Research Article

Changes in Humoral and Cellular Immunity in Tertiary Peritonitis

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Abstract

The objective of the research was to give a comparative characteristic of parameters of humoral and cellular immunity in the development of secondary and tertiary peritonitis.

Materials and methods. The research enrolled 109 patients with secondary peritonitis, 20 of whom developed tertiary peritonitis. Changes in humoral and cellular immunity were evaluated by serial blood tests for the determination of leukocyte count, the relative number of lymphocytes, Ig A, M, and G levels, as well as by counting the phagocytic index, the phagocytic number and the leukocyte intoxication index. The statistical processing of the obtained data was made using the STATISTICA 5.0 software (StatSoft, USA).

Results. All the patients were divided into 2 groups: the group of patients with secondary peritonitis (n=89) and the group of patients with tertiary peritonitis (n=20). In the development of tertiary peritonitis, leukocytosis, relative lymphocytopenia and high values of the leukocyte intoxication index persisted during the entire observation period. In tertiary peritonitis, the phagocytic index was significantly lower only on the day of hospitalization. In the group of tertiary peritonitis, the phagocytic number decreased significantly until the 7th day after surgery. Ig A, M and G levels were lower since admission and subsequently decreased as compared to the results in the group of patients with secondary peritonitis.

Conclusions. 1. Tertiary peritonitis is the most severe form of abdominal sepsis with high rates of mortality and rather difficult early diagnosis. 2. With the development of tertiary peritonitis, leukocytosis increases and relative lymphocytopenia develops. 3. The reduction in phagocytic index is indicative for the prognosis of tertiary peritonitis. 4. Ig A and M levels are significantly lower, and the leukocyte intoxication index is high at the time of hospitalization in patients who subsequently develop tertiary peritonitis.

Keywords

abdominal sepsis; secondary peritonitis; tertiary peritonitis; humoral immunity; cellular immunity

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Problem statement and analysis of the recent research

For decades, abdominal sepsis remains an actual and still unresolved problem of emergency surgery [1, 2]. Present contradictions in the approaches to diagnosis and treatment of its most frequent manifestation - secondary peritonitis (SP) – indicate its special complexity [3, 4]. The nature of the immune response, as one of the leading components of the pathogenesis of sepsis, allows the surgeon to evaluate not only the efficacy of treatment, but also to predict the further course of the disease [5, 6, 7, 8]. Nowadays, the patient’s immune status in tertiary peritonitis (TP) is not sufficiently studied and requires in-depth analysis, namely from the perspective of prediction of changes in its parameters [9, 10].

The objective of the research was to give a comparative characteristic of parameters of humoral and cellular immunity in the development of SP and TP.

1. Materials and methods

We had prospectively examined 109 patients with SP, operated on in the Clinic of Surgery and Endoscopy of Lviv Danylo Halytsky National Medical University (surgical departments No 1 and 3, Lviv City Emergency Hospital) in 2010-2015. Etiology of SP was as follows: acute destructive appendicitis (29.4%), perforated gastric (11%) or duodenal (7.3%) ulcer, perforated colon cancer (11%), perforated colonic diverticulitis (6.5%), abdominal abscess perforation (5.6%), acute destructive cholecystitis with perforation (4.7%), thrombosis of the superior mesenteric artery with small intestine necrosis (3.6%), perforated colon cancer (3.6%), perforated colon cancer (3.6%), Crohn’s disease with the small intestine perforation (3.6%), hernia strangulation with small intestine necrosis (2.8%), severe polytrauma with injury of the small intestine (2.8%), retroperitoneal tumor disintegration and pus formation with its perforation to the abdomen (1.8%), ingrowth of uterine tumor into the small intestine and subsequent necrosis (0.9%), pancreatic necrosis (0.9%), volvulus of the sigmoid colon with perforation (0.9%), ulcerative colitis with necrosis of the colon (0.9%),
perforated cancer of the small intestine (0.9%), pancreatic cancer disintegration (0.9%), gastric perforation by a foreign body (0.9%). Concomitant diseases were diagnosed in 88 (80.7%) patients. Women slightly prevailed – 57 (52.3%). The age of patients was in the range of 18-88 (median - 61). Postoperatively, majority of patients (68; 62.4%) stayed for 1-4 days (median – 2 days) in intensive care unit (ICU). Peritonitis was local non-separated in 104 (95.4%) patients and diffuse - in 88 (80.7%) patients. Postoperative complications arose in 18 (16.5%) cases, being purulent-septic in 50% of patients. Tertiary peritonitis was diagnosed on the 3rd-12th days (median – 5 days) in 20 (18.3%) patients. Criteria for diagnosis of TP were: the persistence of peritoneal symptoms despite the adequate surgical elimination of the infectious focus, the presence of nosocomial microflora (Citrobacter Freundii, Acinetobacter Baumannii, Staphylococcus viridans, Pseudomonas spp., Candida spp., Geotrichum candidum) in peritoneal exudate, multi-organ failure (MOF) and stay in ICU > 3 days [11]. Postoperative mortality in the whole cohort of patients was 30.2%. Tertiary peritonitis resulted in a fatal outcome in 90% of cases with sepsis as the main cause.

The determination of leukocyte count and the relative number of lymphocytes was carried out by counting them in Goryaev camera using light microscopy [12]. The leukocyte intoxication index (LII) was calculated using the formula of V.K. Ostrovsky [13]. Quantitative determination of Ig levels was carried out by radial immunodiffusion by the Mancini method with monospecific Ig A, M, and G serums [12]. The phagocytic index (PI) and as well as the phagocytic number (PN) was calculated by the A.N. Mayansky - D.N. Mayansky method [14].

In order to assess immune changes in the development of both types of peritonitis, serially (at admission, on the 3rd and 7th days thereafter; in the group of TP – on the day of diagnosis of TP and on the 2nd consecutive day) blood sampling was performed to determine the absolute number of leukocytes, the relative number of lymphocytes, the levels of Ig A, M and G, LII, as well as PI and PC were calculated. The statistical processing of the material was made using the STATISTICA 5.0 software (StatSoft, USA). Before choosing the method of intergroup comparison of parametric indicators or repeated researches, the Shapiro-Wilk test to assess distribution normality was performed. Due to non-Gaussian distribution in groups, parametric data were presented as median, minimum-maximum and lower-upper quartiles (25-75%).

2. Results and discussion

All the patients were divided into 2 groups: the group of patients with SP (n=89) and the group of patients with TP (n=20).

In the group of patients with SP, the absolute number of leukocytes decreased as patients recovered. Perioperatively, this indicator showed a tendency (p=0.073) towards higher values in the group of patients with TP (median - 11·10⁹/L (min 4.5 - max 30.4) vs. 13.1·10⁹/L (min 8.6 - max 36.6). In the group of patients with TP, the number of leukocytes increased being significantly higher on the 3rd (12.2·10⁹/L (min 4 - max 21.2) vs. 10.1·10⁹/L (min 4.6 - max 24)) in the group of patients with SP; p<0.05) and on the 7th (11.7·10⁹/L (min 5.9 - max 24.4) vs. 8.95·10⁹/L (min 4.5 - max 25.8) in the group of patients with SP, p<0.001) days after surgery. According to another research, in most cases, the clinical course of TP is accompanied by leukocytosis [15], which is consistent with our data. Most patients with TP may develop only leukocytosis and hyperthermia while other typical symptoms of infection may be absent [2].

The intergroup comparison of the relative number of lymphocytes showed that in the group of patients with TP, it was significantly lower throughout the entire observation period: at admission - 13.0% (min 2 - max 30) vs. 16% (min 2 - max 37) (p<0.05), on the 3rd day - 15% (min 6 - max 29) vs. 17% (min 3 - max 35) (p<0.05) and on the 7th day - 13.5% (min 3 - max 28) vs. 17% (min 3 - max 35) (p<0.01). In the group of patients with TP, lymphocytopenia was confirmed during the entire observation period. Both intensive (compensatory) anti-inflammatory reaction of the organism and stress dyshormonosis, which, in particular, leads to lymphocytopenia were proven to promote immunoparalysis [16].

The LII calculation revealed statistically significant differences between the comparison groups as well. The LII was significantly (p<0.05) higher in the group of patients with TP - 8.15 (min 4.1 - max 10.9) vs. 5.4 (min 2.2 - max 12.1) already on the day of hospitalization. Later, in contrast to the LII in the group of patients with SP, in patients with TP, it was substantially (p<0.001) higher: 8.55 (min 5.6 - max 10.1) vs. 5.6 (min 2.7 - max 12.1) on the 3rd day and 6.3 (min 4.7 - max 11.3) vs. 3.9 (min 1.7 - max 10.8) on the 7th day. In the group of patients with SP, the LII demonstrated downward dynamics. In uncomplicated postoperative course of peritonitis, the LII gradually decreases [17].

The indicators of phagocytic activity had their own peculiarities in each of the comparison groups. At admission, in the group of patients with TP, the PI was significantly (p<0.05) lower, as compared to that in patients with SP: 95.25% (min 89 - max 99.2) vs. 97.1% (min 81.4 - max 99.9). Subsequently, in the group of patients with TP, its value did not significantly differ (p>0.05): 95.55% (min 73 - max 99) vs. 94.7% (min 57 - max 98.7) on the 3rd day; 93.25% (min 68 - max 97.6) vs. 93.25% (min 68 - max 97.6) on the 7th day. In both groups, the PI decreased over time.

However, the PN did not show significant (p>0.05) intergroup differences within the first days after surgery: perioperatively, in the group of patients with SP, it equaled 9.7% (min 8.4 - max 13.2) vs. 9.7% (min 8.9 - max 10.3) as compared to patients with TP on the 3rd day - 9.5% (min 5.4 - max 13.4) vs. 9.4% (min 7.2 - max 10.5). The significant difference (p<0.05) in the values of the PN was found in patients with TP on the 7th day: 9.4% (min 8.7 - max 13.1) vs. 9.1% (min 5.6 - max 17.7). In both groups, the PN gradually decreased. The peak values of the PI and the PN in peritonitis were ob-
Ig levels differed in different monitoring periods depending on their class. In the group of patients with TP, perioperative Ig A concentration tended (p=0.055) to be lower than that in patients with SP: 6.85 g/L (min 4.8 - max 9.4) vs. 7.8 g/L (min 3.2 - max 18.7). In the following days, there were no significant differences in Ig A values between the groups: 6.4 g/L (min 4.1 - max 16.9) vs. 6.5 g/L (min 4.3 - max 10.1) in patients with TP (p>0.05), on the 7th day - 4.8 g/L (min 1.4 - max 12) vs. 5.7 g/L (min 3.7 - max 7.1) in patients with TP (p>0.05). The indicators of Ig A in both groups demonstrated a gradual decrease with time.

Ig M levels had significant intergroup differences in all observation days, in particular towards the lower values in patients with TP. Ig M concentration in this group was 4.65 g/L (min 3.3 - max 6.5) (in patients with SP - 5.4 g/L (min 2.1 - max 11.1), p<0.001) on the day of admission; 4 g/L (min 2.9 - max 5.1) (in patients with SP - 5.1 g/L (min 2.8 - max 12), p<0.001) on the 3rd day; 3.3 g/L (min 1.8 - max 7.5) (in patients with SP - 3.9 g/L (min 1.1 - max 12.4), p<0.05) on the 7th day. Similarly to Ig A, Ig M levels demonstrated a gradual decrease in each of the groups as well.

On the day of admission, Ig G levels between the groups did not differ (p>0.05): 21.75 g/L (min 15.4 - max 29.1) in patients with TP vs. 21.1 g/L (min 6.8 - max 34.5) in patients with SP. Since the 3rd day, in the group of patients with TP, the level of Ig G decreased significantly (p<0.001): 16.25 g/L (min 9.5 - max 20.5) vs. 19.4 g/L (min 10.9 - max 32.9). The same significant (p<0.05) difference was observed on the 7th day as well: 10.2 g/L (min 4.2 - max 24.3) vs. 13.7 g/L (min 4.8 - max 40.2). In general, Ig G levels decreased irrespective of peritonitis type.

In comparison with our results, such dynamics was observed in SP. Ig A levels decrease in peritonitis and for some time after its surgical treatment [18]. According to our data, such changes were observed in all classes of Ig in both SP and TP. The decrease in the concentration of major classes of Ig are considered the indications for immunocorrection to improve the results of sepsis treatment [19].

Peculiar changes in immunity in abdominal sepsis were investigated by other clinicians as well. The available literature, however, does not contain the description of changes in studied parameters in TP. The predictive nature of changes in the investigated parameters of the immune response in TP can be effectively used in the early prediction of the risk of its development.

3. Conclusions

- TP is the most severe form of abdominal sepsis with high rates of mortality and rather difficult early diagnosis.
- With the development of TP, leukocytosis increases and relative lymphocytopenia develops.
- The reduction in the PI is indicative for the prognosis of TP.
- Ig A and Ig M levels are significantly lower, and the LII is high at the time of hospitalization in patients who subsequently develop TP.

4. Prospects for further research

It is reasonable to assess the practical significance of changes in immunity parameters for TP development.

References


Changes in Humoral and Cellular Immunity in Tertiary Peritonitis — 4/4


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