Table 2.8. Case–control/comparison studies of KSHV and multiple myeloma

Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	No. of exposed cases/Total	No. of exposed controls/ Total	Comments
Rettig *et al* (1997)	15 MM Evaluated 100 ng of DNA (equivalent to the amount of DNA from 15,000 cells) from bone marrow mononuclear cells and bone marrow stromal cells from multiple myeloma patients for the presence of KSHV DNA samples	8 MGUS 10 normal individuals and 16 patients with other malignancies	PCR to amplify KS330233 sequence of KSHV	15/15 in stromal cells; 0 / 23 fresh myeloma bone marrow mononuclear cell	2/8 MGUS; 0/26 controls	Selection of cases and controls not clear.
Said *et al* (1997) LA, USA	Biopsy samples from 20 MM cases (9 in remission),	21BM Biopsy samples from Lymphoma / leukemia pts	Dendritic cells Fresh marrow ISH ORF 72	17/20	0/21	Selection of cases and controls not clear. 9 patients in remission
MacKenzie *et al* (1997)	Serum samples from 78 MM cases from UK	37 Healthy controls	Antibodies to HHV-8 lytic (ORF 65.2 ELISA) and latent (IFA on BCP-1cell line). WB Confirmation on + samples	2/78	2/37	Selection of cases and controls not clear
Marcelin *et al* (1997) France.	23 MM 3 MGUS 10 KS	13 NHL	Antibodies to latent HHV8 (IFA on BCP-1cell line).	0/23 MM	0/13	Selection of cases and controls not clear
Whitby *et al* (1997) Italy	37 MM patients from Po Valley, Italy 37 MGUS	241 controls (Lyphoma patients and blood donors from same area)	KSHV LNA-1 by IFA	4/37 MM 2/36 (MGUS)	33/241	Selection of cases and controls not clear
Masood *et al* (1997) USA	Serum samples from 28 MM patients and 25 KS patients 5 Bone marrow MNC samples, 5 Bone marrow stromal cells	24 blood donors	ELISA for whole virus lysate and IFA for lytic antigens (KS-1 cell line) PCR Amplification of the KS 330 sequence.	2/28 MM, 0/5 BM-MNC 0/5 BM-Stroma	2/24	Selection of cases and controls not clear. Sera tested 'blindly'

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Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	No. of exposed cases/Total	No. of exposed controls/ Total	Comments
Olsen *et al* (1998) Columbia, USA	Sera collected from 25 cases of MM, 9 patients with MGUS	70 healthy blood donors 25 Patients with Abnormal serum protein Electrophoresis (SPEP)	LANA IFA	5 / 25.MM 2/9.MGUS	8 /70 donor 11/ 25 abnormal SPEP	Selection of cases and controls not clear
			ORF 65 WB	3 / 25 MM 1/9 MGUS	5 / 70 donor 5 / 25 abnormal SPEP	
Santarelli *et al* (1998) Italy	Sera from 36 patients with MM, 19 with MGUS and 10 with KS	25 Healthy blood donors	IFA Latent	3/36 (MM) 0/19 (MGUS) 5/10 (KS)	1/25	Selection of cases and controls not clear
			IFA Lytic KS-1	0/36 (MM) 0/19 (MGUS) 7/10 (KS)	1/25	
Schönrich *et al (*1998) Heidelberg, Germany.	Sera of 99 patients with advanced MM and 2 with MGUS	14 Patients with NHL, 19 with Breast cancer and 34 normal individuals	IFA Lytic KS-1	4/99 MM 0/2 MGUS	0/14 NHL 1/19 Breast cancer 1/34 healthy individuals	Age matched controls. Selection of cases and controls not clear
Agbalika *et al* (1998) Paris, France	Sera and BM biopsies from 10 patients with MM	10 patients with NHL 10 normal BM samples	IFA – Lytic antigens PCR PCR amplification of the $KS330_{233}$ sequence	5/10 BM biopsy 1/10 serum	0/10 normal BM 1/10 NHL BM	PCR data unusable. No antibodies to lytic HHV-8 antigens were detectable by immunofluorescence in the sera of MM patients or controls. Used long term cultures on MM cases but not in controls
Bélec *et al* (1999a)	Enrolled 15 MM cases without Crow-Fukase syndrome	15 healthy controls	IFA-HHV8 late proteins (KS-1)	0/15	0/15	Selection of cases and controls not clear

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Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	No. of exposed cases/Total	No. of exposed controls/ Total	Comments
Sitas *et al* (1999) Johannesburg, South Africa 1992–1997	Combined 2 studies: First among 1015 black inpatients with newly diagnosed cancer in three tertiary public hospitals in Johannesburg and Soweto completed a 1-page data sheet and provided a serum sample. Second study comprised an interview on 2576 newly diagnosed cancer patients using a 2-page lifestyle questionnaire. Obtained sera from 108 incident cases of MM prior to treatment	3293 incident cancer patients other than KS (n=51) interviewed with a 2-page lifestyle questionnaire and providing a serum sample, and obtained sera from 108 blood donors (only age and sex info provided); matched by age and HIV-1 status	IFA latent BCP-1 cell line	antibody titre (1:100): 24% (95%CI 16–33%) High titre (1:204800): 1.5% (95%CI 0.5–5)	32% (95%CI 28–38%) 3% (95%CI 1.1–3.6)	Histological confirmation rate is high.; Age, sex, education and sex partner adjusted prevalence rates
Azzi *et al* *(*2001) Italy	Obtained BM samples from 25 Hospital patients with MM (66.6 yrs), 22 with MGUS (66.6y)	BM samples from 45 NHL patients (58.3y), and 21 healthy controls (52.2y)	PCR –ORF 26	14/25 MM; 8/22 (MGUS)	26/66	Selection of cases and controls not clear
Beksac *et al* (2001) Turkey.	21 patients admitted to haem dept with MM, 2 with MGUS	12 Controls: 1 plasmacytoma, 6 haem disorders 5 healthy controls	PCR KS330233 ORF26 sequence.	17/21MM; 0/2 MGUS .	1/12	Selection of cases and controls not clear
Patel *et al* (2001) Johannesburg, South Africa	BM aspirates obtained from 34 black patients admitted to Hospital with MM (61.4y), 20 men, 17 had BM cell culture	BM trephine biopsy and BM aspirates from 19 patients	Cultured BM adherent cells PCR ampli-fication of the KS 330-233 sequence.	4/17	0/26	Selection of cases and controls not clear
Zhu *et al* *(*2002) Toronto, Canada	BM aspirates obtained from 12MM patients with >20% marrow plasmocytosis	8 Normal allogeneic donors	Nested PCR ORF65 ORF73 ORFK8.1	 67% 22% 58%	 37% 12.5% 62%	Selection of cases and controls not clear

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Reference, study location and period	Characteristics of cases	Characteristics of controls	Detection method	No. of exposed cases/Total	No. of exposed controls/ Total	Comments
Hermouet *et al* (2003) Western France	BM samples collected prior to treatment from 11 patients with MM (med50y)	BM Samples from 17 Healthy adults (med 41y) 16 AML (55y) 21 B-cell pathologies (66y)	Real time qPCR	1/11	24 / 54	Selection of cases and controls not clear
Santón Roldán *et al* (2002) Madrid, Spain	BM of 41 patients with MM	24 patients with other disorders (NHL, CML, carcinomas, melanoma, cytopaenia, palycytemia and anaemia)	PCR ORF 26	9/41	12/24	A number of patient groups tested, BM aspirates were only available in these groups
De Sanjosé *et al*. (2004) Spain	70 cases of plasma cell myeloma from 4 centres in Spain	598 control blood samples collected from hospital wards and outpatient clinics	K8.1 ELISA or (LANA)	2/70	32/598	Logistic regression used. Adjustment variables not specified
Tsai *et al* (2005) Taipei, Taiwan	Blood samples collected from patients with haematological diseases, 36 MM	229 patients with various heamatological disorders	Indirect IFA (Biotrin, Dublin Ireland)	7/36	57/229	

BM Bone marrow; MM Multiple Myeloma; ELISA, Enzyme-linked immunosorbent assay; IFA, immunofluorescence assay; med, median; y, years of age
*POEMS: Polyneropathy, organomegaly, endocrinoplasty M-protein skin changes; MGUS, monoclonal gammopathy of undetermined significance