DETECTION OF ANTIBODIES TO HUMAN HERPESVIRUS 8 (HHV-8) AMONG WOMEN OF CHILD-BEARING AGE IN THE APULIA REGION (SOUTH-EASTERN ITALY)

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In this study the authors investigated the presence of serum antibodies to Human Herpesvirus 8 (HHV-8) in a group of women of child-bearing age in the Apulia region (South Eastern Italy). A seroprevalence of 16.8% was observed, increasing, although non significantly, with the age of the women (10.6% in women between 19 and 25 years, 25.3% in women aging more than 35 years). The presence of antibodies to Hepatitis C Virus (HCV) was significantly associated to the detection of antibodies to HHV-8. Possible mother-to-child transmission of HHV-8 as well as the outcome of fetuses or children born to HHV-8 positive mothers are still a matter of debate. This study, showing the wide diffusion of HHV-8 infection in healthy women of child-bearing age in our geographical area, highlights the urgency of studies aimed to better clarify these relevant topics.

Human Herpes Virus 8 (HHV-8), first identified in 1994 (1), is the causative agent of all the epidemiological variants of Kaposi sarcoma, including classic, endemic, epidemic (AIDS related) and iatrogenic KS, as well as those of primary effusion lymphoma (PEL) or body cavity-based lymphoma (BCBL) and multifocal Castleman's disease. HHV-8 spread varies widely, depending on the geographical region: the virus seems to be widespread in the general population in regions where the incidence of Kaposi sarcoma is high or intermediate (2). These latter included Southern Italy where a HHV-8 seroprevalence was reported, ranging between 15% and 20% (3).

Although it is known that the incidence of Kaposi sarcoma is higher in men than in women, both in HIV-infected and uninfected individuals, no significant difference in HHV-8 seroprevalence has been generally reported in men as compared to women (2): in addition, a recent study (4) demonstrated (among a group of HIV-seronegative subjects) an even higher seroprevalence in women than in men, although this observation was limited to a single geographical area (northern Thailand). We have previously demonstrated that in the Apulia region (South Eastern Italy) there is a particularly high seroprevalence for HHV-8 (38.7%) among HIV-1 infected pregnant women, which was higher in women that had acquired the infection through needle-sharing than in women who had had sexual intercourse with HIV-1 infected individuals (5). No information is available, however, regarding the

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extent of HHV-8 infection in our region among HIV-seronegative women. This lack of information may be important for two reasons: a) although HHV-8 mother-to-child transmission seems to be relatively rare (6-7) occurrences have been reported (8-10) and co-factors may exist which influence the rate of transmission (11); as a matter of fact, definitive conclusions regarding this modality of transmission have still not been drawn; aa) a correlation between HHV-8 infection and complicated pregnancy (abortion, pre-term labor, low weight at birth) was reported (12), although such observation still needs confirmation.

In this study we therefore aimed to evaluate the seroprevalence for HHV-8 in a population of HIV seronegative women of child-bearing age in a single geographical region (Apulia, South Eastern Italy).

MATERIALS AND METHODS

We enclosed in this study 320 blood samples belonging to two groups of women: 1) 220 female student nurses attending the Clinic of Infectious Diseases, University of Bari, Italy, for HIV and hepatitis virus screening; 2) 100 pregnant women attending the Obstetric and Gynaecological Clinic, University of Foggia, Italy, for delivery. Among the women enrolled in the study, 141 (44%) were aged between 19 and 25 years, 96 (30%) between 26 and 35 years and 83 (26%) were more than 35 years of age. For women from group 1) residual aliquots of serum, previously used for virological analysis, that had been stored frozen at –20 °C were obtained for the study. For women in group 2) residual aliquots were obtained from serum samples that had been used for routine biochemical analysis and stored frozen at –20 °C. The samples were provided in an anonymous fashion along with the corresponding information regarding the HIV, HBV and HCV serostatus.

HHV-8 serum antibodies were detected by means of two commercially available methods (Advanced Biotechnologies, Inc. Columbia, MD): a) an ELISA assay using purified HHV-8 virions; aa) a HHV-8 IgG immunofluorescence assay (IFA) using a primary effusion lymphoma cell line. Sera were analysed at a dilution of 1: 80 in the ELISA and 1:20 in the IFA test.

RESULTS

The results of the study are summarised in Table I: 54 women (16.8%) were positive for HHV-8 antibodies with at least one of the two methods used. None of the women was HIV positive, while 14 (4.3%) were HBV and 12 (3.7%) HCV positive. A concordance between the results obtained using the two methods (ELISA and IFA) was observed in 97.8% of the samples. In 7 cases a discordance was demonstrated instead: four serum samples were positive for HHV-8 antibodies, detection tested by means of the ELISA assay, but negative by IFA. On the contrary, in three cases such antibodies could be demonstrated only in the IFA assay.

Regarding the correlations between HHV-8 seropositive and HBV infection, this latter was demonstrated in 3 (5.5%) and 11 (4%) HHV-8 positive and HHV-8 negative women, respectively, being not statistically signicative. HCV infection was more frequently observed among HHV-8 positive women (5 cases, 9.2%) than among HHV-8 negative women (7 cases, 2.5%): this correlation appeared statistically significant ($p = 0.025$). In addition, HHV-8 infection appeared to be correlated to the age of the women: in fact, antibodies to HHV-8 were demonstrated in only 15 (10.6%) women aged between 19 and 25 years, with the seroprevalence rising to 18.7% (18 cases) and 25.3% (21 cases) in women aged 26 to 35 and more than 35 years, respectively. These differences, however, did not reach a statistical significance.

DISCUSSION

Results reported here, confirm the high diffusion of HHV-8 in our geographical area, not only in HIV-positive, but also in HIV-negative women: the seroprevalence rate in these latter women (16.8%) increases with age, being relatively low in women aged 19-25 years and reaching a particularly high 25.3% in women aged more than 35 years. The finding of a wide distribution of the virus in women is still in contrast with the known lower incidence of Kaposi sarcoma in women than in men: it is therefore conceivable that other, still unrecognised, co-factors are involved in KS pathogenesis. The increasing of HHV-8 seroprevalence with age, observed in our study, although not statistically significant, is in agreement with other studies from our and other groups (3, 13) and it is possibly related to an increase in sexual activity in the women enrolled in the study over the years: as a matter of fact, transmission through sexual contacts still represents the unique definitively recognized modality for HHV-8 spread.

Table I. *Detection of serum antibodies to HHV-8, HIV, HCV and serum HbsAg in a group of 320 women.*

Virus	Student nurses (no. 220)	Pregnant women (no. 100)	Total (no. 320)
		Positive (%)	
HHV-8	36 (16%)	18 (18%)	54 (16.8%)
HIV	0	0	0
HCV	8 (3.6%)	4 (4%)	12 (3.7%)
HBV	9 (4%)	5 (5%)	14 (4.3%)

The number and percentage of women with detectable serum antibodies to HHV-8, HIV, HCV and positive for serum HBsAg for each group (student nurses and pregnant women) are reported: statistical analysis are reported in the results section.

As already reported in HIV-infected women (5), a significant correlation was observed between HHV-8 and HCV infection, suggesting that the two viruses probably share some common route of transmission. Although in agreement with other studies from USA (14-15) this finding is at variance with similar studies from Cambodia (16) and Central (17) and Southern Italy (18) where no correlations between HHV-8 and HCV infection could be demonstrated. Differences in the selection of patients or in the laboratory methods used might account for this discrepancy, but it is noteworthy that we demonstrated such a correlation in two different groups of women (HIV-positive and HIV-negative) and, in the former one, also a correlation between HHV-8 seropositivity and the use of needle-sharing was evident.

The possible perinatal transmission of HHV-8 (in utero, intrapartum or via breast milk), as well as a possible role of the virus in complicated pregnancy needs further study in order to be definitively clarified: the high prevalence of HHV-8 infection in child-bearing age in our region, however, highlight the relevance and the urgency of such studies.

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