collections content was transferred into test tube or other, more spacious, clean, dry labware with 5% sodium citrate solution at a rate of 2–5 ml per 100 ml of the test material in order to stabilize it and prevent the destruction of cellular elements. With a considerable volume of fluid material, it was centrifuged at 1.500 rpm for 5–10 minutes, after which supernatant was discharged, and 4–6 preparations were received from the precipitate with drying for 1 hour and subsequent staining. Further study was performed using BIOLAM and MIKMED-5 light microscopes with a magnification of ×40, ×90, ×100. Microscopy was applied to both native and stained specimen with small and large microscope magnifications (immersion system). The obtained study results were processed using variation statistics of t-test, Fischer test and χ^2.

Results. The obtained study data provided grounds to state that as a result of the aggressive environment effect of the peripenetrating fluid collections with high levels of activated enzymes and proinflammatory cytokines on cellular elements resulted in pathological changes of all cellular elements as determined in cytological specimens. However, the most significant and indicative were the changes in FC mesotheliocytes with intra-abdominal location (37 observations), since these cells, being the main structural elements of serous membranes, in particular parietal and visceral peritoneum, were in direct contact with enzymatically active pancreatic exudate.

Thus, 10 (27%) studies showed dominance in cytological specimens of proliferating mesothelium, characterized by large mesotheliocytes, nuclei and their polymorphism. 15 (41%) cases showed degenerative-dystrophic changes in both cytoplasm and mesotheliocytes in the form of cytoplasmic protrusions, its vacuolation, appearance of foaminess, sometimes with large castration cells. 12 (32%) studies showed the presence of atypically altered mesothelium cells with anisocytosis and anisonucleosis, as well as cytomorphological changes similar to neoplastic process (Fig. 1, 2).

Cytomorphological abnormalities of peripancreatic FC content with their localization in retroperitoneal space (21 observations), in the absence of direct contact of the pancreatic fluid with peritoneum, were most significant in neutrophilic granulocytes. Thus, all studies showed changes in these cells cytoplasm in the form of toxic grains and vacuolations both in individual cells and most neutrophil granulocytes, intensive basophilia, decreased specific graininess and appearance of circular colourless spots, which reflected the initial process of degenerative-dystrophic cell changes.

However, more significant changes were observed in granulocyte nuclei. Thus, in 9 (43%) cases, irreversible structural damages were observed characteristic of the gradually-sequential stages of death, namely karyopyknosis, karyoclasis and karyolysis (Fig. 3, 4).

An analysis was performed of cytomorphological changes in mesotheliocytes and neutrophil granulocytes with intra-abdominal and retroperitoneal FC location depending on the severity of the clinical course of disease according to AP classification criteria (Atlanta, 2012) [2] (Table 1 and 2).

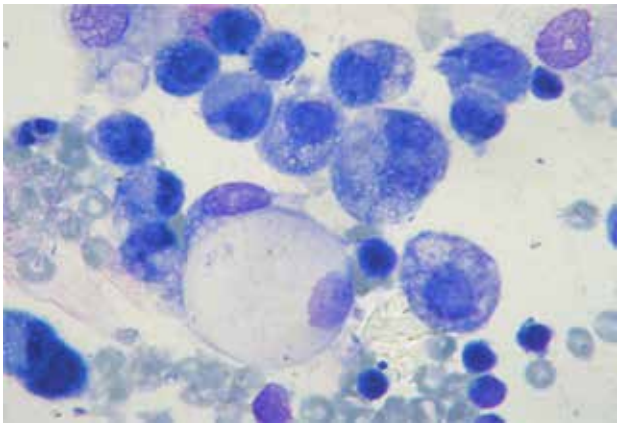

Fig. 1. Degenerative-dystrophic changes in cytoplasm. Castration cell

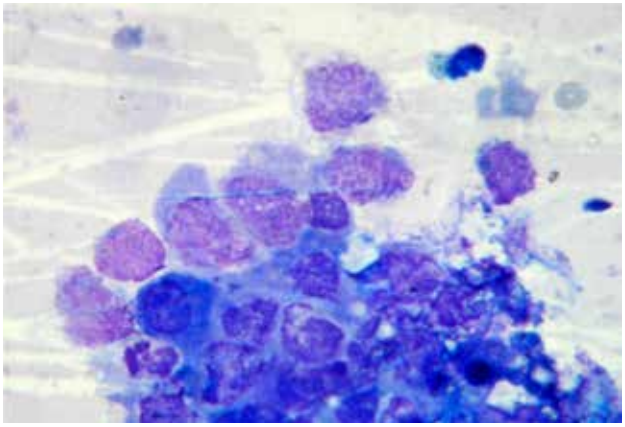

Fig. 2. Atypically altered mesothelium cells. Anisocytosis, anisonucleosis, polymorphism of cells and nuclei

As can be seen from the data presented in tables, in moderately severe ACP, in contrast to the severe clinical course of the disease, the cytological presentation of intra-abdominal FC was characterized by damage to mesotheliocytes structure in the form of their degenerative-dystrophic changes – in 14 (58%) observations vs. 1 (8%) case ($\chi 2 = 6.593$; $p = 0.01$), while the incidence of mesotheliocytes proliferations did not have statistically significant differences – 9 (38%) vs. 1 (8%) of observations ($\chi 2 = 2,438$; $p > 0.05$)

This severe clinical course of the disease was characterized by atypical forms of mesotheliocytes and their nuclei, similar to cells of neoplastic genesis, as observed in 11 (84%) observations vs. 1 (4%) cases ($\chi 2 = 21,368$; $p < 0.001$).

The peculiarities of neutrophil granulocyte changes in the retroperitoneal peripancreatic FC were that both in moderately severe and severe ACP there were cytomorphological damages of cells cytoplasm in the form of degenerative-dystrophic changes. However, in the severe course of disease, in addition to cytoplasm, cell nuclei were also affected by destructive process in the form of karyopyknosis, karyoclasis and karyolysis –5 (71%) observations vs. 1 (7%) case ($\chi 2 = 10,286$; $p = 0,001$). Consequently, the depth of structural changes in mesotheliocytes and neutrophil granulocytes depended on ACP severity. The obtained results provided grounds to work out the “Assessment method of acute necrotic pancreatitis severity” and “Prognostication method for clinical course of acute destructive pancreatitis” [7], according to which the evaluation of cytomorphological changes in mesotheliocytes and neutrophil granulocytes in peripancreatic FC content can serve as a commonly available criterion for determining ACP severity.

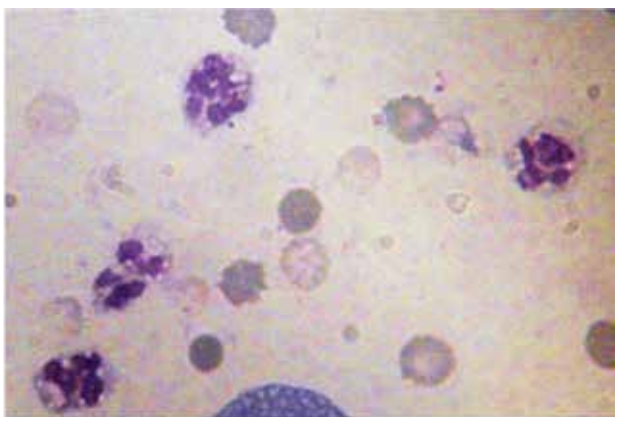

Fig. 3. Vacuolation of the neutrophil granulocytes cytoplasm

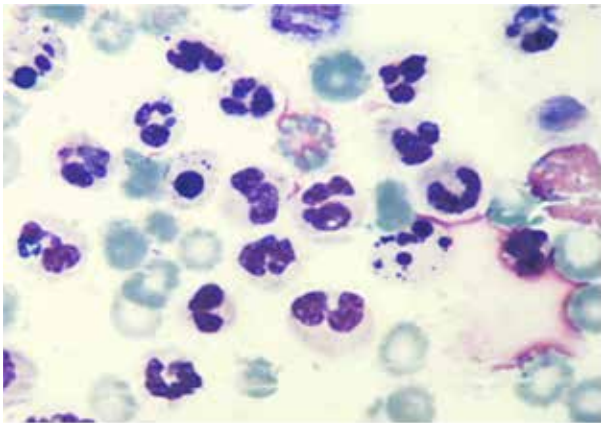

Fig. 4. Changes in granulocyte nuclei. Karyopyknosis, karyoclasis and karyolysis

Table 1

Cytological characteristics of intra-abdominal FC mesotheliocytes with moderately severe and severe ACP

Cytomorphological changes in mesotheliocytes	Moderately severe ACP n=24 (65%)	Severe ACP n=13 (35%)
Mesotheliocytes proliferation	9 (38%)	1 (8%)
Degenerative-dystrophic changes in cytoplasm and mesothelium nuclei	14 (58%)	1 (8%)
Polymorphism of mesothelium cells and nuclei (cellular atypia)	1 (4%)	11 (84%)
Total	24 (100%)	13 (100%)

Table 2

Cytological characteristics of neutrophilic granulocytes of retroperitoneal FC in moderately severe and severe ACP

Cytomorphological changes of neutrophil granulocytes	Moderately severe ACP n=14 (67%)	Severe ACP n=7 (33%)
Degenerative-dystrophic changes in cytoplasm	13 (93%)	2 (29%)
Destructive damages of nucleus – karyopyknosis, karyoclasis and karyolysis,	1 (7%)	5 (71%)
Total	14 (100%)	7 (100%)

Discussion. An unbiased assessment of ACP severity is the basis for determining treatment strategy and tactics in patients with this disease. However, the existing integral prognostication scales for disease severity as a general intensive care profile (APACHE II, SAPS, MODS, SOFA), and specifically adapted for acute pancreatitis (Ranson, Leere, Blamey, Balthazar, BISAP) are quite cumbersome and inaccessible to practical application [5; 7; 9]. Recently, studies have been widely conducted to identify certain criteria for disease severity, the so-called ACP predictors, such as the emergence of hydrothorax [3], changes in erythron parameters and iron metabolism [1], neutrophils damage system [8]. The proposed method is affordable, cost-effective and fast, which greatly contributes to addressing this issue.

Conclusions:

1. Clinical course of ACP shows cytomorphological changes in peripancreatic FC contents, which are the most significant and indicative in mesotheliocytes with intra-abdominal FC localization and neutrophil granulocytes with their retroperitoneal arrangement.

2. Assessment of the extent of identified cytomorphological damage in cellular composition of FC sediment can serve as an objective and publicly available criterion of ACP severety.

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ЦИТОМОРФОЛОГІЧНІ ДОСЛІДЖЕННЯ КЛІТИННОГО СКЛАДУ ПЕРИПАНКРЕАТИЧНИХ РІДИННИХ СКУПЧЕНЬ В ОЦІНЮВАННІ ТЯЖКОСТІ КЛІНІЧНОГО ПЕРЕБІГУ ГОСТРОГО УСКЛАДНЕНОГО ПАНКРЕАТИТУ

Андрющенко Д.В., Андрющенко В.П., Прикупенко О.В., Когут Л.М.

Анотація. Мета – вивчити характер та особливості цитоморфологічних змін клітинного матеріалу осаду перипанкреатичних рідинних скупчень (РС) як критерію об'єктивної оцінки тяжкості клінічного перебігу гострого ускладненого панкреатиту (ГУП).

Матеріали та методи. Піддано аналізу результати цитологічного дослідження осаду перипанкреатичних РС, добутого при виконанні інтервенційної ультрасонографії в 51 (88%) і відеолапароскопії в 7 (12%) спостереженнях у 58 хворих на ГУП.

Результати. Констатовано, що при інтраабдомінальних РС (n=37) у 10 (27%) дослідженнях спостерігалося домінування проліферуючого мезотелію з його поліморфізмом. У 15 (41%) випадках проявлялися дегенеративно-дистрофічні зміни у вигляді вип'ячувань цитоплазми, появи великих «перснеподібних» клітин. У 12 (32%) дослідженнях виявлено атипово змінені клітини мезотелію з проявами анізоцитозу й анізонуклеозу, а також із цитоморфологічними змінами, подібними до неопластичного процесу. При позаочеревинній локалізації РС (n=21) більш істотні зміни спостерігалися з боку ядер гранулоцитів, зокрема в 9 (43%) випадках визначалися незворотні порушення їх структури у вигляді явищ каріопікнозу, каріорексису й каріолізису. Установлено, що глибина структурних змін клітин мезотеліоцитів і нейтрофільних гранулоцитів залежала від ступеня тяжкості ГУП.

Висновки. Оцінка глибини цитоморфологічних порушень клітинного складу осаду РС може слугувати об'єктивним критерієм ступеня тяжкості ГУП.

Ключові слова: *гострий ускладнений панкреатит, рідинні скупчення, цитологічні дослідження.*

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