title

Non-AIDS-defining cancers in the light of recent research

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summary

The results of the recent research which shows twice as high risk of non-AIDS-defining cancers among people diagnosed with AIDS in relation to the general population, make us look for the reasons of this phenomenon. What is taken into consideration are the following: the influence of factors other than HIV, decreased immunity during infection and the direct influence of the antiretroviral therapy on the development of cancerous processes.

key words

AIDS-defining malignancies, cancer, epidemiology, HARRT, HIV infection

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The research has indicated increased incidence of cancers among individuals with suppressed cellular immunity, especially of cancers showing etiopathogenetic relation with infectious factors. It can be clearly observed in the course of HIV/AIDS infections. In case of HIV infection practically all possible cancers can be encountered. However, according to the current classification based on the number of CD4 lymphocytes and the clinical presentation, AIDS-defining cancers include Kaposi's sarcoma among individuals below the age of 60, cervical cancer and non-Hodgkin's lymphoma. The remaining cancers can be ranked as non-AIDS-defining cancers.

The introduction of HAART (Highly Active Antiretroviral Therapy) in 1996 caused significant decrease in the incidence of AIDS-defining illnesses among individuals undergoing antiretroviral therapy. HAART made it possible to use a more aggressive treatment in case of HIV-infected individuals, organ transplantation among others. In the recent years the research observed a worrying increase in the incidence of non-AIDS-defining illnesses and increased mortality related to these cases. A lot of research has been trying to define the reasons and factors of the risk of the incidence of non-AIDS-defining cancers and the role of HAART. It is essential to determine whether the increase of NADM incidence is related to prolonging of lives of HIV-infected individuals treated with HAART or there are other factors which have influence.

The influence of HAART on the incidence and development of cancers among HIV-infected individuals is currently the subject of numerous research. The decreasing incidence of non-AIDS-defining cancers is linked with the antiretroviral therapy and the improved functions of the immune system. The situation looks different in case of NADM – the introduction of HAART seems to result in the increase in the incidence of certain cancers of this group. In spite of numerous research, the relation between the development of NADM and the level of immunosuppression indicated by the number of CD4 cells still remains unclear.

The analysis conducted by E. Engels i R. Biggar (1) can show how huge the scale of the problem is. The analysis has compared the incidence of non-AIDS-defining cancers between 1991 and 2002. Between 1991 and 1995, that is in the times before HAART was introduced, non-AIDS-defining cancers constituted 31% of all cancers among HIV-infected individuals, however between 1996 and 2002, in the age of HAART, they constituted 58% of all cancers.

In their research, M. Shiels i S. Cole (2) analysed 18 examples of research on non-AIDS-defining cancers by means of SIR (Standardised Incidence Ratio). The research was conducted between November 2007 and March 2009. The incidence of cancers among HIV-infected patients was compared with their incidence in general population, taking into consideration gender, HIV/AIDS severity and the use of HAART. Four thousand seven hundred and ninety seven cases of NADM were found among 625,716 HIV-infected individuals. In case of certain cancers, SIRs were particularly high – in case of colorectal cancer SIR = 28, Hodgkin's lymphoma SIR = 11, lung cancer SIR = 2.6, liver cancer SIR = 5.6, oral and throat cancers SIR = 1.9, kidney cancer SIR = 1.7. Graph 1 below shows SIR in case of the most common non-AIDS-defining cancers according to the research by M. Shiels i S. Cole (2).

To summarise this analysis, among HIV-infected individuals NADM was twice as high as in the general population (SIR = 2.0 with 95% confidence interval of 1.8 to 2.2). An interesting observation is the fact that NADM is twice as high in case of men compared to women (SIR = 1.59). The comparison of the clinical phase of HIV infection shows significant increase in the incidence of these cancers among people diagnosed with AIDS (SIR = 3.17), especially in relation to leukaemia (SIR = 8.02), brain cancer (SIR = 4.86), Hodgkin's lymphoma (SIR = 2.77) and lung cancer (SIR = 3.01). No difference was observed in the incidence of colorectal cancer, skin cancers and melanoma among individuals diagnosed with AIDS in comparison to those infected with HIV. The SIR in case of the HIV-infected population undergoing antiretroviral therapy compared to the SIR in case of HIV-infected patients before the introduction of HAART was 0.94, which means no significant relation between the incidence of NADM and the antiretroviral therapy.

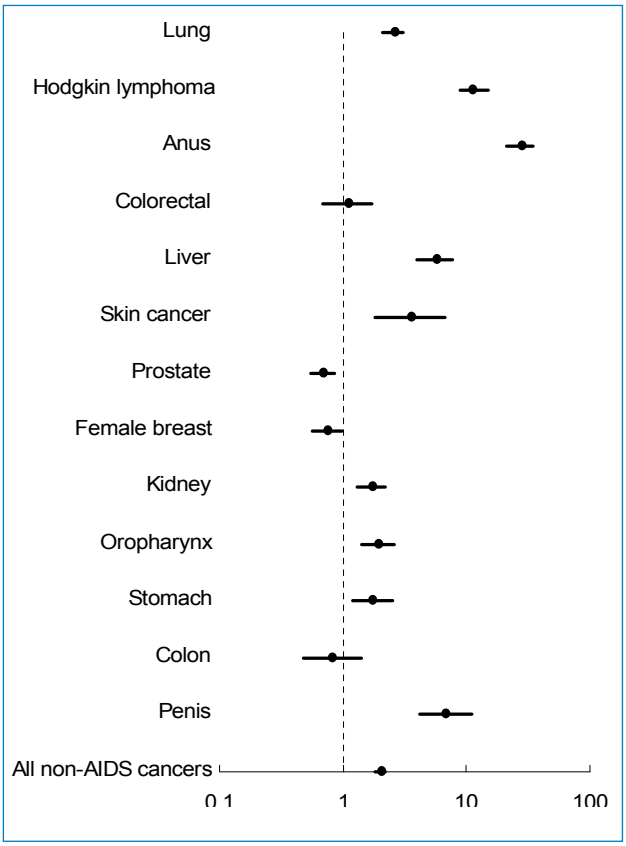

Figure 1. SIR in case of selected cancers according to the research by M. Shiels i S. Cole

The HIV-infected individuals show particularly high incidence of NADM related to the infectious etiology. Colorectal cancer, vaginal cancer and penis cancer connected with HPV virus show high SIR. J. Pafelsky, E. Holly i M. Ralston (3, 4) presented a detailed analysis of the relation between HPV infection and the incidence of colorectal cancer among HIV-infected women and men. A similar situation is observed in cases of liver cancer related to HBV and HCV viruses or Hodgkin's lymphoma and oral and throat cancer related to EBV virus infection. These results suggest that the HIV-infected population is more frequently infected with oncogenic viruses such as HPV, EBV, HCV or HBV compared to the general population. Suppressed immunity along with high percentage of infections with oncogenic viruses among HIV-infected patients can be responsible for the increase in the incidence of NADM related to the infectious etiology. In case of cancers of no infectious etiology, such as pancreas cancer or sigmoid colon cancer, SIR was close to or equal to 1.0.