UDC: 61.616

BACTEREMIA IN PATIENTS WITH DILATED CARDIOMYOPATHY

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БАКТЕРИЕМИЯ У ПАЦИЕНТОВ С ДИЛАТАЦИОННОЙ КАРДИОМИОПАТИЕЙ

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DILATATSION KARDIYOMIOPATIYA BILAN OG'RIGAN BEMORLARDA BAKTEREMIYA KUZATILISHI

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Цель: *исследование бактериемии у пациентов с дилатационной кардиомиопатией.* ***Материал и методы:*** *обследованы 37 пациентов с дилатационной кардиомиопатией (34 мужчины и 3 женщины) в возрасте от 17 до 58 лет (средний возраст 40,9±11,4 года). Диагноз ставился на основании данных анамнеза, результатов клинического и лабораторного обследования и устанавливался при наличии кардиомегалии, расширения полостей сердца и изменений миокарда по данным рентгенографии, электро- и эхокардиографии. У 35 в течение 48 часов с момента поступления пациента в клинику, до проведения зондирования и катетеризации сосудов и полостей сердца, проводилось исследование венозной крови и мочи на наличие бактерий. У 9 пациентов анализ крови на бактерии выполнен через 3-13 дней (8,5-1,4 дня) после начала внутривенного лечения. 8 пациентов были повторно обследованы через 9 месяцев - 2,3 года.* ***Результаты:*** *у 82% обследованных в крови циркулировали бактерии в вегетативной форме, т.е. потенциальные патогены. Кроме того, в крови пациентов была обнаружена L-форма бактерий. У 18% пациентов в крови выявлена только L-форма бактерий, сходная по культуральным свойствам с микоплазмами. Типирование бактерий по биохимическим свойствам позволило идентифицировать различные микроорганизмы в крови пациентов Всего из крови обследованных было выделено 50 штаммов бактерий. Полимикробная инфекция наблюдалась у 7 (18,9%) пациентов. Были идентифицированы Staphylococcus aureus с Enterobacter agglomerans; Staphylococcus epidermidis с Micrococcus spp.; Enterobacter cloaca е с Micrococcus spp. и Staphylococcus epidermidis.* ***Выводы:*** *бактерии, трансформированные в L-формы под воздействием антибиотиков или бактерицидных продуктов активированных макрофагов и нейтрофилов, могут длительное время не вызывать никакой реакции со стороны организма и способствовать длительной персистенции микроорганизмов без видимых клинических проявлений, создавая ложное впечатление клинического и бактериологического выздоровления.*

Ключевые слова: *дилатационная кардиомиопатия, бактериальная инфекция, увеличение левого желудочка.*

Maqsad: *dilatatsiyalangan kardiomiopatiya bilan og'rigan bemorlarda bakteremiyani o'rganish.* ***Material va usullar:*** *dilatatsiyalangan kardiomiopatiya bilan og'rigan 37 bemor (34 erkak va 3 ayol) 17 yoshdan 58 yoshgacha bo'lgan (o'rtacha yoshi 40,9±11,4 yosh) tekshirildi. Tashxis anamnez ma'lumotlari, klinik va laboratoriya tekshiruvlari natijalariga asoslangan va rentgenografiya, elektro- va ekokardiografiya ma'lumotlariga ko'ra kardiomegaliya, yurak bo'shliqlarining kengayishi va miokard o'zgarishlari mavjudligida aniqlangan. 35 bemor klinikaga yotqizilgan paytdan boshlab 48 soat ichida venoz qon va siydik, yurak tomirlari va bo'shliqlarini zondlash va kateterizatsiya qilishdan oldin bakteriyalarga tekshirildi. 9 bemorda bakteriyalarga qon tahlili vena ichiga davolash boshlanganidan 3-13 kun (8,5-1,4 kun) o'tkazilgan. Sakkiz bemor 9 oydan keyin - 2,3 yildan keyin qayta tekshirildi.* ***Natijalar:*** *tekshirilgan bemorlarning 82% ning qonida vegetativ bakteriyalar, ya'ni potentsial patogenlar aylanib yurgan. Bundan tashqari, bemorlarning qonida bakteriyalarning L-shakli aniqlandi. Bemorlarning 18 %ida qonda faqat mikoplazmalarga o'xshash madaniy xususiyatlariga ega bakteriyalarning L-shakli aniqlandi. Bakteriyalarni biokimyoviy xususiyatlari bo'yicha tiplash bemorlarning qonidagi turli mikroorganizmlarni aniqlash imkonini berdi. Tekshirilgan bemorlarning qonidan jami 50 ta bakterial shtammlar ajratildi. Polimikrob infeksiya 7 bemorda (18,9%) kuzatildi. Enterobacter agglomerans bilan Staphylococcus aureus; Micrococcus spp. bilan Staphylococcus epidermidis; Micrococcus spp. bilan Enterobacter cloacae va Staphylococcus epidermidis aniqlandi.* ***Xulosalar:*** *antibiotiklar yoki faollashtirilgan makrofaglar va neytrofillarning bakteritsid mahsulotlari ta'sirida L-shakllariga aylangan bakteriyalar uzoq vaqt davomida organizmdan hech qanday javob qaytarmasligi va mikroorganizmlarning ko'rinadigan klinik ko'rinishlarsiz uzoq vaqt saqlanib qolishiga hissa qo'shishi, klinik va bakteriologik tiklanish haqida noto'g'ri taassurot qoldirishi mumkin.*

Kalit so'zlar: *dilatatsiyalangan kardiomiopatiya, bakterial infeksiya, chap qorincha kattalashishi.*

Introduction Dilatational cardiomyopathy (DCM) is a disease with polymorphic clinical manifestations. The most likely cause of DCM development is considered to be a viral infection, in particular associated with Coxsackie viruses (B1, B2), as well as with influenza viruses type A, herpes simplex, cytomegalovirus and, in some cases, with the human immunodeficiency virus. Patients with DCM are found to have various immunological disorders, the wide spectrum and heterogeneity of which indicate that various mechanisms may be involved in the pathogenesis of this disease. As is known, viral and bacterial infections can lead to damage to blood vessels and myocardium in humans and experimental animals, which is accompanied by a change in immunological reactivity macroorganism. In this case, disorders in the immune system may develop, causing the addition of a secondary infection. This is most clearly manifested in the syndrome of acquired immunodeficiency of the human being (AIDS), in which the development of a secondary infection caused by bacteria, fungi, protozoa and viruses is observed. Patients with immunological deficiency can become infected with low-virulence microorganisms, which are normally commensals. Immunological disorders in patients with DCM are characteristic of the syndrome of immunological deficiency (SID), which is caused by mucosuppressive factors, including viruses and parasites. This work is devoted to the study of bacteremia and bacteriuria in patients with DCM.

Purpose of the study

Study of bacteremia in patients with dilated cardiomyopathy.

Material and methods

From 2018 to 2023, 37 patients with DCM (34 men and 3 women) aged 17 to 58 years (mean 40.9±11.4 years) were examined. The diagnosis of DCM was made based on anamnesis, clinical and laboratory examination and was established in the presence of cardiomegaly, dilation of the heart cavities and myocardial changes

according to X-ray, electro- and echocardiographic examination. The diagnosis was also confirmed using ventriculo- or coronary angiography with myocardial biopsy in 9 patients and at autopsy in 5 patients with DCM.

Venous blood and urine were tested for the presence of bacteria in within 48 hours from the moment the patient was admitted to the clinic, before performing probing and catheterization of the vessels and cavities of the heart in 35 of 37 patients with DCM. In 9 patients, blood was tested for bacteria 3-13 days (8.5-1.4 days) after the start of intravenous treatment. 8 patients were re-examined after 9 months - 2.3 years.

Table 1

Characteristics of bacteria isolated from the blood of patients

Family, genus, species of bacteria	Number of strains	
	abs	%
Neisseriaceae: Moraxella, phenylpyruvica, M-4 Moraxella-like	12 (8.4)	24
Micrococcacea: Staph. aureus, Staph. epidermidis, Staph. xyios, Staph. saprophyticus, Micrococcus spp	16 (2,7.2,1,1)	32
Enterbaceriaceae: Enterbaceriaceae aerogenes, enterobacteriaceae agglomerans, enterbaceriaceae cloacae	7 (1,2,2,2)	14
Pseudomoadaceae: Ps. stutzeri, Ps. dimminita	3 (2,1)	6
Streptococcoceae: Enteroccoceae faecium	1	1
Mycoplasma-like	9	18

Bacteria were incubated under aerobic and anaerobic conditions (in an atmosphere of 5% CO_2 and 95% air) at 37 and 22ºC. Difco media were used to grow L-forms of bacteria Lab.": AC - medium, PPLO - agar Blood Agar Base with and without addition of 10% erythrocyte mass of human blood group 0(I). Bacteria were typed according to their morphological, cultural and biochemical properties determined using microbiological test systems "API-Staph" "API-20E", "API-20A". Patients' sera were stored at 70 degrees C for no more than 6 months before testing. Antibody titer and bacterial autostrain were determined in the agglutination reaction.

Results and discussion

On admission to the clinic, no clinical signs of bacterial infection were detected in patients with DCM. Body temperature, heart rate, respiratory rate, and blood pressure were within normal limits. The total number of leukocytes was also within normal limits, amounting to 5962 +(-)1036 per 1 mm^3, but some hematological indices were altered. Moderate neutropenia within 10-15% was observed in 64% of patients, lymphocytosis in 14%, and eosinophilia in 19%. The source of bacteremia in the patients was not identified [1,3,4].

A comparative analysis of various morphological forms of bacteria circulating in the blood of patients showed that 82% of them had bacteria in the vegetative form circulating in their blood, i.e. potential pathogens. In addition to bacteria in the vegetative form, the L-form of bacteria was found in the blood of patients. Basically, the L-form of bacteria circulates in combination with the vegetative form (63%). In 18% of patients, only the L-form of bacteria was found in the blood, similar in cultural properties to mycoplasmas.

To determine the taxonomic position of L-forms of bacteria, they were transformed into a vegetative form by passaging on nutrient media [2,4,5,7].

Transformation of 18 (66.6%) of 27 cultures isolated from the patients' blood was achieved. The duration of the transition of L-forms into vegetative cells ranged from 5 days to 10 months (99 days on average). L-forms of bacteria incapable of transition into vegetative cells grew well on PPLO-agar, a selective medium for mycoplasmas, and by their biochemical properties belonged to the Mycoplasmataceae family and the Mycoplasma genus. The genus and species of bacteria circulating in the vegetative form corresponded to the genus and species of bacteria transformed from L-forms in 92.8% of the strains studied [1,8,10].

Typing of bacteria by biochemical properties made it possible to identify various microorganisms in the blood of patients (Table 1). A total of 50 bacterial strains were isolated from the blood of 37 patients with DCM. Polymicrobial infection was observed in 7 (18.9%) patients. The following bacterial combinations were identified: Staphylococcus aureus c Enterobacter agglomerans; Staphylococcus epidermidis c Micrococcus spp.; Enterobacter cloaca e c Micrococcus spp. and Staphylococcus epidermidis [6,8,9].

M4 - Moraxella-like with Pseudomonas Stapas stutzeri Microcos. epidermidis; Moraella phenylpyruvice Micrococcus spp. The patient was admitted to the clinic with a deterioration in his condition: acrocyanosis, dyspnea at rest, and edema of the shins were noted. The examination revealed stage II B circulatory failure, and there were no clinical or hematological signs of infection. For 2 months During hospitalization, against the background of antibiotic therapy, body temperature increased to 38.5-39ºC, lymphocytosis increased to 4500/mm and ESR to 22-50 mm/h, activation of humoral and functional insufficiency of cellular immunity were observed, antibodies to autostrains of bacteria were detected in titers of 1:160-1:320. Autopsy data confirmed the diagnosis of DCM. The duration of the disease in patients with DCM with polymicrobial infection was 1-6 years. The development of

polymicrobial infection indicates a profound impairment of the protective functions of the reticuloendothelial system, the functional activity of immune system cells in patients. A study of the dynamics of bacteria circulating in the blood of patients showed that bacteremia persists, but bacteria of one genus and biovar can be replaced by another (Table 2). When studying bacteria in the urine of patients with DCM, colonization of the urinary tract by various bacteria was revealed (Table 3). At the same time, the genus and species of bacteria circulating in the blood and isolated from the urine were not identical in most cases. This indicates the development of dysbacteriosis in patients, in most cases in the decompensation stage. Circulation of bacteria was accompanied by a high level of antibody formation to autostrains of microorganisms (titers 1:160-1:10 240) in 55% of patients. In the remaining patients, antibody titers were 1:20-1:80, some strains had the ability to spontaneously agglutinate in a solution of sodium chloride. In 75% of cases, circulation of bacteria of the genus Moraxella in the blood was accompanied by a high level of antibody formation. It is known that bacteria of this genus can parasitize on human mucous membranes and infect soft tissues. According to the authors, bacteria of this genus can be causative agents of infective endocarditis.

Table 2

Characteristics of recurrent bacteremia

Sick	Survey period	Genus, species of bacteria
Hasan	In 2 years 3 months	M-4 Moraxella-like, Pseudomonas stutzeri, L- shape Enterobacter agglomerans, L-form
Malika	In 1 year 9 months	Staph. Xylosis Stanh. lentus Enterobacter agglomerans
Batir	In 1 year	Staph. aureus, L-form Yersinia Pzeudotuberculosis Moraxella phenylpyruvica, L-form
Murad	In 9 months	Enterobacter cloaceae, Staph. epidermidis, spp., L-form Micrococcus L-shape Propionibacteria acnes, L-form
Safiya	In 1 year 7 months	Orma Moraxella phenylpyruvica, Staph. epidermidis L-shape Form Propionibacteria acnes, L- form
	In 2 years 2 months	Enterococcus faecium, L-for-

What is the role of bacteria circulating in the blood of patients in the development of DCM syndrome?

In a series of experimental works, it was

It has been shown that the creation of a source of infection in the abdominal cavity by E. coli or Staphylococcus aureus leads to bacteremia and cardiovascular disorders similar to those in septic shock in humans and similar to those in DCM (reduced left ventricular ejection fraction, left ventricular dilation, significant changes in diastolic function of the ventricles of the heart without changing the contractility of the myocardium in the first hours of bacteremia). Based on a series of experiments, a concept was proposed according to which the activation of endogenous mediators, in particular tumor necrosis factor interleukin-1, in response to bacterial infection is a common pathogenetic pathway for the development of cardiovascular changes.

Table 3

Comparative data of bacteremia and bacteriuria in patients

Sick	Genus, species of bacteria	
	In the blood	In urine (quantity tank in 1 ml)
Hasan	Staph. epidermidis (haemolyticus)	Staph. aureus 10
Malika	L-shape	Staph. epidermidis
Batir	Staph. xylosis	Staph. epidermidis
Murad	Moraxella phenylpyruvica, Staph. lentus 107 L-shape L-shape	Staph. xylosis 103 Staph. epidermidis 103 E. salt 107
Safiya	Enterobacter aerogenes, L-form	Enterobacter acrogenes 107

This is consistent with modern concepts of the development of the infectious process. In the presence of a focus of infection and the development of bacteremia, microorganisms contact with cells of the immune system, as a result of the activation of macrophages and monocytes, endotoxin of gram-negative bacteria is secreted when macrophages are exposed. Cardiovascular system dysfunction, characteristic of most microorganisms in

the presence of a chronic focus of infection and chronic bacteremia. Mycoplasma-like bacteria, producing active forms of oxygen, H_2O, hemolysins, possessing adhesive capacity, lead to the destruction of blood cells and tissues. Polysaccharides of bacterial glycoproteins suppress the phagocytic activity of macrophages and neutrophils, various toxins have a toxic effect on phagocytic cells, preventing opsonization of bacteria. Bacterial hemolysins (phospholipase C, β-hemolysin) cause hydrolysis of phospholipids, including sphingomyelin, leading to cell death. In L-form bacteria - microorganisms without a cell membrane, but with a preserved cytoplasmic membrane - the phospholipid composition of the membrane changes - cardiolipin is synthesized from phosphatidyl-glycerol. As a result, the rigidity of the cytoplasmic membrane of bacteria increases, their autolysins are inhibited. It can be assumed that one of the factors leading to the development of antiphospholipid syndrome is due to the circulation of L-form bacteria in the bloodstream. Antiphospholipid syndrome, accompanied by accumulation of antibodies to cardiolipin, can be complicated by thrombosis and thromboembolism. Phospholipases of pathogenic and saprophytic clostridia and bacilli hydrolyze phosphatidylcholine of cell membranes, forming lysophosphatidylcholine, which accumulates in tissues during metabolic acidosis, exhibiting arrhythmogenic activity. During acidosis, the formation of lysophosphatidylglycerol by bacteria increases, which has a strong membrane-damaging effect. In addition to the widely studied mitogenic and polyclonal properties of bacterial antigens and products of their vital activity, enzymes that change the primary structure, charge and activity of biologically active molecules of the macroorganism are of great importance. Neuroamidase bacteria and viruses, cleaving negatively charged terminal molecules of sialic acids from molecules of interleukin-2, change the charge of the molecule, as a result of which it loses the ability to interact with cells. The cleavage of neuraminic acid leads to a change in the charge of cells and a violation of their ability to adhesion, necessary for cooperative interactions and proliferation. Changes in the amino acid sequence, a decrease in the content of sialic acids in some cases lead to cryopathy, accompanying chronic hyperimmunization and autoimmune reactions. In addition, the participation of bacteria in glycosylation of molecules of the macroorganism is assumed. Glycosylation of collagen, crystallin, elastin, myelin leads to the formation of compounds that bind cytokines, lipoproteins, which infiltrate tissues. Consequently, bacterial and viral products, changing the structure of the macroorganism's molecules, will maintain an immunopathological state accompanied by autoimmune reactions, creating a complex immunodeficiency that develops as a result of chronic xenogenic hyper-immunization. According to our observations, 50% of patients with DCM have immune reactions to the antigen of the nervous tissue - the basic protein of myelin; other researchers find antibodies to cardiomyocyte antigens, components of the inner membrane of mitochondria, and B1-adrenoreceptors of cardiomyocytes in circulation.

Conclusions

According to our observations, 50% of patients with DCM have immune reactions to the antigen of the nervous tissue - the basic protein of myelin; other researchers find antibodies to cardiomyocyte antigens, components of the inner membrane of mitochondria, and B1-adrenoreceptors of cardiomyocytes in circulation. A promising direction is the study of the mechanisms of interaction of L-forms of bacteria with cells of the immune system, blood and tissues, their participation in the development of autoimmune reactions. Bacteria transformed into L-forms under the influence of antibiotics or bactericidal products of activated macrophages and neutrophils may not cause any response from the body, including the phagocytic system, for a long time and contribute to the long-term persistence of microorganisms without visible clinical manifestations, creating a false impression of clinical and bacteriological recovery.

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Objective: *To study bacteremia in patients with dilated cardiomyopathy.* ***Material and methods:*** *37 patients with dilated cardiomyopathy (34 men and 3 women) aged 17 to 58 years (mean age 40.9±11.4 years) were examined. The diagnosis was based on anamnesis data, clinical and laboratory examination results and was established in the presence of cardiomegaly, dilation of the heart cavities and myocardial changes according to radiography, electro- and echocardiography data. In 35 patients, venous blood and urine were tested for bacteria within 48 hours*

from the moment of patient admission to the clinic, before probing and catheterization of the vessels and cavities of the heart. In 9 patients, blood analysis for bacteria was performed 3-13 days (8.5-1.4 days) after the start of intravenous treatment. Eight patients were re-examined after 9 months - 2.3 years. ***Results:*** *82% of the examined patients had vegetative bacteria, i.e. potential pathogens, circulating in their blood. In addition, the L-form of bacteria was detected in the patients' blood. In 18% of patients, only the L-form of bacteria, similar in cultural properties to mycoplasmas, was detected in the blood. Typing of bacteria by biochemical properties made it possible to identify various microorganisms in the patients' blood. A total of 50 bacterial strains were isolated from the blood of the examined patients. Polymicrobial infection was observed in 7 patients (18.9%). Staphylococcus aureus with Enterobacter agglomerans; Staphylococcus epidermidis with Micrococcus spp.; Enterobacter cloacae with Micrococcus spp. and Staphylococcus epidermidis were identified.* ***Conclusions:*** *Bacteria transformed into L-forms under the influence of antibiotics or bactericidal products of activated macrophages and neutrophils may elicit no response from the body for a long time and contribute to prolonged persistence of microorganisms without visible clinical manifestations, creating a false impression of clinical and bacteriological recovery.*

Key words: *dilated cardiomyopathy, bacterial infection, left ventricular enlargement.*

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