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FEATURES OF THE SEROLOGICAL DIAGNOSIS OF LISTERIOSIS (LITERATURE REVIEW)

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Abstract:

Listeria are widely distributed in the surrounding ecosystems, from food, environmental objects, circulate in the body and cause disease in animals and humans. In this regard, the close attention that has been drawn to listeriosis infection in the last decade, both in terms of clinical and laboratory diagnostics, is natural. Particularly alarming is the growing role of listeria in perinatal and neonatal pathologies, which are characterized by the severity of the course and high mortality

Keywords: Listeriosis, serovariant, cold chain, L. ivanovi, L. innocua.

The increase in the incidence of listeriosis is due to the unique plasticity and ability of Listeria not only to persist, but also to multiply in infected products, even with strict adherence to the "cold chain". It should be noted that a certain role is played by the increase in people suffering from various immunodeficiencies, as well as the predominance of the food route of infection. After a disease, long-term immunity is formed [4, 5, 6, 7].

In order to identify the most significant virulent strains, it is necessary to develop new approaches to Listeria typing [8]. Of the Listeria species studied to date, only L. monocytogenes is dangerous for humans and animals, while L. ivanovii is pathogenic for animals [2]. To date, it has been established that L. monocytogenes is the etiological agent in 98% of cases of listeriosis in humans and in 85% of cases in domestic animals [4].

In 1911, the Swedish scientist G. Hulphers isolated and first described the bacterium L. monocytogenes from a purulent nodule in the liver of a dead rabbit [5], and an accurate and detailed description of the microbe was made later, in 1923 by E. Murray et al. [6]. Continuing the study, scientists have determined that L. monocytogenes is a pathogen for more than 50 species of mammals, including humans, birds, mites, fish and crustaceans. The first cases of human disease with listeriosis were registered in 1929.

It was noted that six species of the genus Listeria have specific antigens that are characteristic of 16 serotypes: 1/2a, 1/2b, 1/2c, 3a, 3b, 3c, 4a, 4ab, 4b, 4c, 4d, 4e , 7, 5, 6a, 6b. The somatic O-antigen of Listeria is indicated by numbers, the letter designation corresponds to the flagellar H-antigen, and the flagellar H-antigens are indicated by the initial letters of the Latin alphabet:

B, C, D. All serovariants were found in L. monocytogenes except for the last three [27, 29]. Strains of the species L. grayi have only one flagellar antigen E. L. ivanovii (serotype 5) and L. innocua (serotype 6) each have one somatic antigen. It should be noted that domestic serological diagnostics has its own characteristics: for example, L. monocytogenes serovars, designated in accordance with the international classification 1/2a 1/2b, 1/2c, 3a, 3b 3c, are combined into the first serological group, and the rest of the serovars - in the second. A wide range of host organisms in which the pathogen can multiply has caused antigenic ecosystems, from food products, environmental objects, circulate in the body and cause disease in animals and humans. In this regard, the close attention that has been drawn to listeriosis infection in the last decade, both in terms of clinical and laboratory diagnostics, is natural. Particularly alarming is the growing role of Listeria in perinatal and neonatal pathologies, which are characterized by the severity of the course and high mortality [1, 2, 3].

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The serological features of isolated cultures are not limited to the described scheme. In the United States, a culture of Listeria serovariant 4b was isolated, which contained genetic sequences characteristic of other serovariants [4]. In addition to intraspecific cross-reactions, Listeria has serological cross-reactions with staphylococci and typhoid-paratyphoid bacteria [9].

When conducting an epidemiological analysis in order to identify the source of infections and ways of its spread, it is of practical interest for medical microbiology to study the antigenic structure of L. monocytogenes [6].

In particular, when studying the serological landscape of strains isolated from patients with listeriosis, it was found that most cases of diseases are associated with serotypes 4b, 1/2a, 1/2b. An analysis of the incidence of listeriosis showed that about 50% of all cases of listeriosis in the world are caused by strains of serovar 4b, although serovars L. monocytogenes 1/2a, 1/2b, 1/2c dominate among the strains isolated from contaminated products. Outbreaks of intestinal diseases 1998-1999 in the USA after eating sausages were caused by the serovar 4b strain, which was the etiological agent of listeriosis in the UK for 30 years. It was found that out of 2232 isolates isolated from diseased people, 60% of cases were serovar 4b, and in 17%, 11% and 4% of cases the disease was caused by serovars 1a, 1/ab and 1c, respectively. The isolation of serovar 1/2a was most frequently reported in Eastern Europe, East Africa, Central Germany, Finland and Switzerland, while the co-isolation of serovar 1/2a and 4b in approximately equal proportions was noted in France and the Netherlands [10, 37 , 38].

It is difficult to determine the diagnosis of "listeriosis" only according to clinical and epidemiological data due to the polymorphism of clinical manifestations and the inability to identify the source of infection - for this reason, laboratory diagnostics is of primary importance. It is possible to give a final diagnosis only after bacteriological examination [28].

Despite the fact that bacteriological isolation of the pathogen culture is recognized as the "gold standard" in the diagnosis of listeriosis, serological methods, being auxiliary, still play an important role in the diagnosis of this infection. The advantages of serological methods include: rapid results, the relative simplicity of setting reactions, as well as the possibility of studying a variety of biological material [2].

One of the methods of serological diagnostics is the determination of antibodies to the secreted pathogenicity factor of Listeria - listeriolysin O. This method is more specific, and yet the authors recommend using it only to detect non-invasive asymptomatic forms of the disease during epidemic outbreaks of listeriosis [3] . It has been shown that the

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terminal polypeptide fragment of the recombinant listeriosin O molecule is the most specific in screening sera of people with listeriosis compared to other protein antigens. To detect non-invasive asymptomatic forms of the disease in epidemic outbreaks of listeriosis, as well as in the analysis of sera of donors and patients with listeriosis, it is advisable to use a specific technique based on the humoral response to listeria protein antigens (JrpA, JnlB and ActA) associated with pathogenicity. [12].

To determine the serological affiliation of crops, according to the world classification, it is recommended to use the multiplex PCR method in practical and scientific work, based on the correlation between the serogroup affiliation of an isolate and the presence of specific open reading frames in its genome [8, 11]. The use of this method makes it possible to identify the diversity of L. monocytogenes cultures circulating in different geographical areas of Russia with the differentiation of strains that are epidemically significant and dangerous to humans [14].

Most immunological methods for detecting Listeria are based on the use of monoclonal antibodies. The first panel of monoclonal antibodies for the detection of Listeria was proposed by J.M. Farber (1987). The method detected the common flagellar H-antigen of Listeria in L. monocytogenes, L. ivanovi, L. innocua, L. weishimeri, and L. seeligeri and did not cross-react with 30 cultures of other species, including staphylococci and streptococci [17, 44] . The genus-specific panel of monoclonal antibodies developed by T. Butman et al. [nine]. In enzyme immunoassay and dot-blot, monoclonal antibodies did not cross-react with 21 types of other microorganisms, including streptococci. The panel consisted of 15 monoclonal antibodies specific to the genus Listeria, which detected a thermostable genus-specific protein with a molecular weight of 30,000 to 38,000 Da. Two monoclones from this panel were further used to create a commercial enzyme immunoassay (Listeria - EEK) for the detection of Listeria spp. [five]. The test system has been widely used as an additional, but not alternative, method for the detection of Listeria in food [6].However, monoclonal antibodies, as well as polyclonal antibodies previously used in the method of immunofluorescence, are currently practically not used for the diagnosis of listeriosis. According to a number of researchers, this group of methods remains of practical importance only when conducting seroepidemiological examinations and sanitary and hygienic measures at livestock facilities for the prevention of listeriosis in animals and service personnel [14].

There are a number of serological methods that are used in clinical laboratory diagnostics and are aimed at identifying specific antibodies to Listeria. Their use is advisable from the second week of the disease. Antibodies against Listeria persist for several years after the disease. The serological tests used to diagnose listeriosis include: enzyme-linked immunosorbent assay (ELISA), agglutination test (RA), complement fixation test (RCC), indirect hemagglutination test (RIHA). The material for the study is blood and cerebrospinal fluid (CSF). The result is considered positive by the presence of antibodies in the titer from 1:250 to 1:5000 [7].

In the Russian Federation, for the serological diagnosis of infections in farm animals, drugs are produced for setting RSK and RNGA, as well as two types of sera, 1 and 2, which allow assessing the antigenic affiliation of Listeria to two serogroups. Currently, a dry complement is offered for the RSC produced by the ShchelkovskyBiocombinat (Moscow Region). Analysis of the antigenic structure of L. monocytogenes using domestic sera of two types showed a relatively low specificity of this differentiation system [8, 11].

It is well known that Listeria serovars and serotypes are not species-specific. They can be common to different types of Listeria, regardless of human pathogenicity. Analysis of the serological structure of Listeria showed that it is extremely inconvenient for diagnosis. L. monocytogenes, shares one or more antigenic determinants with Listeria species other than L. welshimeri. Therefore, the determination of the serovar alone without the use of other methods does not make it possible to establish the diagnosis of an infection caused by L. monocytogenes [8].

Serological methods that are currently used have a number of disadvantages: the study has low specificity (listeriosis antigens are very similar in structure to the antigens of other microorganisms, therefore, false positive or false negative results are often obtained), and the method itself does not detect the pathogen, but detects antibodies; the results are of low reliability; on their basis, listeriosis can only be suspected; in severe immunodeficiency states, the body loses the ability to form antibodies, while ELISA will be negative even with the most severe course of listeriosis; analysis is possible only in the later stages of the disease, starting from the second week from the first symptoms. The diagnosis of "listeriosis" can be suspected or made with a significant difference in antibody titers in paired sera of patients with a characteristic clinical picture (RA with a color diagnosticum, RSK, indirect immunofluorescence reaction (IRIF), RNAG), in the study of CSF (IRIF, PCR, ELISA, microscopy) and

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bacteriological study by enrichment with carbon immunoglobulin sorbent [2, 14].

Nevertheless, in the practice of domestic bacteriologists, serological methods for the laboratory diagnosis of listeriosis remain the main ones and make it possible to establish a presumptive diagnosis of listeriosis infection with further confirmation by bacteriological method. Of course, the results of a serological examination carry certain information about the contact of various population groups or risk groups with the pathogen, but do not allow diagnosing listeriosis with a high degree of accuracy even when several serological methods are used. The method of slide agglutination remains simple and reliable, for the implementation of which agglutinating listeriosis sera are required. The main factor limiting the diagnostic capabilities of bacteriological laboratories is the lack of commercial, registered preparations for typing cultures of L. monocytogenes.

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