CHANGES HUMORAL IMMUNITY AND ANTIGENS HLA SYSTEM IN ACUTE PANCREATITIS

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In patients with acute pancreatitis noted antibodies to endogenous antigens: s-DNA – 58,5%, d-DNA – 53,7%, n-DNA – 51,2%, trypsin – 42.7%, insulin – 28,1% and pancreatic tissue antigens – 19,5%, and increase in the level of serum immunoglobulins and circulating immune complexes. In conjunction with an increase in frequency of detection in patients with acute pancreatitis antigen system HLA A1, B8, B18, associated with dysregulation between T- and B-functioning immune system, changes in the state of humoral immunity are genetic and humoral mechanisms that mediate the development of autoimmune reactions in acute pancreatitis.

Keywords: acute pancreatitis, humoral immunity, antigens of HLA system

Acute pancreatitis in recent decades continues to be one of the most common disease among acute diseases of the abdominal cavity, there is an increase in the number of patients with acute pancreatitis and increase the share of destructive forms of lesions of the pancreas.At present, the immune changes detected in acute surgical diseases of the abdominal cavity, considered as a factor that largely determines the course of the disease, contributing to the maintenance of the inflammatory process and reducing the effectiveness of reparative processes [1–3, 16, 17, 20, 21]. The study of humoral and cellular immunity in pancreatitis indicates a change in the main humoral factors [4, 9, 13, 14]. Study Association of HLA phenotype, and the intensity of the humoral immune response to antigens of the pancreas, the level of production flogogennys agents humoral and cellular genesis in pancreatitis matters to define the role of genetically determined mechanisms in the pathogenesis of inflammatory diseases of the pancreas and introducing prospects pathogenetically oriented methods of treating a disease using anticytokine correction methods [7, 8, 15, 19, 23].

Aim. To study the frequency of detection of antibodies to structural and secretory component of the pancreas in patients with acute pancreatitis and to consider possible changes in humoral immunity association with certain HLA phenotypes.

Materials and methods of research

We examined 110 patients with acute pancreatitis who have studied the condition of humoral immunity to structural (antigens from the tissues of the pancreas) and secretory (insulin and trypsin) pancreatic components, to DNA: single- stranded (s-DNA), denatured (d-DNA), a native (n- DNA)- in the reaction of passive hemagglutination by Boyden. According to the classification of acute pancreatitis patients studied were divided into two groups: patients with dropsical (regressing, abortive) form of acute pancreatitis – 79 patients and patients with acute destructive pancreatitis (fatty and hemorrhagic pancreatic necrosis) – 31 patients. Among patients with dropsical form of acute pancreatitis were 45 women and 34 men, with a destructive form – 17 women and 14 men.

Identification of HLA antigens were determined by complement-dependent cytotoxicity [15, 16]. We have panels 28 – I and 28 – II Institute of Hematology and Blood Transfusion (Saint-Petersburg) of 116 sera to identify specific antigens of locus A – 14, locus B – 18 and locus C – 5 of HLA system. The immunoglobulins of the main classes (A, G, M) were investigated by radial immunodiffusion by G.Mancini, using monospecific serum immunoglobulin A, G, M. Circulating immune complexes were determined by a method based on the selective precipitation of antigen-antibody complexes in 3,75% polyethyleneglycol solution, followed by photometric examination.

Results of research and their discussion

In patients with acute pancreatitis, we noted the presence of humoral immunity responses to all antigens studied. Of antibodies to s-DNA found at 58,5% in the d-DNA – 53,7%, n-DNA – 51,2% trypsin – 42,7% insulin – 28,1%, and the antigen of pancreatic tissues – in 19,5%. The appearance of circulating antibodies, presumably, is the body's response to organ tissue damage. The greatest manifestation of the immunological changes observed in destructive forms of acute pancreatitis: s-DNA in 62,1% (56,6% – in dropsical form of acute pancreatitis), d-DNA – 62,1% (49,1%), n-DNA – 55,2% (49,1%), trypsin – 48,3% (39,6%), insulin – 37,9% (22,6%) and pancreatic tissue antigens – 27,6% (15,1%).

The appearance of antibodies to DNA in the literature is regarded as an indicator of autoimmune process [16, 17]. Antigenic properties in acute pancreatitis acquire structural (pancreatic tissues antigen) and

secretory (trypsin, insulin) components pancreas. In acute pancreatitis revealed distinct autoimmune reaction to structural and secretory pancreas components. It should be noted that the deoxyribonucleic acid (DNA) in a large amount is in the nuclei of pancreatic acinar cells. When released from the cell as a result of degradation, the DNA is contacted with immunocompetent cells. In this regard, antibodies to DNA (s- DNA and d-DNA) can also be regarded as a structural component of the pancreas, along with the pancreatic tissue antigen, which is specific but not pancreas.

We have noted a correlation between the presence of antibodies to endogenous antigens and a number of clinical and laboratory parameters, which were more pronounced in acute destructive pancreatitis. Detection of antibodies to DNA, tissue antigens and pancreatic trypsin was associated with an increase in general indicators of inflammatory activity (ESR and leukocytosis). The presence of antibodies to trypsin correlated with serum levels of trypsin in acute pancreatitis: the level of antibodies in the presence trypsin thereto was 17,24 ± 0,9 (μmol/Min.-ml.), which was significantly higher ($P < 0,05$) than patients who lacked the antibody – 11,12 ± 0,8 (μmol/Min.-ml.) The level of trypsin for patients with various forms of acute pancreatitis was also dependent on the presence of antibodies to trypsin: in acute pancreatitis destructive antibodies in the presence trypsin – 17,63 ± 1,1 (μmol/Min.-ml.), and absence of antibody to trypsin – 13,40 ± 0,8 (μmol/Min.-ml.) with dropsical form – in the presence of antibody to trypsin – 16,99 ± 0,9 (μmol/Min.-ml.) and the absence of antibodies to trypsin – 9,60 ± 0,7 (μmol/Min.-ml.). Therefore, the determination of antibodies to DNA, tissue antigens of pancreatic trypsin and characterize the activity of the inflammatory process in the pancreas.

The presence of antibodies to insulin was correlated with the level of blood glucose: at acute destructive pancreatitis in the presence of antibodies to the insulin increase in blood glucose was observed in 63,6 % of patients, with the absence of antibodies to insulin – significantly less ($P < 0,05$) – 23,5 % at dropsical form in the presence of antibodies to the insulin increase in blood glucose was observed in 41,7 % of patients in the absence of antibodies to insulin in 2,4 % ($P < 0,01$). We suggest that insulin in acute pancreatitis becomes antigenic properties, due to the destruction of beta cells with active inflammatory-destructive process in the pancreas that characterizes the extent and depth of the pathological changes in the body. Further, the presence of antibodies to insulin can occur picture is beta-cell insufficiency insular with clinical diabetes.

In the dynamics of antibody titers to endogenous antigens in patients with acute destructive pancreatitis in the 2nd week it was slightly higher than in the 1 st week. In patients with acute pancreatitis dropsical form dynamics titers of antibodies to endogenous antigens were reversed, with the exception of pancreas tissue antigen. The gradual decline in antibody levels subside as the pathological process, probably a reflection of the protective reaction of the organism.

On the severity of antibody indirectly indicates the level of serum immunoglobulins. We investigated the level of IgA, IgG and IgM in 44 patients with acute pancreatitis. In the control group (40 healthy donors) major classes of immunoglobulins level was: IgA – 1,67 ± 0,06 g/l, IgG – 8,65 ± 0,04 g/l and IgM – 1,05 ± 0,01 g/l. Compared with the control group of patients with acute pancreatitis was significantly increased ($P < 0,05$) Contents IgM – 1,51 ± 0,04 g/l and IgA – 1,88 ± 0,07 g/l. Lowered ($P < 0,01$) as compared with the control group the level of IgG – 7,73 ± 0,09 g/l.

At the destructive forms of acute pancreatitis increased content of immunoglobulins of all classes compared to dropsical form: IgA – 1,92 ± 0,07 g/l, IgG – 8,46 ± 0,08 g/l and IgM – 1,59 ± 0,04 g/l. In dropsical form of serum immunoglobulin content below: Ig A – 1,85 ± 0,07 g/l, IgG – 7,32 ± 0,12 g/l and IgM – 1,47 ± 0,04 g/l. A statistically significant difference in the IgG content with destructive and dropsical forms ($P < 0,05$).

A significant elevation of serum immunoglobulins was observed in seropositive patients with acute pancreatitis in relation to all studied endogenous antigens. Level of IgM was statistically significantly increased in patients with the presence of antibodies to s-DNA (respectively 1,58 ± 0,04l and 1,42 ± 0,06 g/l) and d-DNA (respectively 1,59 ± 0,05 and 1,43 ± 0,03 g/l) at a confidence ($P < 0,05$), in pancreatic tissues antigens (respectively – 1,80 ± 0,05 and 1,44 ± 0,03 g/l), trypsin (respectively – 1,61 ± 0,02l and 1,42 ± 0,03 g/l) and insulin (respectively 1,75 ± 0,04 and 1.44 ± 0,03 g/l) at a confidence ($P < 0,01$). Level of IgG was statistically significantly

increased in patients with the presence of antibodies to insulin (respectively 8,77 ± 0,11 and 7,43 ± 0,14 g/l) for pancreatic tissues antigens (respectively – 8,64 ± 0,12 and 7,58 ± 0,11 g/l) at a confidence ($P < 0,05$) and of s-DNA (respectively, 8,35 ± 0,11 and 6,84 + 0,13 g/l), d-DNA (respectively, 8,30 ± 0,12 and 7,11 ± 0,14 g/l), n-DNA (respectively – 8,31 ± 0,12 and 6,89 ± 0,13 g/l) and trypsin (respectively – 8,58 ± 0,09 and 6,96 ± 0,14 g/l) at a confidence ($P < 0,01$). The level of Ig A was statistically significantly increased in patients with the presence of antibodies to DNA-n (respectively – 1,93 ± 0,05 and 1,79 ± 0,04 g/l).

The average level of circulating immune complexes in patients with acute pancreatitis was 179,04 ± 6,84 units, which was significantly higher ($P < 0,01$), than in the control group – 94,72 ± 3,52 units. The level of circulating immune complexes in destructive form was higher (209,37 ± 9,83 units). Than in the dropsical form of acute pancreatitis (159,17 ± 7,82 units.). The level of circulating immune complexes was increased in patients with the presence of endogenous antibodies to all antigens except trypsin.

When comparing the frequency of the HLA antigen distribution in patients with acute pancreatitis and healthy individuals from among the alien population of Western Siberia [15, 16] in a group of patients with acute pancreatitis observed a significant increase in the frequency of determining the HLA antigens A1 ($P < 0,01$), B8 ($P < 0,001$), B18 ($P < 0,05$), Cw1 ($P < 0,001$). For antigen detection rate which was significantly increased in acute pancreatitis, the magnitude of the relative risk were as follows: A1 – 2,14; B8 – 3,66; B18 – 3,58; Sw1 – 5,93. In patients with different forms of acute pancreatitis we observed statistically significant differences, expressed in the absence of B16 antigen in acute destructive pancreatitis ($P < 0,05$) and B27 antigen in the dropsical form of acute pancreatitis ($P < 0,05$). HLA antigens B8 A1i associated with dysregulation between T- and B-functioning immune system, which manifests itself primarily as a defect of T-suppressors as a result of the immune response is enhanced and becomes inadequate autoimmune [14, 17]. Patients with phenotype A1, B8 in chronic pancreatitis smaller effect than all patients generally gave protease inhibitors, more – immunomodulators thymic origin enterosorption and intravenous laser irradiation of blood [14]. Sw1 antigen associated with a low activity tripsinsvyazyvayuschey alpha-2-macroglobulin, HLA B18 antigen system deficiency associated with severe and suppressor T-cell to autoserotherapy pancreatic tissue [9]. The antigen HLA B27 system is associated with the immunocomplex pathology – ankylosing spondylitis, Reiter's disease, diffuse connective tissue diseases [14, 15] and the development of pancreatitis in patients with gallstone disease [14, 18].

Conclusion

Immune cells developing immune disorders and play an important role in the pathogenesis of acute pancreatitis and determine the severity of the disease [5, 6, 11, 10, 22]. It is shown that the assessment by APACHE II score of 16 points or more in the clinic is a predictor of excessive immune response and premature immunosuppression, and expressed local and systemic complications in acute pancreatitis [12].

Identified by us in patients with acute pancreatitis: improved circulation of autoantibodies to an endogenous antigen, serum immunoglobulins, immune complexes, combined with the presence of the phenotype antigens HLA A1, B8, B18 associating with dysregulation between the T and B-functioning immune system, which manifests itself primarily as a defect of T -supressorov [14, 16, 17] are genetic and humoral mechanisms mediating autoimmune reactions in acute pancreatitis.

Knowledge of HLA-phenotype in patients with acute pancreatitis allows to predict the development of immune disorders affecting the outcome of the disease, and accordingly plan the use in the treatment of patients with immunosuppressive therapies and sorption.

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