the future, further studies including genetic factors are necessary to elucidate the pathology of AA with AD, and it may lead to greater insight into the pathomechanisms responsible for AA. ■

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Familial Kaposi's Sarcoma in HHV8 infected subjects presenting the G-174C allele of the IL-6 promoter: a possible role for EBV?

Classical Kaposi's Sarcoma (cKS) is a vascular tumor associated with HHV-8 infection [1]. Close contacts in the familial environment may play an important role in HHV-8 transmission. In fact, beside the sexual route, saliva is the most likely source of HHV-8 transmission [2]. However, both genetic and environmental factors have also been implicated in the pathogenesis of KS. A recent analysis of cancer clustering performed on 878,593 patients to estimate familial occurrence of different types of tumors, reports a striking familial aggregation of KS [5], pointing to either a genetic predisposition or environmental factors, or both. Previously suggested predisposing factors include immune suppression or an imbalanced immune response [3, 4]. Further, an association between the G-174C allele of the IL-6 promoter and the risk of KS development has been suggested [6]. Among the environmental factors, secondary infections may play a role, directly or indirectly, by a reactivation of HHV-8 [7]. We describe a familial case of cKS presenting peculiar characteristics. The son and the non-consanguineous husband of a cKS female patient developed KS lesions almost concomitantly to a clinical relapse in the woman. The latter was diagnosed with cKS in 2004 when she presented erythemato-oedematous and angiomatous papular lesions on the left leg. Endoscopic and radiologic investigations excluded visceral tumour involvement. Consequently, the patient underwent local treatment with electrochemotherapy and intravenous administration of bleomycin [8]. Subsequent clinical examinations, performed every six months, showed a complete remission of the disease until June 2012, when she relapsed, with the occurrence of skin lesions on both legs. During the same visit, both her husband and son underwent medical examination due to the appearance of papular, violaceous lesions, localized on the lower limbs, which had appeared two months before the visit on the husband and very recently on the son. Histological examination confirmed in both cases the suspected diagnosis of KS. Subsequent medical investigations, performed for clinical staging, showed no visceral involvement. All three patients were negative for HIV infection and had high titers of anti-HHV-8 antibodies towards both lytic and latent phase antigens. HHV-8 DNA was detected in sera from the wife and husband, while viral load was undetectable in the son's serum. Analysis of the genetic variants of HHV-8 showed that all patients were infected by a type A virus, which is the most represented HHV-8 genotype present in our geographical area and has been previously reported in association with severe forms of KS [9]. Other herpes virus infections, including Herpes Simplex Viruses 1 and 2, (HSV1/2) Cytomegalovirus (CMV), Epstein-Barr Virus (EBV), were assessed with determination of the number and distribution of lymphocyte subsets and assessment of genetic polymorphisms of the IL-6 promoter *(table 1)*. Written informed consent was obtained from the patients for publication of this report. The patients did not show any significant alterations in the number and distribution of lymphocyte subsets, which were within normal ranges. However, genetic assessment showed that all patients presented the putative KS-predisposing allele of the IL-6 promoter, the wife presenting a homozygosis and the newly affected relatives a heterozygosis, respectively. The determination of concomitant viral infection, performed by either serological or molecular analysis, revealed the possible occurrence of a recent EBV infection/reactivation. They had anti-BZLF1 antibodies, which have been associated either to recent infection or to viral reactivation [10]. Moreover, the wife and husband had IgM against p138 EA antigens as well as IgG anti-EBNA, associated with a past infection, while the son had no anti-EBNA IgG. Conversely, anti-CMV IgG were present only in the wife, as a result of a past infection but were absent in the husband and son, while HSV1 and HSV2 were excluded by real time-PCR of sera or skin biopsies in all patients. Although these serological results were gathered on a single sample, and thus require future confirmation, they suggest that, even if clinically silent, reactivation of EBV (which similarly to HHV-8 infects B lymphocytes, establishes a latent infection in target cells and controls the host's

Table 1. Clinical, genetic, immune and virological parameters in the family members in relation to KS relapse in the affected wife/mother and KS onset in her husband and son

		Wife (63 yrs)	Husband (64 yrs)	Son (40 yrs)
Elapsed time from diagnosis (months)		90	2	0
Clinical stage		A1	B1	A1
IL-6 promoter polymorphism G-174C		Homozygosis (GG)	Heterozygosis (CG)	Heterozygosis (CG)
CD4 lymphocytes (n/mmc) (540-1600)		1497	790	1180
CD8 lymphocytes (n/mmc) (270-930)		1330	345	830
NK lymphocytes (n/mmc) (210-740)		700	263	815
B lymphocytes (n/mmc) (100-810)		372	511	750
HHV-8	Antibodies (titer)	1:25600	1:25600	1:25600
	Viral load GenEq/mL	125	100	<10
	Genotype PBMC/lesion	A	A	A
EBV	IgG anti-EBNA	+++	+++	Neg
	IgG anti-VCA	+++	++	++
	IgG anti-BZLF1	+++	+++	+++
	IgM anti-EA 138	++	++	Neg
CMV	IgG	+++	Neg	Neg
	IgM	Neg	Neg	Neg

adaptive immune response), might cause HHV-8 reactivation in genetically predisposed individuals, and, in turn, cKS relapse/development. ■

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