DUPUYTREN'S CONTRACTURE AND SARCOMA

S. WILBRAND, A. EKBOM and B. GERDIN

From the Department of Hand Surgery, University Hospital, Uppsala, the Department of Medical Epidemiology, Karolinska Institute, Stockholm, and the Department of Plastic Surgery, University Hospital, Uppsala, Sweden

In order to study possible connections between Dupuytren's contracture and sarcoma we analysed the records of 18 patients who developed sarcoma 5 years or more after surgery for Dupuytren's contracture. We found an increased frequency of fibrosarcoma and malignant fibrous histiocytoma, but these patients did not differ from the other patients in the study group. Our analysis suggests that neither smoking, diabetes nor cancer syndromes can explain why patients with Dupuytren's contracture have a higher incidence of sarcoma.

Journal of Hand Surgery (British and European Volume, 2002) 27B: 1: 50–52

INTRODUCTION

Dupuytren's contracture is classified as a benign superficial fibromatosis, but has some histological features of a neoplasm, including marked fibroblast proliferation within the palmar nodules (Gabbiani and Majno, 1972). The histological similarity to fibrosarcoma is well recognized and mid-thigh amputation has mistakenly been carried out for plantar Dupuytren's disease (Bowser-Riley et al., 1975). Like fibrosarcoma, Dupuytren's disease arises from mesenchymal cells and is characterized by infiltrative growth, proliferation, lack of apoptosis and a tendency towards recurrence. However, unlike sarcoma, Dupuytren's contracture never metastasizes.

Fibroblasts derived from Dupuytren tissue show in vitro properties similar to those of solid tumours and exhibit leukaemia-like chromosomal abnormalities and the capability to bind monoclonal antibodies derived from human sarcomata (Bartal et al., 1987).

In a previous study of patients who had undergone surgery for Dupuytren's contracture at least 5 years previously, we observed an increased risk of developing sarcomas of bone and connective tissue (SIR = 2.00, 95% CI = 1.10–3.36) (Wilbrand et al., 2000). This could be an indication that there are coexisting risk-factors for the development of Dupuytren's contracture and sarcoma, or that they share a common pathophysiological pathway. Apart from in certain cancer syndromes such as Li–Fraumeni, exposure to various physical and chemical factors or ionizing radiation, and inherited or acquired immunological defects, the pathogenesis of most connective tissue tumours remains unknown (Enzinger and Weiss, 1995). In order to further study a possible connection between Dupuytren's contracture and sarcoma we studied the records of the 18 patients identified in our previous study who developed a sarcoma after surgery for Dupuytren's contracture (Wilbrand et al., 2000).

PATIENTS AND METHODS

Study group

We used the Swedish register data to identify all 15 212 patients treated surgically for Dupuytren's contracture as inpatients between 1965 and 1994. We then followed them up for the development of cancer through the Swedish Cancer Register. In addition to national registration numbers (NRNs, unique personal identifiers assigned to all Swedish residents (Lunde et al., 1980)), each Swedish register record contains medical data, including surgical and anaesthetic procedures, hospital department, and up to eight discharge diagnoses which are coded according to the International Classification of Diseases (ICD). The codes for the main diagnoses are estimated to be correct at the detailed five-digit level in 83 to 86% of the records (Nilsson et al., 1994). Since there is almost no private inpatient treatment in Sweden, patients are obliged to use the public hospitals in the county where they live. The Inpatient Register is essentially population-based and referable to the population of the counties covered by the registration.

By record linkage to the Cancer Register, which was established in 1958 and is virtually complete (Mattsson, 1977, 1984), we identified that 2151 (24%, 1920 men and 231 women) of the 15 212 Dupuytren's patients were later diagnosed as having a malignancy. Among these cases we found an increased risk for sarcomas of bone and connective tissue at 5 years or more after surgery for Dupuytren's contracture (Wilbrand et al., 2000). The patient records of these 18 cases were obtained from their discharging hospitals and were studied for details of sex, age at time of initial surgery for Dupuytren's contracture, frequency of surgery for Dupuytren's contracture, presence of other diseases, age at time of sarcoma diagnosis, type and localization of sarcoma, the presence of other malignancies and the possible cause and age at death.

RESULTS

Among the 18 patients diagnosed with sarcomas (15 men and three women) there were 14 cases (78%) of soft-tissue sarcoma and four cases (22%) of bone neoplasms. Among the 14 cases with soft-tissue sarcoma there were seven cases of malignant fibrous histiocytoma, three cases of fibrosarcoma, and one case each of xanthomatous fibrous histiocytoma, liposarcoma, leio-

Downloaded from jhs.sagepub.com at UNIV ARIZONA LIBRARY on November 30, 2015

Table 1—Patient data

Sex	Age at first op for DC	Operations for DC		Other illness or cancer	Age at sarcoma diagnosis	Type of sarcoma	Localization of sarcoma	Age at death	Cause of death
		Left	Right						
M	47	1	1	Prostate cancer, alcohol abuse	65	Chondrosarcoma	Left hand	69	Prostate cancer
F	72	2	4	Diabetes	79	MFH	Left arm	Alive	–
M	76	–	1	Pyelonephritis, cardiac	79	Chondrosarcoma	Left thumb	81	Cardiac infarction
M	69	1	–	Diabetes	74	MFH	Left leg	Alive	–
M	71	–	1	Colloid goitre, hypertension	82	Fibrosarcoma	Left bottom	88	Fibrosarcoma with lung metastasis
M	59	1	1	Hypernephroma	68	Leiomyosarcoma	Intraabdominal	67	Intraabdominal Leiomyosarcoma
M	63	1	–	Diabetes, hypertension, lung	72	XFH	Left axilla	82	XFH with lung metastasis
M	60	–	1	–	74	MFH	Left thigh	74	MFH with cerebral metastasis
M	59	–	1	Hypertension, carotid stenosis	61	Chondrosarcoma	Left Arcus costae	70	Unknown
F	76	1	1	Colon cancer, hypertension	77	MFH	Right scapula	82	Colon cancer
M	65	1	1	Basalioma genu dx, Cardiac	81	Liposarcoma	Left groin	88	Pneumonia
M	53	2	2	–	66	MFH	Left popliteal	67	MFH with lung metastasis
F	75	3	2	Thyreotoxicosis	89	Osteosarcoma	Left femur	89	Osteosarcoma, lungembolization
M	52	–	2	–	61	Fibrosarcoma	Right scapula	Alive	–
M	66	1	–	Lung tuberculosis	73	Fibrosarcoma	Retroperitoneal	80	Unknown
M	62	1	–	Hypertension, cardiac infarction	79	MFH	Left arm	83	Unknown
M	73	2	1	Asthma, alcohol abuse	82	Mal	Retroperitoneal	82	Metastasizing Mal. mesenchymoma
M	48	2	1	–	52	MFH	Right bottom	Alive	–

MFH = malignant fibrous histiocytoma; XFH = xanthomatous fibrous histiocytoma; Mal = Malmesenchymoma.

myosarcoma, and malignant mesenchymoma. Among the four cases with bone cancer there were three cases of chondrosarcoma and one of osteosarcoma (Table 1). Eight patients underwent surgery once for unilateral and four patients for bilateral Duputyren's disease. Six patients underwent surgery for recurrent Dupuytren's contracture. The mean age at the initial operation for Dupuytren's contracture was 64 years (62 for the men and 75 for the women). The mean age at diagnosis of the sarcoma was 73 years (71 for the men and 82 for the women). The mean age at death among the 14 patients who had died was 79 years (78 for the men and 85 for the women). Four patients are still alive, 7, 8, 9 and 23 years after the diagnosis of sarcoma. Three of the patients still alive had malignant fibrous histiocytoma and one had a fibrosarcoma.

Three of these 18 patients suffer or suffered from diabetes mellitus, five from hypertension and five from other malignancies (prostate cancer, hypernephroma, colonic cancer, lung cancer and basalioma). In two cases there was a history of alcohol abuse (Table 1) and eight patients smoked. The cause of death in seven of the 14 deceased patients was metastasizing sarcoma, in another two it was another malignancy (prostate cancer, colon cancer), in one case it was pneumonia and in three the cause of death was unknown.

DISCUSSION

In our previous study we found a mean age at first operation for Dupuytren's contracture of 61 years (men 62 years and women 60 years). In the present study the mean age was somewhat higher at 64 years (men 62 years and women 75 years). The difference in age for men is small and, as there were only three women, no conclusions can be drawn. The male:female ratio (5:1) is comparable with previous studies (Wilbrand et al., 1999) and the frequency of operations for Dupuytren's contracture is also similar to previous studies. In the present study six cases (one-third) were operated on because of recurrent disease, which is identical with the findings of our previous study (Wilbrand et al., 1999). Cigarette smoking is known to be a risk-factor for the development of Dupuytren's contracture (Burge et al., 1997) and eight of our patients, all men, were smokers, compared with 72% in another study (An et al., 1988). The reported prevalence of Dupuytren's contracture in patients with diabetes varies from 14 to 56%, depending on age and ethnic origin (Arkkila et al., 1997; Eadington et al., 1991; Noble et al., 1984). Earlier studies by Arkkila have shown a prevalence of Dupuytren's contracture in 14% of subjects with type I (insulin-dependent) and II (non-insulin-dependent) diabetes. In the present study-group only two cases had a positive history of type I diabetes mellitus. Thus patients with Dupuytren's contracture

Downloaded from jhs.sagepub.com at UNIV ARIZONA LIBRARY on November 30, 2015

and subsequent sarcoma do not obviously differ from other patients with Dupuytren's contracture. Sarcoma is known to be an important component of inherited cancer-prone conditions such as neurofibromatosis, retinoblastoma, Gardner's syndrome, Werner's syndrome and Li–Fraumeni syndrome (Zahm and Fraumeni 1997).

In the present study there were four patients with malignancies other than sarcoma, all of which had been diagnosed after the initial diagnosis of soft-tissue sarcoma or bone neoplasm (Table 1). This finding does not differ from the expected cancer incidence in the elderly. The Li-Fraumeni syndrome is characterized by the combination of early-onset of bone and soft-tissue sarcoma and breast cancer, brain tumours, leukaemia and adrenocortical carcinoma in children and young adults (Hisada et al., 1998). It is caused by a germ-line mutation in the p53 gene (Zahm and Fraumeni, 1997). No abnormalities in tumour suppressor gene p53 have been detected in patients with Dupuytren's disease (Muller et al., 1996).

Sarcoma accounts for approximately 1% (230 cases/year) of all cancers diagnosed in Sweden. The distribution between soft-tissue sarcoma (78%) and bone cancer (22%) in our study is similar to the data in the Swedish Cancer Registry for the same period 1965 to 1994 (76.5 and 23.5% respectively). In a Swedish population-based study, the annual incidence of soft-tissue sarcoma was 18 per million (Gustafson, 1994). 41% of these sarcoma were malignant fibrous sarcoma, 13% leiomyosarcoma, 10% liposarcoma, 7% synovial sarcoma and 3% fibrosarcoma. The annual incidence of primary malignant bone tumours in Sweden is 10 cases per million. Osteosarcoma is the most frequently diagnosed (29%) and chondrosarcoma the second (23%) (Nilsonne, 1982; Stark et al., 1990). Thus the excess number of sarcomas in this patient study seems to be confined to malignant fibrous histiocytoma 7/14 (50%) and fibrosarcoma 3/14 (21%), although our number of cases is small.

In conclusion, this record analysis suggests that neither smoking, diabetes nor cancer syndromes can explain why patients with Dupuytren's contracture have a higher incidence of sarcoma. Further research focusing on the underlying biological mechanism for Dupuytren's contracture might enhance our understanding of the aetiology of sarcomas.

Acknowledgements

Supported by the Swedish Medical Research Council, project number 9102 and by the Thureus foundation.

References

An HS, Southworth SR, Jackson WT, Russ B (1988). Cigarette smoking and Dupuytren's contracture of the hand. Journal of Hand Surgery, 13A: 872–874.

Arkkila PET, Kantola IM, Viikari JSA (1997). Dupuytren's Disease: association with chronic diabetic complications. Journal of Rheumatology, 24: 153–159.

Bartal AH, Stahl S, Karev A, Lichtig C (1987). Dupuytren's contracture studied with monoclonal antibodies to connective tissue differentiation antigens. Clinical and Experimental Immunology, 68: 457–463.

Bowser-Riley S, Bain AD, Noble J, Lamb DW (1975). Chromosome abnormalities in Dupuytren's disease. Lancet, 27 ii (7948): 1282–1283.

Burge P, Hoy G, Regan P, Milne R (1997). Smoking, alcohol and the risk of Dupuytren's contracture. Journal of Bone and Joint Surgery, 79B: 206–210.

Eadington DW, Patrick AW, Frier BM (1991). Association between connective tissue changes and smoking habit in type 2 diabetes and in non-diabetic humans. Diabetes Research and Clinical Practise, 11: 121–126.

Enzinger FM, Weiss SW. Soft Tissue Tumors, 3rd edn. St Louis, Mosby, 1995: 1–94.

Gabbiani G, Majno G (1972). Dupuytren's contracture: fibroblast contraction? An ultrastructural study. American Journal of Pathology, 66: 131–146.

Gustafson P (1994). Soft tissue sarcoma. Epidemiology and prognosis in 505 patients. Acta Orthopaedica Scandinavia (suppl) 259: 1–31.

Hisada M, Garber JE, Fung CY, Fraumeni JF, Li FP (1998). Multiple primary cancers in families with Li-Fraumeni syndrome. Journal of the National Cancer Institute 90: 606–611.

Lunde AS, Lundeborg S, Lettenstrom GS, Thygeson L, Huebner J (1980).The person-numbers systems of Sweden, Norway, Denmark and Israel. (DHHS publication no 80-1358) Washington DC, US Government Printing Office, 1980 (Vital and Health Statistics. Series 2: data evaluation and methods research No 84).

Mattsson B. The completeness of registration in the Swedish Cancer Registry, Stat rep HS. Report no. 15. Stockholm, Swedish Board of Health and Welfare, 1997.

Mattsson B. Cancer registration in Sweden. Studies on completeness and validity of incidence and mortality registries. Stockholm, Department of Oncology and Cancer Epidemiology, Radiumhemmet, Karolinska Hospital, 1984.

Muller E, Castagnaro M, Yandel DW, Wolfe HJ, Alman BA (1996). Molecular genetic and immunohistochemical analysis of the tumor suppressor genes Rb and p53 in palmar and aggressive fibromatosis. Diagnostic Molecular Pathology 5: 194–200.

Nilsson AC, Spetz CL, Carsjö K, Nightingale R, Smedby A (1994). Slutenvårdsregistrets tillförlitlighet. Diagnosuppgifterna bättre än sitt rykte. Läkartidningen, 91: 598–605.

Nilsonne U (1982). Epidemiology and some prognostic factors in osteosarcoma in Sweden. Semaine des Hospitaux, Paris, 58, (30–31): 1727–1728.

Noble J, Heathcote JG, Cohen H (1984). Diabetes mellitus in aetiology of Dupuytren's disease. Journal of Bone and Joint Surgery, 66B: 322–325.

Stark A, Kreicbergs A, Nilsonne U, Silfersward C (1990). The age of osteosarcoma patients is increasing. An epidemiological study of osteosarcoma in Sweden 1971 to 1984. Journal of Bone and Joint Surgery, 72B: 89–93.

Wilbrand S, Ekbom A, Gerdin B (1999). The sex ratio and rate of reoperation for Dupuytren's contracture in men and women. Journal of Hand Surgery 24B: 456–459.

Wilbrand S, Ekbom A, Gerdin B (2000). Cancer incidence in patients treated surgically for Dupuytren's contracture. Journal of Hand Surgery, 25B: 283–287.

Zahm SH, Fraumeni JF (1997). The epidemiology of soft tissue sarcoma. Seminars in Oncology, 25: 504–514.

Received 1 December 2000
Accepted after revision: 31 May 2001
Dr Stephan Wilbrand, Dept of Hand Surgery, University Hospital, S-751 85 Uppsala, Sweden
E-mail: stephan.wilbrand@plastik.uu.se

© 2002 The British Society for Surgery of the Hand
doi: 10.1054/jhsb.2001.0652, available online at http://www.idealibrary.com on IDEAL®

Downloaded from jhs.sagepub.com at UNIV ARIZONA LIBRARY on November 30, 2015