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THE ROLE OF HERPESVIRUSES IN THE DEVELOPMENT OF CORONARY HEART DISEASE COMPLICATIONS

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Putting forward a virus hypothesis of atherogenesis, G. Fabricant assigned the leading part to representatives of Herpesviridae family in this process [4]. The question about etiological role of these viruses is discussed [1,2], but the influence of a virus infection on aggregative properties of blood corpuscles and on the function of endotheliocytes which are a target for persistent viruses of herpes simplex (HSV) and for a cytomegalovirus (CMV) [3,7] is specified. Recently there have appeared messages, that it is possible to consider CMV as an independent risk factor of restenosis after angioplasty [5] and the accelerated development of atherosclerosis in the patients who had a transplantation of heart [6]. The role of viruses in vascular smooth muscle cells proliferation [7,8] is shown. A virus infection including herpes viral infection can complicate considerably a course of any disease, a course of coronary heart disease in particular.

Death rate from cardiovascular diseases, and first of all from myocardial infarctions, has the lead in developed countries as before. It is the myocardial infarction that frequently leads to fatal complications of coronary heart disease (CHD). First of all these are cardiogenic shock, acute left ventricular insufficiency (ALVI), ventrical fibrillation and flutter, thromboembolism, cardiac rupture and tamponade.

The purpose of our work was to reveal the influence of herpesvirus infection, of cytomegalovirus and a herpes simplex virus in particular, on complicated course of CHD.

Materials and methods

129 patients with CHD, which were undergoing a course of treatment in infarction and cardiological departments of clinic *N* 8 of Kharkov. Among them, there were 83 men and 46 women. The average age of patients was 57,4 ± 3,6 years.

The control group was composed of 26 persons comparable for sex and age. During meticulous examination including electrocardiography (ECG), veloergometry, echocardiography, chest radiography none of the control group had clinical signs of CHD. Examined people in the control group had no lesions of heart valvular apparatus, arterial hypertension (AH), myocardial diseases. When analyzing the autopsy data, the group consisting of 19 died as a result of diseases not connected with an atherosclerosis, was used to control.

CHD was represented by following clinical forms: a stable angina (SA) of II-IV functional classes –39 patients, an unstable angina (UA) – 22 patients (a progressive exertional angina) and an acute myocardial infarction (AMI) – 68 patients. The diagnosis was established on the basis of patient's complaints, the antecedent anamnesis, clinical, laboratory and tool research methods. A functional class of a stable angina was defined according to the classification of the Canadian association of cardiologists.

The most frequent complication, which accompanies the course of AMI is recurrence anginous pains in the form of a recurrent angina, and also the presence of various forms of arrhythmia. The most frequent among them were sinus tachycardia and extrasystolic arrhythmia, which have made 44 % of general number of complications and 75 % of all rhythm disturbances.

We used the methods directed on coronary heart disease diagnostics, analysis of haemodynamic indicators and also virologic and immunologic methods of laboratory diagnostics.

The determination of HSV and CMV antigens in lymphocytes was carried out through indirect immunofluorescence method (IIFR) with the help of monoclonal serum against FITC-labeled HSV and CMV (Dako Corporation, Carpinteria, CA).

Results and discussion

The analysis of herpesvirus (CMV and HSV) infections of patients with CHD has revealed certain differences among clinical groups. The highest level of infection (90,9 %) is observed in the group of patients with unstable angina. The infection in the group with AMI and SA differs not so considerably – 72,0 % and 61,5 % respectively. Analyzing these total infection indicators of various CHD clinical groups it is possible to assume that destabilization of CHD clinical course can be connected with reactivation of HSV and CMV latent infections. Moreover when estimating the association of HSV and CMV, it is necessary to notice that every second patient with AMI has joint infection (48,5 %), the indicator is almost twice as low in the group with UA (22,7 %) and it is almost four times as low in patients with SA (12,8 %).

It appears that the infection by two representatives of Herpesviridae family (HSV and CMV) is the factor which aggravates CHD course. Literature information indicates that the probability of myocardial infarction appearance having UA increases under simultaneous HSV and CMV infections [7].

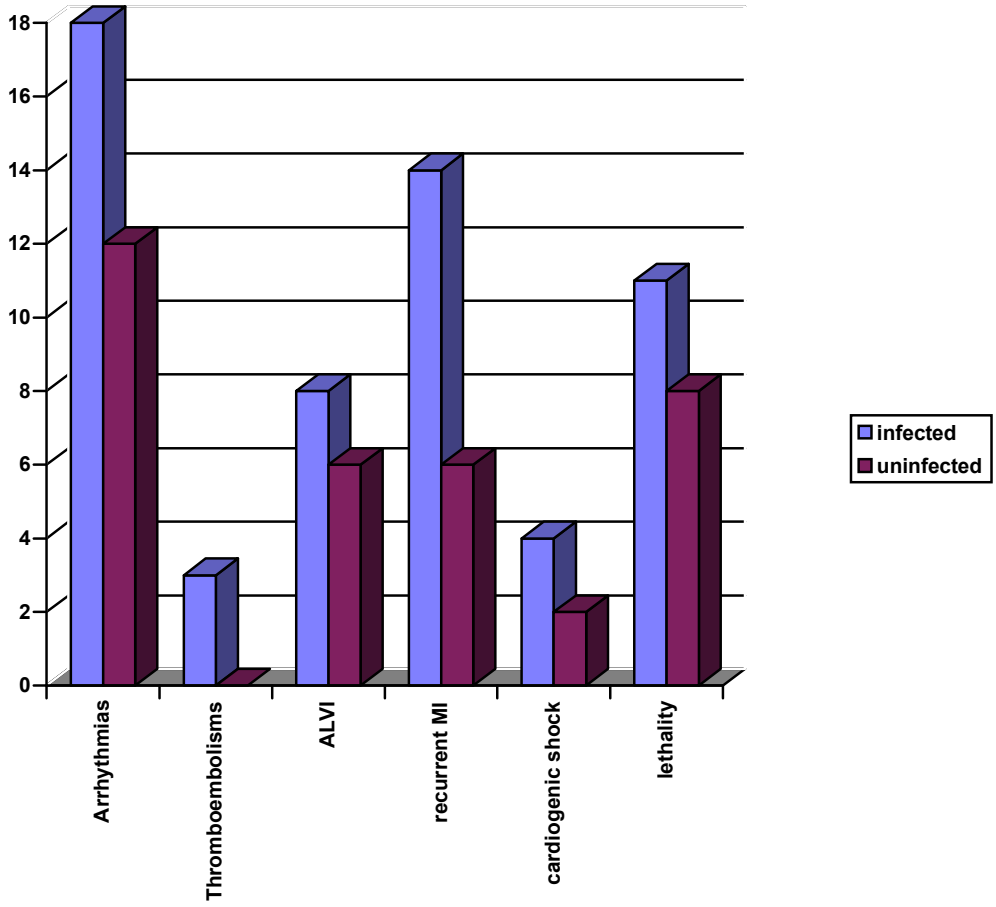
The important risk factor causing the development of atherosclerosis is lipidic metabolism disorder. In our work we analyzed the content of various lipoprotein fractions in patients with acute myocardial infarction. The analysis of the obtained data indicates the presence of dislipoproteinemia in the group of AMI-infected patients as well as in the group of uninfected patients. Correlation

between herpesvirus infection and the content level increase of low-density and very-low-density lipoproteins was revealed.

The obtained data give the evidence of the increase of general cholesterol, triglyceride, low-density and very-low-density lipoproteins indicators in patients with AMI in comparison with the control. VHDL cholesterol level of HSV and CMV-infected patients is reduced in comparison with uninfected patients. The possible reason of VHDL cholesterol decrease in infected patients is liver function disorder and ApoA-I (the basic protein which is a part of these lipoproteins) decrease. The atherogenity index, which is twice as high for AMI-patients infected with herpesviruses than for uninfected patients indicates the risk of the recurrent myocardial infarction development. The revealed characteristics of dislipoproteidemia for patients with AMI give the reason to assume that their appearance is connected with virus persistence characteristics in a human organism as well as with coronary vessel architectonics, which can be the factors of atherosclerosis progression promoting under infection conditions.

Significant content changes of inflammation markers such as leukocyte, ESR, sialic acid and fibrinogen ones were not observed in herpesvirus-infected patients with AMI as well as in uninfected patients with AMI. However, the tendency to fibrinogen level increase in herpesvirus infected patients was noted.

It was interesting for us to study characteristics of AMI clinical course, development of its complications depending on herpesvirus infection. When estimating the complications the development of arrhythmias, thromboembolic complications, recurrent myocardial infarction, acute left ventricular insufficiency (ALVI), cardiogenic shock and fatal outcome was taken into account.



Pic 1. Frequency of complication development in the course of acute myocardial infarction in infected and uninfected patients

Complications in the group of CHD infected and uninfected patients are shown in this diagram. The development of arrhythmias is found one and a half times as often among herpesvirus infected patients. It may be connected with tropism peculiarities of herpesviruses. The more frequent development of thromboembolisms in the group of uninfected patients can also be connected with the presence of endothelium "active zones" which are the most probable sites of thrombosis. At first sight ALVI syndrome and cardiogenic shock were also noted in patients infected with herpesviruses. But both of these syndromes were observed in patients with thromboembolic complications. Therefore we can consider their development as thromboembolism consequence. The development of ALVI and cardiogenic shock of various degrees in patients with AMI which were not noted with thromboembolic complications in the groups of infected and uninfected patients practically were not revealed.

More frequent development of recurrent myocardial infarction among herpesvirus infected patients is marked. Their frequency is twice as high in comparison with CHD uninfected patients. It may be the result of virus persistence in the organism. It is long persistent virus and factors effecting the organism lead to the formation of infectious causative agents which initiate pathological process [3]. According to researchers, there are cause-and-effect factors which influence the transition of the "silent" virus in active state [1]. It is proved by the presence of CMV and HSV association in CHD-patients. So among 20 patients who have recurrent myocardial infarction in the process of development 70 % were infected by herpesviruses. And 10 patients had CMV and HSV infection simultaneously.

Conclusions

Thus, in CHD patients with acute myocardial infarction the infection by the association of CMV and VHS is twice as high in comparison with patients with unstable angina and four times as high in patients with stable angina. Lipidogram changes of herpesvirus infected patients with acute myocardial infarction are characterized by the increase of general cholesterol level, atherogenicity index and by the decrease of high-density lipoproteins level in comparison with uninfected patients. Heart rhythm disturbance, thromboembolisms and recurrent infarction development are observed 1,5-2 times as often.

References

1. Roivainan V., Viik-Kajander V., Palosuo T. et.al. Infections, inflammation, and the risk of coronary heart disease // Circulation.-2000.-Vol.101.-P.252-257
2. Fong I.W. Infections and the Cardiovascular System: New perspectives – New York; Kluwer Academic/Plenum Publishers,2003.-270 p.
3. Goldschmidt-Clermont P.J., Creager M.A., Lorsordo D.W., et.al. Atherosclerosis 2005:Recent Discoveries and Novel Hypotheses // Circulation.-2005.-Vol.112,N 21.-P.3348-3353.
4. Mayr M., Kiechl S., Willeit J., et al. Infections, Immunity and Atherosclerosis // Circulation.-2000.-Vol.102,N 8.-P.833-839.
5. Isakov V.A., Borisova V.V., Isakov L.V. Herpes: pathogenesis and laboratory diagnostics. St. Petersburg,-1999. - P.190.
6. Frolov A.F. Virus persistence – Vinica, -1995. - P.233.
7. Horvath R., Cerny J.,Benedik J.Jr, Hokl J The possible role of human cytomegalovirus (HCMV) in the origin of atherosclerosis // J Clin Virol.- 2000.-Feb;16(1).-p.17-24.
8. Ibrahim AI, Obeid MT, Jouma MJ, Moasis GA, et al Detection of herpes simplex virus, cytomegalovirus and Epstein-Barr virus DNA in atherosclerotic plaques and in unaffected bypass grafts // J Clin Virol.-2005 Jan.-32(1).-p.29-32.

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The research results of CMV and HSV influence on CHD course and acute myocardial infarction in particular, of complication developments and outcomes are given in this article. It is defined that 48, 5 % of patients with AMI, 22,7 % of patients with unstable angina and 12,8 % of patients with stable angina have CMV and HSV association. The increase of general cholesterol level, of atherogenity index and the decrease of HDL level are detected in herpesvirus infected patients with AMI in comparison with uninfected patients. Heart rhythm disturbances, thromboembolisms and recurrent infarction development are observed 1,5-2 times as often.

Keywords: herpesviruses, coronary heart disease

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РОЛЬ ГЕРПЕСВИРУСОВ В РАЗВИТИИ ОСЛОЖНЕНИЙ ИШЕМИЧЕСКОЙ БОЛЕЗНИ СЕРДЦА

Перемот С.Д., Смелянская М.В., Мартынов А.В., Перемот Я.А.

В статье приведены результаты исследования влияния ЦМВ и ВПГ на течение ИБС и в частности острого инфаркта миокарда, развития осложнений и исходов. Установлено, что ассоциация ЦМВ и ВПГ встречается в 48, 5 % случаев у больных с ОИМ, в 22,7 % - у больных с нестабильной стенокардией и в 12,8 % - у больных со стабильной стенокардией. У больных с ОИМ, инфицированных герпесвирусами, выявлено повышение уровня общего холестерина, коэффициента

атерогенности, снижение ЛПВП по сравнению с неинфицированными. У больных ОИМ, инфицированных герпесвирусами, в 1,5-2 раза чаще наблюдаются нарушения ритма сердца, тромбоэмболии и развитие повторных инфарктов.
Ключевые слова: герпесвирусы, ишемическая болезнь сердца

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РОЛЬ ГЕРПЕСВІРУСІВ У РОЗВИТКУ УСКЛАДНЕНЬ ІШЕМІЧНОЇ ХВОРОБИ СЕРЦЯ

Перемот С.Д., Смілянська М.В., Мартинов А.В., Перемот Я.О.

У статті приведені результати дослідження впливу ЦМВ і ВПГ на перебіг ИБС і в особливості гострого інфаркту міокарду, розвитку ускладнень і результатів. Встановлено, що асоціація ЦМВ і ВПГ зустрічається в 48, 5 % випадків у хворих на ГІМ, в 22,7 % - у хворих з нестабільною стенокардією і в 12,8 % - у хворих із стабільною стенокардією. У хворих з ГІМ, інфікованих герпесвірусами, виявлено підвищення рівня загального холестерину, коефіцієнта атерогеності, зниження ЛПВП в порівнянні з неінфікованими. У хворих на ГІМ, інфікованих герпесвірусами, в 1,5-2 рази частіше спостерігаються порушення ритму серця, тромбоемболії і розвиток повторних інфарктів.
Ключові слова: герпесвіруси, ішемічна хвороба серця