A review of the epidemiology of soft tissue sarcoma

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Incidence

Soft tissue sarcoma (SST) represents a heterogeneous group of tumor diseases originating from connective tissue and accounting for less than 1% of all malignant tumors in Sweden. The incidence increases with age (Cancer Incidence in Sweden 1995). During recent years, there has also been a dramatic increase in Kaposi sarcoma associated with HIV infections. Previously, Kaposi sarcoma was diagnosed mainly in older men, but the disease is now common in HIV–infected young and middle–aged men (Zahm et al.1996). When Kaposi sarcoma is excluded, the incidence of other soft tissue sarcomas has not increased dramatically in developed Western countries, although some registers such as the Cancer Register in Connecticut, show an increase in incidence between 1935–1989 (Ries et al. 1993). This increase has been slightly greater in men than in women. Because of the inherent difficulty of classifying SST, international variations and geographic patterns cannot be evaluated in a meaningful way.

Blood vessel sarcomas (mainly Kaposi sarcoma), fibrosarcomas, rhabdomyosarcomas and liposarcomas occur more often in men, while leiomyosarcomas are seen oftener in women (Zahm et al. 1996). In the USA the 5–year survival is best in patients with liposarcoma (75%) and worst in those with blood vessel sarcoma (15%) (Zahm et al. 1996).

Risk factors

The heterogeneity of sarcoma and the relative rarity of various types have impeded etiologically oriented studies. Risk factors in soft tissue sarcomas are therefore little known, but thought to include exposure to herbicides and radiation as well as a positive family history (Hardell et al. 1979, Eriksson et al. 1981, Hardell et al. 1988, Wingren et al. 1990, Vineis et al. 1987, Karlsson et al. 1996, Zahm et al. 1996).

The latency time (start of radiation exposure to diagnosis of SST) has varied between 2–40 years (median 8 years) and various types of sarcomas have been seen (Laskin et al.1988, Karlsson et al. 1996, Zahm et al. 1996). An unusual type of sarcoma, lymphangiosarcoma, developing in an arm with lymphedema is commoner in patients exposed to radiation, but is not considered to be caused not by the ionizing irradiation but by long–standing lymphedema (Dubin et al. 1974, Karlsson et al. 1996).

While to exposure radiation and a family history have shown more or less convincingly a relationship to development of sarcoma, it is still debated, whether herbicide exposure especially as exposure to phenoxyacetic acids increases the risk of sarcoma (Dick et al. 1997). The results of meta–analysis have been conflicting (Johnson et al. 1990). In these studies the role of contamination with dioxins has been discussed (Zahm et al. 1996). Likewise, exposure to chlorophenol has been incrimated as a possible risk for development of sarcoma (Hardell et al. 1979, Zahm et al. 1996). These occupational risk factors have mainly been studied in men with sarcoma because only a few women have been exposed to these substances.

Other factors suggested to be associated with development of SST include thorotrast, arsenic pesticides and medications, vinyl chloride, immunosuppressive drugs, alkylating agents, androgen–anabolic steroids, human immunodeficiency virus, and exposure to human herpes virus type 8 (Popper et al. 1978, Falk et al. 1979b, Falk et al. 1981, Kinlen et al. 1979, Klepp et al. 1978, Zahm et al.1996, Zahm et al. 1997, Moore et al. 1995). Trauma with local injury has been discussed as a risk factor, although conclusive evidence of a relationship is abscent (Ott et al. 1970, Rock et al. 1990).

In families soft tissue sarcoma in childhood has in families been linked to breast cancer, adrenal tumors, leukemia, brain tumors and lung cancer in the Li–Fraumeni syndrome (Hodgson et al. 1993, Zahm et al. 1996). Mutations in the p53 gene on chromosome 17p have proved to be the molecular correlate to the syndrome (Hodgson et al. 1993, Zahm et al. 1996). Other syndromes associated with an increased risk of SST include retinoblastoma, Gardner's syndrome, Wern-

er's syndrome, nevoid basal cell carcinoma syndrome, neurofibromatosis type 1, and some immunodeficiency syndromes (Hodgson et al. 1993, Zahm et al. 1996).

Hormonal factors have been implicated as etiologic factors in patients with some rare subgroups of soft tissue tumors such as benign leiomyoma, uterine sarcoma and liver angiosarcoma (Schwartz et al. 1996, Falk et al. 1979b, Ham et al. 1980).

Prevention

Apart from prevention of infections with HIV and herpes virus type 8 and exposure to ionizing irradiation and thorotrast it is unclear whether reduction of other exposures can be expected to reduce the incidence of SST.

Resumé

In Scandinavia ongoing studies addressing the role of ionizing irradiation, herbicide exposure, constitutional and hormonal factors during childhood, puberty and adulthood. Some of these studies are being carried out within the scope of the Scandinavian Sarcoma Group. Two case control studies in the SSG have been completed and abstracts of the results are presented below.

Study 1. A case control study encompassing 79 cases and 226 matched referents in Sweden and Finland were interviewed about risk factors of sarcoma within the scope of a randomized trial (SSG 1). Some of the results presented in the thesis of Alvegård (1989) are shown in Table 1.

Study 2. Between 1990–1998, in a population, based case control study, 353 cases and 697 parish controls and 703 county controls were interviewed about risk factors using a standardized questionnaire. Cases and referents were living in the south Swedish health care region. Table 2 shows some of the more noteable risk factors from the preliminary analyses.

In study 2 no significant effect was found for smoking or alcohol exposure.

However, the risk factors described hither to generally weak and can only explain a small proportion of new cases. It is therefore important to investigate new risk factors and to confirm the importance of suspected factors. Some of these factors may stimulate further epidemiologic studies of the genetic and environmental determinants of various forms of STS.

Table 1. Study 1

Risk factor	OR [a]	95% CI
Herbicide exposure (occupational)	2.4	0.8–7.0
Family history of cancer	1.9	1.0–3.5
Past smoking	0.9	0.5–2.4
Present smoking	0.3	0.1–0.8
Liquor consumption (moderate vs. high)	0.9	0.5–2.1
Solvent exposure (occupational)	0.9	0.5–2.1
Wine consumption (moderate vs. high)	0.8	0.5–1.5

[a] conditional logistic regression, adjusted simultaneously for the other factors

Table 2. Study 2

Risk factor	OR [a]	95% CI
Family history		
First–degree relative with sarcoma	5.4	0.9–32
First– or second– degree relative with sarcoma	10.8	2.2–54
First–degree relative with other malignant tumor	1.5	1.2–1.9
First– or second–degree relative with other malignant tumor	1.3	1.0–1.7
Radiation exposure		
Previous history of radiation treatment	2.0	1.1–3.4
Occupational exposures		
Herbicide	1.5	0.8–2.6
Agriculture work	1.4	1.1–1.9
Paint	1.8	0.9–3.4
Constitutional factors		
Height at sixth school year		
shorter than average	1.0	
average	1.3	0.9–1.9
taller than average	1.6	1.1–2.4

[a] conditional logistic regression, adjusted simultaneously for other factors

The south Swedish research group working on the epidemiology of soft tissue sarcoma also includes Dr. Thor A Alvegård, Dept. of Oncology, Dr. Anders Rydholm, Dept. of Orthopedics, Dr. Helena Willén and Dr. Måns Åkerman, Dept. of Pathology, University Hospital, Lund.

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