Epidemiological trends in dermal sarcoma in Australia

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Abstract

Background: Sarcomas comprise a heterogenous group of malignant tumours of mesenchymal origin and can arise in the skin. Definitive management of skin sarcoma usually entails surgical resection with wide margins, often requiring reconstruction. The incidence and demographics of these neoplasms in Australia are poorly understood.

Method: Incidence, gender and age distribution data for skin sarcomas for the period 1982–2009 were obtained from the Australian Cancer Database (ACD). Morphology and topographical region coding via the International Classification of Diseases for Oncology third edition (ICD-O-3)[1] were used to identify the data.

Results: A total of 5453 cases of skin sarcoma in the Australian population were identified over the 28-year period. Anatomically, 1610 cases (29%) occurred on the limbs, 1416 (26%) on the head and neck area, 957 (18%) on the trunk and 1470 (27%) had an unspecified skin origin. Overall incidence was 2.09 per 100,000 population. Males were more commonly affected (70%), most commonly in the 30–49 years and 70+ years age groups. The most common pathological subtypes were fibromatous sarcoma (including dermatofibrosarcoma protuberans), Kaposi's sarcoma and pleomorphic dermal sarcoma.

Conclusion: The Australian Cancer Database data used to describe the pattern and epidemiological trends for skin sarcoma in Australia demonstrated variation from international trends and highlight the need for further research into the aetiology of these tumours.

Keywords: sarcoma, skin neoplasms, incidence, Australia, malignant fibrous histiocytoma

Background

Sarcomas are a rare group of malignancies that arise from bone or soft tissue of mesenchymal origin and account for approximately 1 per cent of all malignant tumours.[2,3] There are a wide variety of pathological subtypes that can occur in any anatomical location, affect a wide range of age groups and have variable prognostic outcomes. Dermal sarcomas are a distinct subset of sarcoma that are poorly understood and may occur in cosmetically and functionally important areas. Dermal sarcomas may be encountered by clinicians in general and specialist clinical practice. This paper seeks to outline the Australian experience with dermal sarcomas.

The heterogenous histopathological types of dermal sarcoma are classified by the mature cell they most resemble. These include pleomorphic dermal sarcoma (PDS; formerly known as malignant fibrous histiocytoma—MFH), which has no distinct origin cell line; fibromatous sarcoma (including dermatofibrosarcoma protuberans—DFSP); Kaposi's sarcoma; myomatous sarcoma; and angiosarcoma lesions.[2,3] Atypical fibroxanthoma (AFX) is a confounding lesion that is sometimes included in dermal sarcoma classifications.[1,2] Current pathological classification considers AFX a benign but locally aggressive condition confined to the dermis and without metastatic potential. Once this tumour type invades deep into the dermis, it is considered a pleomorphic dermal sarcoma with metastatic potential. Other rare forms of dermal sarcoma are grouped together.

Kaposi's sarcoma has an established carcinogenesis link with herpesvirus-8 and human immunodeficiency virus (HIV). Causative agents for other pathological subtypes remain obscure, although certain industrial chemicals, radiotherapy and ultraviolet (UV) radiation have been implicated.[4–7]

While multiple different pathological types of dermal sarcoma exist, diagnosis and management follow similar pathways. Dermal sarcomas can pose diagnostic challenges as they have few distinguishing features, may mimic other lesions and are rare. Dermatoscopy has been used in diagnosis of cutaneous sarcoma lesions, although this technique relies on individual clinical expertise and pathological sampling is still required to confirm the diagnosis.[8,9] Accurate diagnosis relies on formal biopsy, usually excisional, although use of core biopsy may be dictated by lesion size and location.[10–12] Of note, resection prior to referral to a specialist centre is associated with poorer outcomes.[13] Following routine histopathology, a specialist pathology opinion may be required.[13]

Depending on the pathological subtype, regional imaging with MRI or CT for local staging and CT or PET CT to assess for metastatic disease may be required.[15] Most commonly the tumour node metastasis (TNM) system is used for staging, with lesion size being of key importance.[16] Currently there is no evidence to support the use of sentinel node biopsy in dermal sarcomas, consistent with their predisposition for local invasion and haematogenous spread rather than lymphatic spread.[17,18]

The mainstay of treatment for dermal sarcoma is surgical resection with or without radiotherapy. Due to their rarity, discussion of the management of cutaneous sarcoma as part of a specialist sarcoma multidisciplinary team should be considered.[19,20] Such specialist groups are well-placed to advise on resection planning, reconstruction options and follow-up and to determine the role of chemoradiotherapy and novel therapies in those patients who may benefit.[19,20] Wide surgical margins are routinely used to obtain adequate clearance and to reduce local recurrence.[2] Internationally accepted recommendations for clearance advocate at least a 30 mm margin peripherally and deep-tissue clearance to the next tissue plane, either fascia or periosteum.[21] Obtaining satisfactory surgical margins may be challenging when, as is common with dermal sarcomas, the lesion occurs in the head and neck region or in a functionally significant area like the hands or feet. Indeed, part of the morbidity from dermal sarcoma may directly result from extensive surgical margins and the consequent functional and cosmetic limitations. Micrographic surgery ('slow mohs') has

been proposed as an option to facilitate resection in particularly challenging areas such as the face, although this technique is not widely accepted.[22]

Outcomes are dependent on the completeness of resection. Adjuvant radiotherapy may be indicated to assist in local control or to manage local recurrence.[2,7,23,24] Neoadjuvant radiotherapy and brachytherapy have a well-established role in the management of sarcoma, although few studies have exclusively examined dermal sarcoma.[7,25,26] Chemotherapy has limited efficacy in the treatment of dermal sarcoma and should be reserved for select cases, or if there is evidence of metastatic progression.[7,27] Notably, Kaposi's sarcoma may respond to medical therapies depending on the causative agent; that is, antiviral therapies in individuals with HIV.[28]

While uncommon, there is anecdotal evidence that the incidence of dermal sarcomas is increasing in Australia but the epidemiology of this group of tumours is poorly understood. European and North American populations have published incidence and prevalence of dermal sarcomas but Australian epidemiological data are limited.[2,3,29–33] This is in part due to the rarity of this tumour group, making accurate data collection difficult. Recent changes have standardised classification of sarcomas, and networked national registries have increased the data available and knowledge of this rare group of tumours.[34] These changes should improve future data collection but it will take time to see the effects due to the low incidence/rarity of dermal sarcomas. This paper aims to report epidemiological information about dermal sarcomas in Australia, using Australian Cancer Database (ACD) data, and compare this with international trends.

Methods

A retrospective analysis was conducted on data obtained from the ACD for the years 1982–2009 for dermal sarcomas. The ACD requires mandatory reporting of every episode of malignancy that generates a histopathology report, for all of the Australian population.[35] The data cover approximately 97 per cent of the population, as statistics for the Australian Capital Territory and

the Northern Territory were not available.[35] The ICD-O-3 coding system[1] was used by the ACD to identify sarcomas originating in the skin and which regions of the body they affected (codes C44.0-9). Initial analyses examined gender, age, year and pathological subtype for trends. Incidence per 100,000 population was calculated using Australian Bureau of Statistics (ABS) historical population numbers and dividing the observed frequency by the population then multiplying by 100,000.[36] An average incidence across the length of the study was also calculated. These data were further categorised by pathological subtypes, anatomical location and trends over time.

Results

The data collected from the ACD reported a total of 5453 cases of dermal sarcoma in the Australian population over a 28-year period. Fibromatous sarcoma, which includes dermatofibrosarcoma (DFSP), was the most common dermal sarcoma subtype, followed by Kaposi's sarcoma (**Figure 1**). During the period of the study there was a steady increase in the number of cases of myomatous sarcoma, which includes leiomyosarcoma and pleomorphic dermal sarcoma, while Kaposi's sarcoma had the greatest frequency during the early 1990s before declining thereafter. Other forms of cutaneous sarcoma had stable incidence during the study period.

Overall, dermal sarcomas occurred more commonly in males (male:female=2.3:1). An increase in prevalence and incidence was observed during the study period, with males being particularly affected (**Figure 2**). The average incidence of dermal sarcomas across the study was 2.09 per 100,000.

The highest incidence of dermal sarcomas was observed in males in the 30–49 years and 70 years and older age groups. Few cases of dermal sarcoma were reported in the 0–19 year age cohort and the majority of these were fibromatous tumours which appeared to affect males and females evenly. The incidence of both Kaposi's sarcoma and fibromatous sarcoma steadily rose from the age of 20, peaked in the 30–49 years age group and slowly
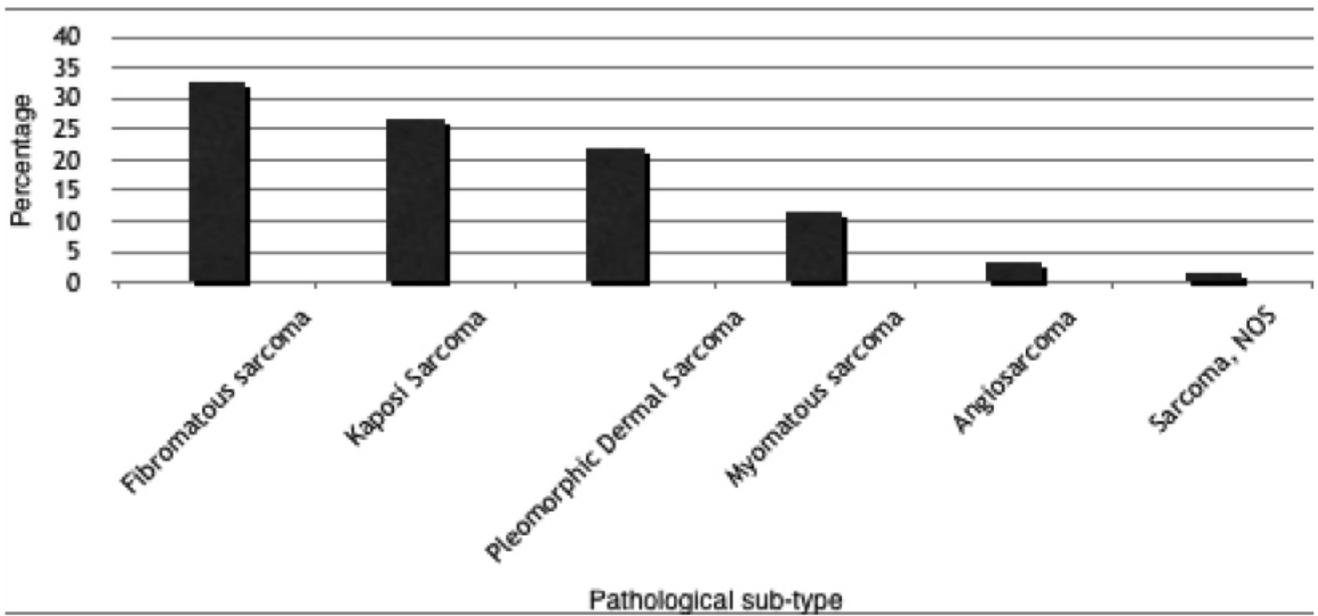
Fig 1. Frequency of pathological subtype as a percentage of all dermal sarcomas (subtypes with prevalence <1 per cent excluded)

declined in older cohorts. This was in contrast to cases of pleomorphic dermal sarcoma, myomatous sarcoma and angiosarcoma which all increased after age 60 years in both men and women but were more pronounced in males. Of note, fibromatous sarcoma affected men and women relatively equally while the other four pathological subtypes affected males more commonly.

There was a clear predilection for dermal sarcomas affecting males in the head and neck region, comprising 39 per cent of cases when cases without an anatomical location were excluded while no anatomical preference was observed in females. The face, scalp and neck were the most commonly affected areas in the head and neck region. In both genders, fibromatous sarcoma had a predilection to affect the trunk while pleomorphic dermal sarcoma and angiosarcoma most commonly affected the head and neck region. In contrast, cases of myomatous sarcoma were most frequently observed in the head and neck region in males, although no anatomical preference was observed in females. Kaposi's sarcoma affected the lower limbs most frequently in this study.

Discussion

This is the first study to describe the epidemiology of dermal sarcomas in Australia and is one of the largest series in the world. The increased incidence
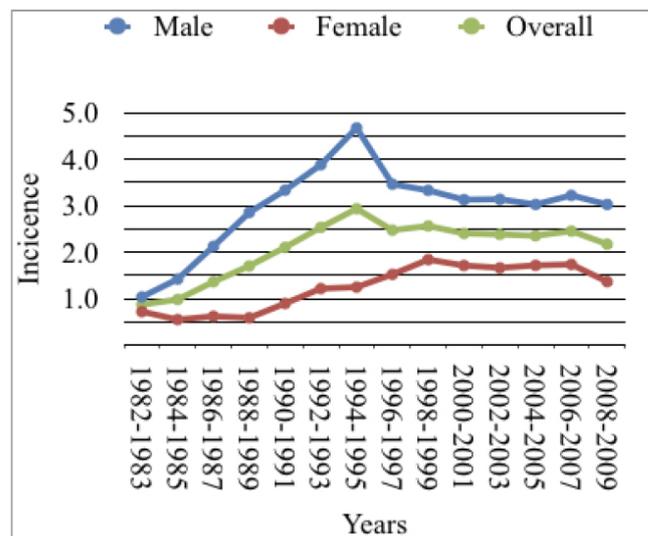

Fig 2. Incidence of dermal sarcomas per 100,000 Australian population overall and by gender

of tumours in males is consistent with other studies of dermal sarcomas, although this dataset has a number of unusual features.[29–33] The anatomical location of cutaneous sarcomas in the current study demonstrated higher rates of incidence in the head and neck region of males but a more even anatomical spread in females. This gender difference in anatomical variation is not easily explained, although the anatomical distributions of pleomorphic dermal sarcoma, myomatous sarcoma and angiosarcoma, which affect men and occur in the head and neck region most commonly, may partly account for this observation.

Known carcinogens for sarcoma include ionising radiation (including therapeutic radiotherapy), some chemicals and HIV infection. Ultraviolet radiation may be a causative agent in the pathogenesis of pleomorphic dermal sarcoma, consistent with the observed distribution of this cancer in sun-exposed areas, and mirroring the distribution of known UV-related malignancies such as melanoma.[37,38] Genetic changes induced by UV in melanoma have been noted to occur in pleomorphic dermal sarcoma.[37] The higher incidence in males is consistent with this hypothesis, as males have traditionally undertaken outdoor-intensive occupations in Australia and may undergo balding of the scalp, predisposing them to UV radiation. There is increasing evidence of a role for UV radiation in the aetiology of pleomorphic dermal sarcoma, although such a link with myomatous sarcoma and angiosarcoma has not been made and the reason for these two tumour subtypes favouring the head and neck region is not readily apparent. Notably, the other pathological subtypes, Kaposi's sarcoma and fibromatous sarcoma, did not demonstrate the same preference for affecting the head and neck area. Kaposi's sarcoma had greatest incidence in the lower limbs in this Australian study while the trunk was more common in previous international studies.[29]

The incidence of different pathological subtypes in this study contrasts with epidemiological trends from other countries. Kaposi's sarcoma is the most commonly reported type of cutaneous sarcoma globally, although this may be skewed by the inclusion of several geographic regions with particularly high rates of HIV.[30,31] In this Australian dataset, Kaposi's sarcoma was the second most common subtype and noted to be on the decline. This may be due to the relatively low prevalence of HIV in Australia, as well as access to antiviral therapies.[40] Fibromatous sarcoma is the most common type of dermal sarcoma overall in Australia and the second most common in all age groups in the US.[29] Fibromatous sarcoma appears to affect men and women equally and is observed in all age brackets but particularly in the 30–50 age group. This contrasts with pleomorphic dermal sarcoma, myomatous sarcoma and angiosarcoma, which are observed more frequently in those over 60 years of age. Our data demonstrated an increasing incidence of pleomorphic dermal sarcoma, particularly in elderly males, which was not evident in the US.[29]

This study used ACD data, which requires compulsory registration of cancers and uses standardised coding information. As such, this study has a large number of cases and a high degree of data accuracy. However, there are limitations to these data. The data represent 97 per cent of the Australian population as data from the Australian Capital Territory and the Northern Territory were not available. The ethnic makeup of Australia changed significantly during the period of the study but unfortunately data relating to racial heritage were not accessed, limiting epidemiological analysis. Finally, as with most cancer registries, the ACD does not collect information pertaining to exposure to carcinogens or patient comorbidities and it was therefore not possible to include these in this study.

Conclusion

This is the first paper to describe the epidemiology of dermal sarcomas in the Australian population. Compared with published data from Europe and North America, this study demonstrated variation in anatomical distribution and incidence in pleomorphic dermal sarcoma among elderly males.[29] These findings are in keeping with the hypothesis of a causal link between pleomorphic dermal sarcoma and UV radiation.[37] Further research to establish the epidemiology of dermal sarcomas in particular racial groups, and the role of genetics and aetiological agents, may lead to improved understanding of this disease. This in turn may lead to identification of potential preventive strategies and targeted treatments. This paper provides a foundation and reference point on which further research can be based and to ultimately improve outcomes for patients affected by dermal sarcoma.

Disclosures

No financial support for this study was requested or received. The authors have no commercial or financial interests to declare.

A variation on these data was presented at the RACS ASC in Brisbane 2016. Part of these data contributed to the thesis component of a Masters of Surgical Science through the University of Edinburgh for Dr Edward LMG Gibson.

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