DUPUYTREN’S CONTRACTURE AND SARCOMA

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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.

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).

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-
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 Dupuytren’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 basaloma). 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...
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 adenocortical 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%) (Nilssonne, 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.

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