

## Familial Kaposi's Sarcoma: Case Reports and Review of the Literature

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We report 4 new families with Kaposi's sarcoma, occurring in 2 members of the same family (2 pairs of brothers, uncle and nephew and father and son) in a series of 160 patients with Kaposi's sarcoma. In addition, HLA typing was also carried out for 6 of the 8 patients. A detailed review of the literature is also presented. The total number of familial cases of Kaposi's sarcoma is low (only 30 cases are described); the great majority of these cases consist of siblings and Italians. *Key words: familiarity; HLA.*

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Kaposi's sarcoma (KS) within the same family has rarely been encountered: in fact, since the first report of a familial case in 1909 by Radaeli (1), there have been only 30 cases published in the literature (2–27). Over the last 20 years, at the Department of Dermatology of the University of Sassari, epidemiological studies on KS (28–29) have been under way, and although a great number of cases have been collected, only 4 documented cases of familial KS have been found.

### MATERIALS AND METHODS

A study of 160 consecutive cases of KS collected in our Department over 15 years included familial KS occurrence in 4 instances. An accurate examination of the family history of the 8 patients from 4 different families revealed that there had been no other cases of KS in the preceding generations. They all came from north-east Sardinia. Clinical and histological examination of these patients showed the typical features of KS. Routine hematochemical tests and X-rays (chest, gastrointestinal tract) were normal. Test for HIV was negative. HLA typing was also carried out for 6 of the 8 patients, as summarized in Table I.

Table I. HLA antigens in 8 male patients in 4 different families

Family	Age	Antigens
1	84	
	54	A3 A33 CW6 CW- B18 B65 DR1 DR- DQ1
2	71	A32 A33 CW1 CW- B5 B14 DR1 DR- DQ1
	65	
3	62	A2 A24 CW4 CW7 B17 B35 DR2 DR10 DQ1
	44	A24 A- CW4 CW- B35 B- DR3 DR10 DQ1
4	64	A2 A- CW4 CW5 B35 B44 DR2 DR3 DQ1 DQ2
	60	A2 A32 CW4 CW- B35 B39 DR2 DR4 DQ1 DQ3

### CASE REPORTS

#### Family 1

An uncle and a nephew, 84 and 54 years old: at clinical examination the uncle showed angiomatous lesions on his left foot, while his nephew presented a nodular angiomatous lesion on his right ear. The uncle later died of unknown causes.

#### Family 2

Two brothers, 65 and 71 years old: the older brother presented wine-red spotted elements and numerous angiomatoid nodules on his lower limbs. The younger brother had a single nodular lesion on the right hand.

#### Family 3

Father and son were affected. The disease developed on both the father's feet at the age of 62. Ten years later, his son, at the age of 44, showed bluish-red macules on the left foot. The father later died of unknown causes.

#### Family 4

Two brothers, 60 and 64 years old: the older brother showed angiomatoid papules and nodules on the distal portions of the lower extremities. The younger brother was referred and examined elsewhere.

### DISCUSSION

The observation of 2 or more cases of KS within the same family is exceedingly rare. We have found 30 documented cases of familial KS reported in the literature, as summarized in Table II. As the Table shows, the great majority of the familial cases consist of siblings. There have been no cases reported in identical twins. Brownstein et al. (13), in a survey of 100 patients with KS, described only one familial KS case: 2 brothers, of whom one died from lymphosarcoma. DiGiovanna & Safai (18), in their review of 90 patients with KS seen and treated at the Memorial Hospital of New York between 1954 and 1975, found only one documented familial case. Other authors have reported cases of KS in 4 or more members of the same family. Grinspan (6), for example, described 9 members of the same family affected by KS over several generations. Martinotti (3) described a family containing 4 siblings (3 brothers and a sister), of whom one of the brothers and one child of each sibling developed KS. Rabbiosi (8) reported a family in which KS developed in the mother, her son and 2 nephews.

There is a strong predominance in Italians, as has been observed in classic KS in general; in fact, 13 of these 30 familial cases were Italian. Of the remainder, 6 were Jewish, 4 were Greek, 2 were Russian, one was American, one was Ugandan and 2 were unknown.

It is known, although results have been contradictory, that immunogenetic studies on patients with classical KS have shown an increased incidence of the HLA DR5 antigen. In the familial cases reported in the literature, 20 patients,

Table II. Cases of Kaposi's sarcoma in 2 or more members of the same family

Authors	Date of publ.	Cases of familial Kaposi's sarcoma	Origin
Radaeli (1)	1907	Two brothers	Italy
Ragusin (2)	1937	Four brothers	Italy
Martinotti (3)	1938	Four cousins, the father of one and an uncle	Italy
Greco (4)	1938	Three brothers and a son of one of them	Italy
Jackson (5)	—	Three members of the same family	USA
Grinspan (6)	1954	Nine members of the same family	Unknown
McGinn (7)	1955	Uncle and a nephew	Italy
Rabbiosi (8)	1959	Mother, her son and two cousins of the latter (brothers)	Italy
Zeligman (9)	1960	Father and son	Jew
Grupper (10)	1967	Father and son	Jew
Pisani (11)	1968	Father and two sons	Italy
Epstein (12)	1972	Two brothers	Latvia
Browenstein (13)	1973	Two brothers	Unknown
Templeton (14)	1975	Two half-brothers	Uganda
Kalamkarian (15)	1978	Two brothers	Russia
Gange (16)	1979	Brother and sister	Jew
Finlay (17)	1979	Mother and son	Italy
Di Giovanna (18)	1981	Two brothers	Jew
Friedman (19)	1983	Two brothers	Jew
Brambilla (20)	1985	Brother and sister	Italy
Brambilla (21)	1986	Father and son	Italy
Kalamkarian (22)	1986	Two sisters	Russia
Manganoni (23)	1987	Two sisters	Italy
Amerio (24)	1989	Brother and sister	Italy
Neefe (25)	1989	Three brothers and one cousin	Jew
Invernizzi (26)	1993	Father and son	Italy
Kaloterakis (27)	1995	Four families (three brothers and sisters, one mother and son)	Greek

members of 9 unrelated families with KS, were serotyped for HLA-A, B and DR antigens. Twelve of the 20 family members possessed HLA-DR5 (20, 23–27). In our own experience of 160 cases of KS, we have found only 4 cases; this finding confirms the rarity shown by the detailed review of the literature. Our familial cases presented the typical features of classic KS: male predominance, an over 40 age range and a slow course. In addition, our genetic studies reveal that not one of the patients presented the HLA DR5 antigen, which has been found in about 72% of Sardinian patients with classic KS (30). Over 10 estimable haplotypes the expected number of the DR5 allele is 3.6.

Probably, the genetic susceptibility to KS given by the DR5 allele does not have an important role in the development of familial KS. The marked infrequency of familial cases suggests that though genetic factors are important in the development of the disease, other factors must be taken into account, such as environmental, geographic, viral and immunological ones.

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