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ACUTE PHASE PROTEINS IN PATIENTS WITH BRUCELLOSIS



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Abstract: In the Republic of Uzbekistan, brucellosis is widespread not only among farm animals, but also among people. Human brucellosis cases are often an indicator of a problem with brucellosis in farm animals, since they are often detected in areas considered safe for animal brucellosis.

Key words: brucellosis, agriculture, people, animals, disease, region.

БРУЦЕЛЛЁЗ БИЛАН ОҒРИГАН БЕМОРЛАРДА ЯЛЛИГЛАНИШ ЎТКИР ФАЗА ОКСИДЛАРИ

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Аннотация. Ўзбекистон Республикасида бруцеллёз нафакат қишлоқ хўжалиги ҳайвонлари, балки одамлар орасида ҳам кенг тарқалган. Одамларда бруцеллёз билан касалланиш ҳоллари кўпинча қишлоқ хўжалиги ҳайвонларида бруцеллёз муаммосининг кўрсаткичидир, чунки улар кўпинча ҳайвонлар бруцеллёзи учун хавфсиз деб ҳисобланган ҳудудларда аниқланади.

Калит сўзлар: бруцеллёз, қишлоқ хўжалиги, одамлар, ҳайвонлар, касалланиш, ҳудуд.

ПОКАЗАТЕЛИ БЕЛКОВ ОСТРОЙ ФАЗЫ ВОСПАЛЕНИЯ У БОЛЬНЫХ БРУЦЕЛЛЁЗОМ

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Аннотация. В Республике Узбекистан распространен бруцеллёз не только среди сельскохозяйственных животных, но и среди людей. Заболевания людей бруцеллёзом часто являются индикатором неблагополучия по бруцеллёзу сельскохозяйственных животных, так как они нередко выявляются на территориях, считающихся благополучными по бруцеллёзу животных.

Ключевые слова: бруцеллез, сельское хозяйство, люди, животные, болезнь, регион.

Introduction. Brucellosis, as a widespread zoonotic infection, causes significant economic and social damage in many countries around the world where livestock farming is developed [2,4,10]. In the Republic of Uzbekistan, brucellosis is widespread not only among farm animals, but also among people [1,2]. Human brucellosis is often an indicator of brucellosis problems in farm animals, since it is often detected in areas considered free of animal brucellosis [1,2,4]. This pathology occurs in several clinical forms (acute, subacute, primary and secondary chronic), and the acute and especially subacute forms often (50% to 70%) progress to chronic brucellosis [1, 2, 5]. Chronicization of the process, with impairment of ability to work, and a long-term course, sometimes leading to disability, also requires a solution.

As is known, the causative agent of brucellosis has an intracellular location, during which it recognizes cells of loose connective tissue and binds to their receptors, the signals from which indicate the activity of the innate immune system. The presence of exogenous pathogens in the environment promotes the synthesis and secretion of proinflammatory cytokines into the blood in loose connective tissue [7]. In response to the synthesis of primary mediators (cytokines), hepatocytes induce the synthesis of a complex of acute-phase inflammation proteins, which include C-reactive protein, glycoproteins, macroglobulin, antiproteases, etc. Each of these acute-phase inflammation proteins performs an individual function [7,8,9], and therefore the study of acute-phase inflammation protein indices in acute forms of brucellosis is of particular interest. The aim of this work is to study the content of acute phase inflammation proteins in the blood serum of patients with acute forms of brucellosis.

Material and methods of research. We observed 50 patients with brucellosis who were hospitalized in the Republican Clinical Infectious Diseases Hospital at the Research Institute of Epidemiology, Microbiology, and Infectious Diseases of the Ministry of Health of the Republic of Uzbekistan in the period from 2015 to 2017. The diagnosis was made based on the clinical classification of N. I. Ragoze (1955) with the addition of K. D. Dzhililov (1988). All patients were divided into 2 groups: 20 (40%) patients with acute brucellosis; 30 (60%) patients with subacute brucellosis.

Clinical and epidemiological examination with specific laboratory diagnostics (enzyme-linked immunosorbent assay with determination of antibodies to brucellosis pathogens (*Br. melitensis*) of class IgG and IgM, Heddleson plate agglutination reaction, Wright agglutination reaction in test tubes, indirect hemagglutination reaction with brucellosis diagnosticum; additional methods include clinical, biochemical and instrumental (X-ray of joints and spine, ultrasound of



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abdominal organs) studies. Blood was collected from a vein in patients with brucellosis in the morning on an empty stomach in 3.8% sodium citrate at a ratio of 1:9. After centrifugation of the patient's blood at 1500 rpm, the content of acute phase proteins in plasma (α 1-acid glycoprotein, α 1-antitrypsin, α 2-macroglobulin, ceruloplasmin, C-reactive protein) was analyzed on a Copas Emira biochemical analyzer using ROSH kits. Interleukin-4 (IL-4), γ -interferon (γ -IFN) were determined by solid-phase enzyme immunoassay using test systems from Cytokine LLC, St. Petersburg.

Statistical processing of the obtained results was carried out using the variation statistics method using Microsoft Excel 11.0 (Windows 10). To determine the reliability of differences, Student's t-test was used with the calculation of the error probability (P). Differences in mean values were considered reliable at a significance level of $P < 0.05$.

Results and discussion. During the primary epidemiological diagnosis of brucellosis, the majority of patients (67.3%) were found to have a professional nature of the disease with contact and mixed routes of infection: 48.5% were farmers and shepherds who were directly involved in animal husbandry and did not always use personal protective equipment (gloves), had scratches, cuts, and bruises.

The remaining patients were infected through foodborne transmission (18.8%), consuming undercooked foods (meat, meat products, milk, and dairy products). By age: 26.9% were 18 to 30 years old; 47.2% were 30 to 40 years old; 17.4% were 40 to 50 years old; and 8.5% were 50 to 60 years old. Patients by place of residence: 32.8% were urban residents and 68.2% were rural residents.

Table 1.

Serum levels of acute phase proteins and cytokines in patients with acute brucellosis

№	Indicator	Patients with brucellosis (main group)		Healthy individuals (control group) (n=15)
		acute form (n=20)	subacute form (n=40)	
1	CRP, g/l	0,07±0,003*	0,09±0,002*	0,007±0,0005
2	Alpha-1-acid glycoprotein, g/l	1,99±0,08*	2,89±0,09*	0,89±0,08
3	Alpha-1-antitrypsin, g/l	2,47±0,15*	3,07±0,11*	1,41±0,09
4	Alpha-2-macroglobulin, g/l	3,03±0,10*	4,15±0,14*	1,99±0,08
5	Ceruloplasmin, g/l	0,39±0,01*	0,57±0,05*	1,38±0,07
6	Interleukin-4 (IL-4), pg/ml	176,9±6,8*	187,5±9,8*	74,6±4,2
7	γ -interferon (γ -IFN), pg/ml	398,7±9,2*	412,7±7,4*	76,9±3,8

Note: * — significance of differences $P \leq 0.05$ compared to healthy individuals.

Our research revealed increased cytokine concentrations in patients with acute brucellosis. This was accompanied by significant changes in plasma levels of acute-phase proteins, indicating signs of an inflammatory response. This was confirmed by a significant increase in plasma C-reactive protein ($P \leq 0.05$). In this situation, C-reactive protein can be synthesized by peripheral cells of loose connective tissue (interstitial tissue), and when the inflammatory process involves the



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entire body, C-reactive protein is synthesized centrally by hepatocytes [7,8]. Serum levels of acute-phase proteins and cytokines in patients with acute brucellosis are presented in Table 1.

Analysis of acute-phase proteins in the peripheral blood plasma of patients with acute and subacute brucellosis revealed a significant increase in their levels compared to the control group ($P \leq 0.05$). For example, alpha-1-antitrypsin levels exceeded baseline levels by 1.7–2.1 times, and alpha-2-macroglobulin levels by 1.5–2.1 times (respectively), indicating increased antiprotease activity in the blood ($P \leq 0.05$).

It should be noted that the saturation of the blood with endogenous toxins, peptides and oligopeptides contributes to an increase in the protease activity of the blood in patients with acute forms of brucellosis, which leads to a compensatory increase in the activity of alpha-1-antitrypsin, alpha-2-macroglobulin. Thus, in patients with acute forms of brucellosis, against the background of general intoxication and the synthesis of primary mediators, the synthesis of acute phase inflammation proteins, which play a certain role in the pathogenesis of the disease, also increases.

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