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Clinical aspects of diagnosis and prognosis of acute necrotic pancreatitis

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Aim – to evaluate diagnostic markers of acute pancreatitis.

Materials and methods. The study was conducted in the period from 2014 to 2023 and was based on the assessment of the severity of acute pancreatitis (AP) in 237 patients. All patients were divided due to the severity of AP. Mild AP was detected in 85 (35.86%), moderate – in 90 (37.97%), severe – in 44 (18.56%), critical – in 18 (7.59%) patients. Also, two study groups were formed: the Group 1 (patients with mild and moderate AP) and the Group 2 (severe and critical AP).

Results. The level of procalcitonin in the blood was increased in 29 (12.23%) patients of the Group 2 (severe and critical AP) and was >2.0 ng/ml. Among them in 25 (86.2%) patients early surgical treatment was perfomed and septic inflammation was detected in operating room. Typical ultrasound signs of AP were in 207 (87.34%) patients. Correlation roots between amylase and diastase on the first day of illness were: r=0,71 in the Group 1 and r=0.73 in the Group 2.

Conclusions. The diagnosis of AP should be based on a comparative evaluation of the results of instrumental, laboratory tests and clinical symptoms. Levels of PCT, amylase, blood glucose, and urine diastase together with other clinical parameters helped to confirm the diagnosis of AP on admission to the hospital in 162 (92.57%) and 54 (87.09%) patients of the Group 1 and the Group 2. PCT should be used to predict complications and evaluate the efficiency of antibacterial therapy.

The study was performed in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee for all participants.

The informed consent of the patient was obtained for conducting the studies.

No conflict of interests was declared by the authors.

Keywords: acute pancreatitis, infected pancreatic necrosis, procalcitonin.

Клінічні аспекти діагностики та прогнозу гострого некротичного панкреатиту

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Мета – оцінити діагностичні маркери гострого панкреатиту.

Матеріали та методи. Дослідження проводилось у період із 2014 по 2023 роки і базувалося на оцінці ступеня тяжкості гострого панкреатиту (ГП) у 237 пацієнтів. Усіх пацієнтів було розподілено за ступенем тяжкості ГП. Легкий ГП було виявлено у 85 (35,86%), середньої тяжкості – у 90 (37,97%), важкий – у 44 (18,56%), критичний – у 18 (7,59%) пацієнтів. Надалі сформовано дві досліджувані групи: група 1 (пацієнти з легким та середньотяжким ГП) та група 2 (тяжкий та критичний ГП).

Результати. Рівень прокальцитоніну (ПКТ) у крові був підвищений у 29 (12,23%) хворих 2-ої групи та становив >2,0 нг/мл. Із них у 25 (86,2%) хворих проведено раннє оперативне лікування та під час операції виявлено гнійно-септичне запалення. Типові УЗД ознаки ГП були у 207 (87,34%) хворих. Кореляційні зв'язки між рівнями амілази крові та діастази сечі в першу добу хвороби становили: r=0,71 у групі 1 та r=0,73 у групі 2.

Висновки. Діагностика ГП повинна ґрунтуватися на порівняльній оцінці результатів інструментальних, лабораторних досліджень і клінічних симптомів. Рівні ПКТ, амілази, глюкози крові, діастази сечі з іншими клінічними показниками допомогли підтвердити діагноз ГП при надходженні у стаціонар у 162 (92,57%) пацієнтів групи 1 та 54 (87,09%) групи 2 груп. Для прогнозування ускладнень та оцінки ефективності антибактеріальної терапії слід використовувати визначення ПКТ у крові.

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної в роботі установи. На проведення досліджень отримано інформовану згоду пацієнтів.
Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: гострий панкреатит, інфікований панкреонекроз, прокальцитонін.

Introduction

Acute pancreatitis (AP) is the number one gastrointestinal diagnosis prompting inpatient admission, ranking 21st on the list of all diagnoses requiring hospitalization [1,2,9]. The incidence of AP ranges from 13 to 45/100,000 with equal affinity for each gender (though with different etiologies) [10]. Recently, the prevalence of AP has periodically ranked second or third place among urgent diseases of the abdominal organs [7]. AP represents a disorder characterized by acute necroinflammatory changes of the pancreas and is histologically characterized by acinar cell destruction [3]. This disorder is associated with early activation of the digestive enzymes that are released into the small intestine during the digestive process, instead of being activated at the appropriate time to digest food, these enzymes attack the pancreatic tissue, causing damage [4]. In 15% of patients, there is an infected pancreatic necrosis (IPN), which is a surgical problem [7]. IPN is severe surgical disease with high mortality (approaching 100% in the absence of treatment) [11]. IPN is considered to be the cardinal feature of the late phase of AP, however, several attacks of acute inflammation of the pancreas can result in a diagnosis of chronic pancreatitis as well [10]. AP sometimes causes problems to the patient and to the doctor due to the unpredictable course that require timely and correct solution. Moreover, the role of early diagnosis based on specific complex of laboratory and instrumental methods of examination, is significant. The determinants of disease severity of AP continue to be the subject of discussion [8]. There is no single doctrine of conservative and surgical treatment of IPN, either in Ukraine or abroad. Literature discussions are based on forecasting, timing of surgery, techniques of performing surgeries [9]. The problem of non-invasive diagnosis of infected acute necrotizing pancreatitis (ANP) is meaningful, despite the fact that instrumental visualization of the pancreas has reached a very high level [1,11]. One of possible ways to solve the problem of treating this disease is timely determination of the nature and extent of the destruction of the pancreas and retroperitoneal fat and making prognosis of the IPN [5]. The diagnostic value of determining the level of procalcitonin in blood – a biochemical marker for the early diagnosis of sepsis in surgical pancreatology has not been studied enough, so the scientific research in this area is more than relevant.

Aim – to evaluate diagnostic markers of acute pancreatitis.

Materials and methods of the study

The study was conducted at the Ternopil University Hospital and Ternopil Municipal City Hospital No.2 in the period from 2014 to 2023 and was based on the assessment of the severity of AP in 237 patients. All patients were divided in two groups: patients with moderate AP (presence of sterile (peri)pancreatic necrosis and/or intermittent organ failure) constituted the Group I (n=175); patients with severe AP (presence of infected (peri)pancreatic necrosis or resistant organ failure) and critical AP (availability of infected (peri)pancreatic necrosis and resistant organ failure) made up the Group II (n=62). The average age of patients was 44.6±1.52 in the Group I and 47.8±1.55 – in the Group II.

It is actual to distinguish local and system determinants. Local determinants include pancreatic necrosis and/or peripancreatic tissue necrosis, which is represented by the term «(peri)pancreatic necrosis», and system determinants – a presence of organ dysfunction due to AP. All laboratory and instrumental methods, as well as some special ones, were used, particularly the procalcitonin (PCT) levels in the blood. Moreover, a correlation analysis of all these data was carried out to determine the prognosis of the disease.

All statistical calculations were performed using Microsoft Excel version 2010 spreadsheets and the program «STATISTICA for Windows 10» (Stat Soft Inc). All statistical calculations of the results were carried out in compliance with the criteria of statistical analysis, which are acceptable for research in biology and medicine. Statistical processing of normally distributed indicators, that is, indicators with a normal distribution of data, was carried out by the method of Student–Fisher variation statistics with the determination of the arithmetic mean (M), the error of the arithmetic mean (m), Student's test (t). All data are given as their mean value with root mean square error (M±m), where M is the arithmetic mean of the sample, m is the standard deviation (mean squared deviation). The correlation coefficient was evaluated according to generally accepted criteria: r<0.3 – weak connection; r=0.3–0.49 – moderate; r=0.5–0.69 – significant; r=0.7–0.89 – strong; r>0.9 – very strong, close to a functional relationship. The study was performed in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee for all participants.

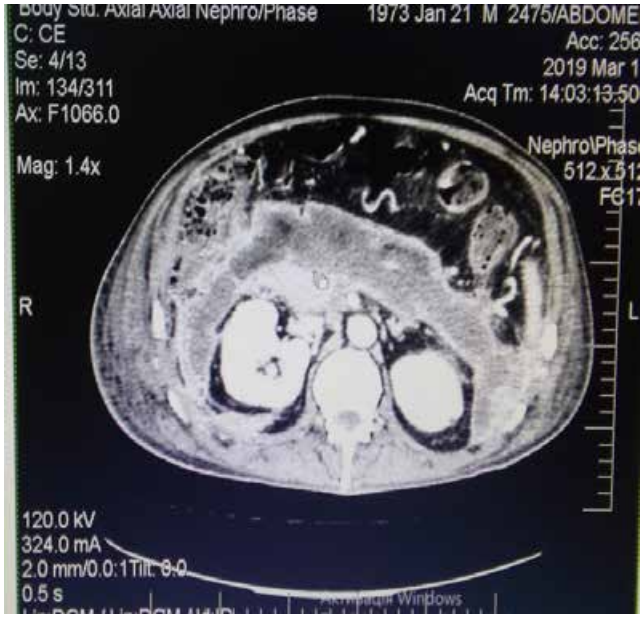

Fig. 1. Retroperitoneal phlegmon as a septic complication of pancreatic necrosis

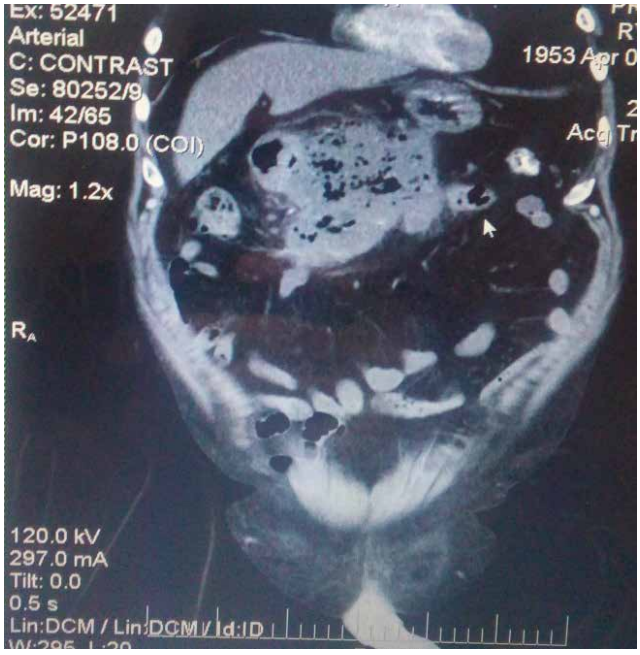

Fig. 2. Intra-abdominal abscesses

The informed consent of the patient was obtained for conducting the studies.

The results of the study and discussion

Mild AP was diagnosed in 85 (35.86%) patients, moderate – in 90 (37.97%), severe – in 44 (18.56%), critical – in 18 (7.59%) patients. Ultrasonography was informative on the first day in 139 (79.4%) patients of the Group I and 31 (50%) of the Group II. The main difficulties were associated with the excess weight of patients. In onset patients with AP moderate, severe and critical diagnostic value of sonographic diagnosis is reduced compared to mild AP light, which can cause false diagnosis of AP. Computed tomography (CT) was performed in 19 (8,01%) patients with severe AP (n=11) and critical (n=8) in the Group II. The high diagnostic value of CT in patients with critical AP was in 62.5% (5 patients), with severe – in 72.2% (8 patients) in the Group II. CT signs of destructive process, which assign patients to the Group II (severe and critical AP), were presented by retroperitoneal phlegmonas (Fig. 1) as septic complications of pancreatic necrosis or intra-abdominal abscesses (Fig. 2). We didn't perform CT in patients with mild and moderate AP, due to our experience and literature data about no specific changes on the first days of AP.

In patients of the Groups I and II, 41 parameters reflecting the status of individual body functional systems on the 1st, 2nd, 3rd, 5th, 7th day of the disease were analyzed. Of all the 41 parameters, 8 were selected (amylase, diastase, PCT, alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, protein, glucose), with a probable difference.

The average levels of these laboratory biochemical parameters on the first day of disease are presented in Table. A significant leukocytosis in the blood, increasing anemia in combination with hypoproteinemia ($p<0.05$) was

Table

Laboratory parameters in patients of both groups on the first date of AP

Parameters	Group I (n=175)	Group II (n=62)
Amylase, U/L	147.34±14.37	269.16±34.7**
Diastase, U/L	898.45±134.22	1546.23±246.25**
Glucose, mmol/l	7.2±0.2	7.9±0.15
Bilirubin, μm/l	14.71±0.9	21.15±1.78
ALT, U/L	34.6±1.16	79.14±10.82**
AST, U/L	31.48±1.54	72.73±10.32**
Leukocytes, $\times 10^9$ l	7.56±0.16	12.26±0.37*
Hemoglobin, g/l	123.2±1.64	123.4±2.17
Total protein, g/l	58.27±0.23	49.27±1.34*

Notes: * – data reliability between the Groups I and II $P<0.05$; **– data reliability between the Groups I and II $P<0.01$.

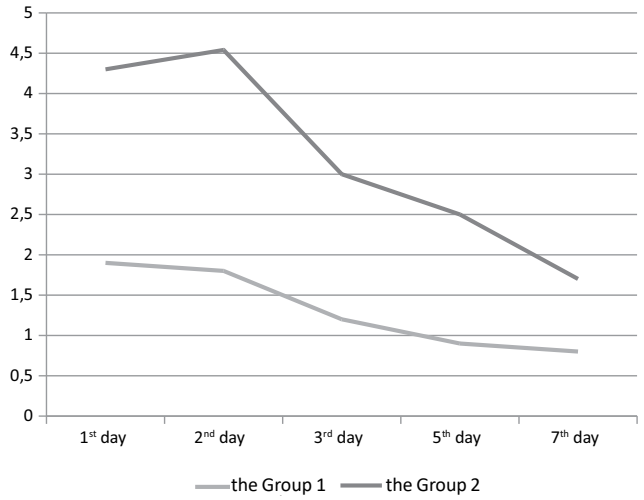

Fig. 3. Levels of PCT in Group I and Group II on different days of disease, ng/ml

Fig. 4. Macroscopic: necrotic tissues of pancreas after necrectomia

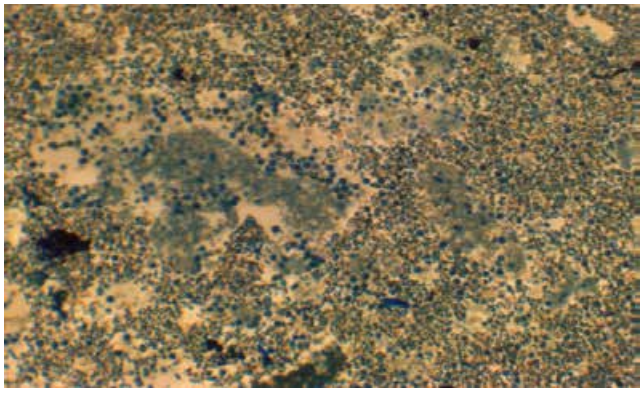

Fig. 5. Histological examination of resected part of pancreas

in the Group II of patients on the first day of illness. Also, patients of the Group II was diagnosed a significant level of cytolysis (the contents of AST, ALT) and significantly high levels of amylase in blood and urine diastase on the first day of the disease that caused exocrine dysfunction.

In both observation groups, a tendency to hyperglycemia was observed, so inflammatory-destructive process effected endocrine function of pancreas. Normalization of these indicators in both groups was mostly possible after a week of observation due to a correct treatment.

Our attention was also paid to PCT, a marker of septic inflammation. We noticed that among patients in the Group I, an increase in PCT levels was detected only in 3 (1.71%) patients, when in the Group II in 15 (24.19%) and it indicated a septic nature of inflammation in this group. The marker levels were increased (>2.0 ng/ml) on the first and second days and decreased during next days due to the influence of antibacterial therapy (Fig. 3). It means that levels of PCT were indicators of the efficiency of antibacterial therapy and were used to control treatment.

All patients of the Group II with high level of PCT on admission to hospital in combination with high intra-abdominal pressure were operated and septic inflammations were detected in operating room (Fig. 4). Histological examination of resected part of pancreas revealed necrosis of the gland, as an evidence of destructive process (Fig. 5).

To make prognosis of the disease, it was significant to built correlation analysis of all these criteria. It means that all paramaters were compared to make correlations and find relations.

The connection matrix had 1976 correlation coefficients. The majority of relationships were formed by such factors as urine levels of diastase, amylase in blood, PCT in blood serum, glucose levels that correlated with each other and with other parameters of the system. Amylase and diastase on the first day of illness had correlations: r=0.79 in the Group I and r=0.76 in the Group II. On the third day: r=0.74 and r=0.71 in the Groups I and II, respectively. In the Group II, PCT and diastase on 2nd day of the disease had correlations: r=0.81.

The importance of these parameters in predicting the course of AP can be evaluated by timely diagnosis and proper treatment, which helps to prevent complications in those patients in which those parameters were detected.

We found that the level of PCT, amylase, blood glucose, and urine diastase in comparison with another clinical parameters on admission helped to cofirm AP diagnosis in 162 (92.57%) and 54 (87.09%) cases in the Groups I and II, respectively.

Reevaluation of laboratory data on next days especially such indicators as the number of white blood cells, level of PCT, urine diastase level, and the level of glucose in blood is meaningful for controling the course of disease.

The blood levels of amylase, urine diastase urine and PCT on admission correlated with the severity of pancreatitis, concerning the importance of these parameters in predicting the course of AP and diagnosis, which was confirmed in 162 (92.57%) and 54 (87.09%) cases in the Groups I and II, respectively. Ultrasonography on admission to hospital re-

vealed changes in the pancreas that were characteristics of AP in 139 (79.4%) patients of the Group I and 31 (50%) patients of the Group II. The diagnostic value of sonographic diagnosis in patients with moderate, severe and critical AP was reduced compared to mild AP, which can lead to errors in diagnosis of AP. CT was useful in patients with severe and critical AP, but not earlier than on 10–14th day of illness. Our instrumental data are indicated in the results of other researchers [6,10]. Amylase and diastase on the first day of illness had strong correlations: r=0.79 in the Group I and r=0.76 in the Group II and it is also mentioned in other studies [5,7]. But there is still a wide area for research into the prediction of ANP and the choice of the tactics of treatment.

Conclusions

1. The diagnosis of AP should be based on a comparison of the results of instrumental and laboratory tests and clinical symptoms.

2. Levels of PCT should be used in prognosis of AP to prevent complications, as well as indicators of the efficiency of antibacterial therapy and control of treatment.

3. The ultrasound method requires further examination to achieve diagnostic value.

4. Levels of PCT, amylase, blood glucose, and urine diastase in comparison with another clinical parameters on admission helped to cofirm AP diagnosis in 162 (92.57%) and 54 (87.09%) cases in the Groups I and II.

5. Reevaluation of laboratory data on next days is meaningful for controling the course of disease.

No conflict of interests was declared by the authors.

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