

CLASSIC KAPOSI'S SARCOMA AND OTHER SYNCHRONOUS OR HETEROCHRONOUS TUMOURS: A POPULATION-BASED STUDY

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ABSTRACT

Introduction: The aim of this study was to define the incidence of classic Kaposi's sarcoma in Sardinian patients with another synchronous or heterochronous malignancy, and to evaluate the role of classic Kaposi's sarcoma as a risk factor for cancer.

Materials and methods: Data from the cancer registry of Sassari province, including all incident cases of classic Kaposi's sarcoma, as well as all other types of cancer during an 18 year period (1992–2010) were used for analysis.

Results: The European adjusted incidence rates of Kaposi's sarcoma in North Sardinia was high in both males (2.25/100,000) and females (0.85/100,000). However, a decreasing incidence trend was observed in the period under investigation. Odds ratio between these patients and those with multiple neoplasias other than Kaposi's sarcoma was 3.40.

Conclusions: A high incidence but a decreasing trend of classic Kaposi's sarcoma was detected in North Sardinia during the period under investigation. Our data suggest that classic Kaposi's sarcoma may have a role in the development of further malignancies in affected patients.

Key words: Kaposi's sarcoma, synchronous, heterochronous tumours, risk factor, Sassari, Italy.

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Introduction

Kaposi's sarcoma (KS) is a malignant tumour arising from the vascular endothelium. Four clinical-epidemiological forms have been proposed to classify Kaposi's sarcoma: classic Kaposi's sarcoma (CKS), African sarcoma, AIDS-related Kaposi's sarcoma, and immunosuppressive therapy associated Kaposi's sarcoma. All forms are characterised by infection with human herpesvirus-8 (HHV-8)⁽¹⁾. At the early stages, HHV-8 infection causes immune imbalance that favours oncogenesis, likely by stimulating lymphocyte proliferation via virally-encoded cytokine homologues or proteins that interfere with cell cycle control^(2,3).

The spread of AIDS in the last few decades has renewed interest in KS because of variations in the world incidence pattern of the disease. CKS is a rare neoplasia, showing heterogeneous distribution in different geographic areas, with high incidence

rates registered in the Mediterranean region (4). Before the AIDS era, it was uncommon in the USA and England^(5,6). CKS is a relatively common disease in Sardinia, according to epidemiological reports⁽⁷⁾.

A very high incidence of CKS has been described in some recent Italian studies, whereas a decline in CKS in the older population and a steady increase in AIDS-related KS have been described in some areas in Italy^(8,9). Furthermore, a relevant correlation between the AIDS-related form and immunoblastic lymphomas has been demonstrated⁽¹⁰⁾. Although some authors have not observed an increased risk for additional cancers among individuals affected by CKS, others have reported an increased risk of onset of new malignancies in patients with CKS, or alternatively, a higher risk for CKS in patients with a diagnosis of cancer of a different type⁽¹¹⁻¹³⁾.

The aim of this study was to define the incidence of CKS in Sardinian patients with another synchronous or heterochronous malignancy. Furthermore, we evaluated the role of CKS as a risk factor for the development of additional tumours.

Materials and methods

Data from the cancer registry of Sassari province including all incident cases of CKS, as well as all other types of cancer during an 18 year period (1992-2010) were used for analysis. In 2010, the province had an estimated population of 490,000. Cases were identified according to standardised criteria and procedures employed for population cancer registries, based on accurate collection of record files from all hospitals and health care institutions across the province⁽¹⁴⁾. Data from the registry have been used for periodical publication of epidemiological reports⁽¹⁵⁻¹⁹⁾.

Inclusion criteria for CKS cases were based on pathological referrals. The histological diagnosis of CKS was made according to generally accepted morphological and immunohistochemical parameters⁽²⁰⁾. Furthermore, all patients with KS underwent a blood test for detecting HIV infection after written informed consent was obtained. Data on previous transplant and/or immunosuppressive therapy were obtained from clinical records. All tumours registered were classified according to the International Agency Cancer Research classification system⁽²¹⁾.

Crude incident rates were calculated using the number of cases detected and the official population estimated in the province during the period considered (1992-2010). Standardised rates were adjusted for the European population using the direct standard method (EAR = European adjusted rates). Finally, odds ratios were calculated for cases of CKS with other synchronous or heterochronous tumours compared with patients with multiple tumours other than KS during 1992-2010.

Results

From 1992 to 2010, 44,247 cases of malignant neoplastic disease were registered in the province. During the same period, 240 CKS cases, 10 AIDS-associated cases, and two KS in patients undergoing immunosuppressive therapy were detected. Among the CKS patients, 171 were males and 69 were females (male to female ratio 2.5:1). The incidence

was significantly higher in males >70 years of age. Crude, specific, and EAR incidence rates are reported in Table 1.

Age class	Males		Females	
	n°	Rate	n°	Rate
40-49	4	0.62	2	0.31
50-59	10	1.84	1	0.17
60-69	24	5.52	3	0.83
70-79	53	19.38	20	5.65
80+	80	23.08	43	21.14
Total	171	3.94	69	1.53
EAR		2.25		0.85

Table 1: Age-class number of cases and incidence rates of CKS per 100,000 inhabitants in North Sardinia. (EAR: European adjusted rates)

CKS incidence decreased over time in males, whereas it increased in females since 2001 and decreased thereafter (Figure 1).

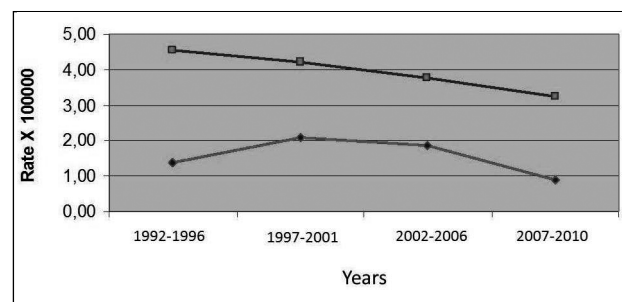


Fig. 1: Incidence trend of classic Kaposi's sarcoma in North Sardinia (1992 - 2010). (M: males, F: females).

CKS was associated with at least one additional tumour in 60 (54 males and six females) of the 240 patients. Among them, 40 cases (16.7%) presented with CKS as the first tumour diagnosed, and CKS was diagnosed in the remaining 20 patients with at least another previous or synchronous tumour (Tables 2 and 3).

Among the 44,247 cancer cases registered, 3,933 (8.9%) were cases with more than one malignancy. Therefore, the odds ratio of CKS multineoplastic patients compared with multineoplastic patients without CKS was 3.40.

Discussion

Classic KS mostly affects individuals >60 years old and rarely occurs earlier than the 4th or 5th decade of life. In northern Sardinia, the specific and standardised incidence rates are higher than in other, particularly northern, areas of the country^(8,9).

Second malignancy	Age Classes						Total
	40-48	50-59	60-69	70-79	80-89	90+	
Squamous cell carcinoma			1	3			4
Basal cell carcinoma			2		2		4
Adenocarcinoma	1	2	2	3	3	4	15
Colangiocarcinoma				1			1
Neuroendocrine carcinoma					1	2	3
Bcell Malignant lymphoma	2		2				4
Lymphoid leukemia				2		1	3
Acute myeloid leukemia					1	1	2
Chronic myeloid leukemia					2		2
Essential thrombocythemia				1			1
Cancer not specified					2	1	3
Total	3	2	7	10	11	9	40

Table 2: Age-class distribution of CKS diagnosed as first tumor in patients with multiple malignancies.

First malignancy	Age classes				Total
	60-69	70-79	80-89	90+	
Squamous cell carcinoma	2	1	1		4
Basal cell carcinoma	3	1	1	1	6
Transitional cell carcinoma			1		1
Adenocarcinoma		5			5
Non-Hodgkin's Lymphoma	2				2
Acute myeloid leukemia		2			2
Total	7	9	3	1	20

Table 3: Age-class distribution of CKS diagnosed as second tumor in patients with multiple malignancies.

In a previously published epidemiological study reporting data from 1992 to 1997 and conducted in the Sardinia region, the incidence of CKS was lower than that estimated in the present study⁽²²⁾. This suggests an increasing trend for the incidence of CKS in recent years. However, considering the years from 1992 to 2010, we found a decrease in incidence in males and a temporary increase in females (from 1992 to 2001). This may be due to two major events observed in the general local population in the last 30 years: the ageing of individuals who had not had malaria and the transformation of occupational, social, and economic conditions, particularly a shift from agriculture activities to industry and tourism businesses, with progressively increased involvement of females in the labour force. Such events may have influenced the trend in disease incidence, although some authors did not find any occupational risk for CKS⁽²³⁾.

The association between KS and other tumours (particularly immunoblastic lymphoma) is widely described in patients affected by AIDS⁽¹⁰⁾. The role of CKS as a risk factor for additional primary tumours is still controversial⁽¹¹⁻¹³⁾. Our data suggest that males with CKS present a significant risk for developing multiple tumours, but this result was not confirmed in females.

The AIDS- and immunosuppressive therapy-associated cases indicate that a dysregulation of the immunological system may be involved in KS pathogenesis. However, this hypothesis alone does not fully explain the differences observed between the sexes and the higher neoplastic risk in male patients with CKS. Thus, further studies are necessary to better comprehend the pathophysiological mechanisms and associations of this disease.

Conclusions

A high incidence of CKS was detected in Sassari province, mainly involving males > 60 years of age. However, a decreasing trend in the incidence was observed during the period under investigation. Our data suggest that CKS may have a role in the development of further malignancies in affected patients.

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