Immune Reactions in the Body Based on Listeriosis.

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ABSTRACT

The review presents data on the antigenic structure of Listeria and the modern classification of epidemically significant Listeria serovariants. Information is given on the characteristic species-specific properties of Listeria serovariants, which may be common to two or more species, and also have common antigens with staphylococci, typhoid-paratyphoid bacteria.

Keywords: listeria, paratyphoid bacterium, antigenic scheme, listeriosis, pathogen serotyping

It has been shown that only the antigenic scheme of Listeria monocytogenes, the only type of Listeria pathogenic for humans, is of practical interest for medical microbiology. The importance of serotyping in epidemiological analysis in order to identify the source of infections and ways of its spread has been determined. Information about the discovery of the causative agent of listeriosis is presented. The data concerning the differences in the designation of serovariants in the diagnosis of listeriosis in domestic and foreign medical practice are given. The inextricable association of Listeria serotypes with a particular host, a particular type of disease and a geographical origin is displayed, which is confirmed by the isolation of food isolates. Thus, the most frequently isolated serotypes are 1 and 4. It is shown that the high level of adaptive properties of Listeria, their ability to reproduce in an abiotic environment, including food, an increase in persons with various immunodeficiencies, as well as the predominance of the food way of infection represent significant risk of increased incidence of listeriosis. The review provides information on such methods of immunochemical studies recommended as express diagnostics, such as immunofluorescence reaction, enzyme immunoassay, and polymerase chain reaction. The review considers the current state of the problem of serological diagnosis and promising areas for serotyping pathogenic Listeria. Serological diagnosis of Listeria has not been developed in detail, and existing serological methods are aimed at identifying specific antibodies to Listeria. The advantages of the serological method include: quick result; the possibility of studying any biological material. Currently available serological methods have a number of disadvantages, such as low reliability of the results, low specificity of the study.

Listeria are widespread in the environment, they are isolated from soil and water 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].

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, 9, 10, 11, 12]. Of the listeria species studied so far, 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 [25] from a purulent nodule in the liver of a dead rabbit, 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. For the first time, cases of listeriosis in humans were registered in 1929 [8].

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:

A, B, C, D. In L. monocytogenes, all serovariants were found 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, serovars of L. monocytogenes, designated in accordance with the international classification 1/2a 1/2b, 1/2c, 3a, 3b3c, are combined into the first serological group, and the remaining serovars - into second. A wide range of host organisms in which the pathogen can multiply has determined the antigenic heterogeneity of the outer coat of L. monocytogenes [12]. R.H. Orsis et al. [14] demonstrated that, using molecular typing methods, L. monocytogenes can be divided into three evolutionary lines characterized by different pathogenic potentials: the first line - strains associated with epidemic outbreaks of listeriosis (serotypes 1/2b, 3b, 4b, 4d, and 4e); the second line - strains isolated during sporadic cases of listeriosis (serotypes 1/2a, 1/2c, 3a and 3c); the third line - strains rarely associated with cases of listeriosis (serotypes 4a and 4c). At the same time, no patterns were found between the serovars of the isolated strains and the biological type of the host, as well as the severity of the disease. Host specificity and the course of the pathological process are determined by Listeria pathogenicity factors: listeriolysin, internalins A and B [13]. According to foreign authors, sequences encoding pathogenicity factors were found much more frequently in serovar 4b strains [19].

The serological features of isolated cultures are not limited to the described scheme. In Uzbekistan, a culture of Listeria serovariant 4b was isolated, which contained genetic sequences characteristic of other serovariants [14]. 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 [16].

In particular, when studying the serological landscape of strains isolated from patients with listeriosis, it was found that most of the 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. monocytogenes1/2a, 1/2b, 1/2c dominate among the strains isolated from contaminated products. Outbreaks of intestinal diseases 1998-1999 in the US after eating sausages were caused by the serovar 4b strain, which has been 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].

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 [18].

Despite the fact that the "gold standard" in the diagnosis of listeriosis is recognized as bacteriological isolation of the culture of the pathogen, serological methods, being auxiliary, still play an important role in the diagnosis of this infection. The advantages of serological methods include: an express result, the relative simplicity of setting up reactions, as well as the possibility of studying a variety of biological material [12].

One of the methods of serological diagnostics is the determination of antibodies to the secreted pathogenicity factor of Listeria - listeriolysin O. This technique 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 [39]. It has been shown that the 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 identify 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 (Jrp A, JnlB and Act A) 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 Uzbekistan 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 Listeria H-antigen in L. monocytogenes, L. ivanovi, L. innocua, L. weishimer, and L. seeligeri and did not cross-react with 30 cultures of other species, including staphylococci and streptococci [17, 4]. 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 revealed 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 Listeriaspp. [5]. 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 surveys and sanitary and hygienic measures at livestock facilities for the prevention of listeriosis in animals and staff [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 [17].

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 allow the diagnosis of an infection caused by L. monocytogenes [18].

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 in 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 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 slide agglutination method remains simple and reliable, for the implementation of which agglutinating listeria sera are required. The main factor limiting the diagnostic capabilities of bacteriological laboratories is the lack of commercial, registered preparations for typing L. monocytogenes cultures. Roszdravnadzor are urgent tasks.

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