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Prognostic factors and treatment strategies for adult head and neck soft tissue sarcoma

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Abstract. Adult head and neck soft tissue sarcomas are rare and display a variety of histological types and clinical characteristics; they are also associated with a variety of mortality risks. The purpose of this study was to examine all patients treated at the Instituto Nacional de Cancerologia for head and neck sarcoma during a 5-year period. Fifty-one adult patients were examined and treated for head and neck sarcomas from 2004 to 2009. The 51 tumours were histologically re-evaluated by expert pathologists and classified as low, intermediate or high grade sarcomas. A multivariate analysis was performed to evaluate the surgical margins, histological grades, and clinical stages as prognostic factors for the disease. Adult head and neck soft tissue tumours are rare, and they are associated with poor prognosis for patients, especially at clinical stages III and IV. The average survival rate after 2 years is 45%, and most of these patients die because of disease progression and metastases.

Key words: head; neck; sarcoma; soft tissue; prognosis; treatment.

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Soft tissue sarcomas (STS) are a group of heterogeneous tumours that have their origin primarily in the embryonic mesoderm; more than 50 histological subtypes and diverse clinical behaviours have been identified. STS can range from relatively slow growing cancers that cause limited destructive spread to those that are locally aggressive, regionally destructive and associated with great potential for systemic metastases.[1] The approximate incidence for this type of neoplasia is 3–4.5 in 100,000 people, representing approximately 1% of all malignant adult neoplasias.[2] STS in the head and neck region are rare and comprise 5–15% of all adult sarcomas and less than 1% of all head and neck neoplasias.[3] The age at presentation is variable, with a mean of 50–55 years (the minimum is 3 months and the maximum is 89 years). The male/female ratio is approximately 2:1, which varies depending on the review series. The symptoms depend on location, although the most frequently reported symptoms are: headache, nasal obstruction, dysphagia, hoarseness and dyspnoea, but most patients are asymptomatic.[4] The most frequently reported sites of involvement are the: face, neck, scalp, nasopharynx, maxillary antrum, cranial base, and parotid gland. Frequencies at each site differ depending on the published series.[4,5] There is much histological diversity, although the most frequent types are malignant fibrous histiocytoma and fibrosarcoma.[5] In Mexico, 27 cases were reported by the Instituto Nacional de Cancerologia between 1982 and 1993. The most frequent histological types were rhabdomyosarcoma and malignant peripheral nerve sheath tumors.[6] The General

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Hospital of Mexico reported 29 head and neck sarcomas cases between 1993 and 1997, with the most frequent histological types being neurogenic sarcomas and leiomyosarcomas.[7] The natural history of head and neck sarcomas is similar to that of sarcomas in other parts of the body, but because of their location, they present greater surgical difficulty. There is often residual disease, which reduces the patient's life expectancy.[6] The main prognostic factor for STS is histological grade and tumour size. Staging is performed according to the American Joint Committee on Cancer (AJCC) staging, which defines four clinical stages (I–IV),[8,9] and a second classification system proposed by Memorial Sloan-Kettering Cancer Center (MSKCC).[10] The evolution of disease in head and neck soft tissue sarcomas (HNSTS) frequently involves metastases, most commonly lung metastases. As such, initial management includes a chest X-ray or computed tomography scan. The absence of metastatic lesions excludes the possibility of a systemic disease.[9] In paediatric cases, head and neck sarcomas respond when children are treated with chemotherapy and radiation therapy. In adults, the main treatment modality is surgical, although multidisciplinary treatment is also important because these tumours frequently invade, or are in close proximity to, vital structures. As a result, surgical resection could be incomplete, necessitating local control of disease with adjuvant therapies.[11] The purpose of this study was to review retrospectively adult head and neck sarcomas treated at the Mexico City-based National Institute of Cancerology (Instituto Nacional de Cancerología, INCan) between 2004 and 2009. The aim was to identify prognostic factors and share the authors' experience regarding treatment performed at this institute.

Materials and methods

One thousand sixty-nine soft tissue tumour cases were registered at INCan between 1 January 2004 and 31 December 2009. Of these, 575 (54%) cases corresponded to STS. Ninety-five (16.5%) cases were located in the head and neck region. Seventy-three (77%) were treated at INCan. As in the study performed by de Bree et al.,[5] patients with carcinosarcomas and aggressive fibromatosis (desmoid tumours) were excluded from the study because those lesions are not formally considered sarcomas. The following variables were analysed: age (over 15 years), gender, location, symptoms, histological subtypes, tumour size, metastases (N1, presence of lymph nodes; M1, distant metastasis), treatment performed, and surgical margins. Margins were classified as: R1, microscopically positive; R2, macroscopically positive with margins >10 mm; R0, surgical margins ≤ 10 mm, negative. Tumour size was categorized as ≤ 5 cm or >5 cm. Treatment was dichotomized into radiotherapy (RT) and chemotherapy (CT). The 51 sarcomas were histologically re-evaluated by two experienced pathologists, who reached a consensus after taking into account the National Cancer Institute (NCI) standards (all tumours were graded I–III) and the French Fédération Nationale des Centres de Lutte Contre le Cancer Classification (FNCLCC).[8] The pathologists evaluated tumour differentiation (score of 1, 2 or 3), number of mitoses by 2 mm^2 (score of 1, 2 or 3), tumour necrosis (score of 0, 1 or 2) and histological grade (classified as: G1, low; G2, intermediate; G3, high grade), as in the work of Van Damme et al.[10] TNM classification and staging related to the AJCC and MSKCC staging systems were used. For analytical purposes, patients presenting with dermatofibrosarcoma protuberans were grouped as AJCC clinical stage I because these are low-grade tumors.[8] The authors evaluated overall survival (OS). Disease-free survival (DFS) and disease-specific survival (DSS) were analysed for all possible prognostic factors such as gender, age, size, site, margins, RT, QT, metastasis, extension, grade (NCI and FNCLCC), and staging systems (MSKCC and AJCC). The follow-up period was 23.8 months on average (minimum 6 months and maximum 60 months).

Statistics

The estimated survival distribution was calculated using the Kaplan–Meier method. The significance test for estimated survival was performed using the log-rank test. The results were considered significant at $P < 0.05$. The data were tabulated and analysed using SPSS 15.0 statistical package (SPSS Professional Statistics, SPSS Inc., IL, USA).

Results

Fifty-one (100%) patients with HNSTS were admitted to INCan. The male/female ratio was 1.5:1, with 31 male (60.7%) and 20 female (39.2%) patients. The average age was 43.1 years (range 15–92 years). Localisation of HNSTS was at the scapula/face in 37 (72.5%) patients, parotid/neck in 7 (13.7%) patients and upper airway in 7 (13.7%) patients (Table 1). The most frequent histological subtypes were malignant peripheral nerve sheath tumour in 9 (17.6%) patients, followed by rhabdomyosarcoma in 7 (13.7%) patients. Among the latter, 4 (7.8%) had alveolar rhabdomyosarcoma, 2 (3.9%) had embryonal rhabdomyosarcoma, and 1 (1.9%) had pleomorphic rhabdomyosarcoma. The most frequent symptoms included painful tumour (37.2%), bleeding (17.64%), trismus (11.7%), weight loss (11.7%) and nasal congestion (7.8%). The remaining patients were asymptomatic (41.17%). Only 12 patients (23.5%) had a history of probable predisposing risk factors including trauma (15.6%, $n = 8$), exposure to chemical agents (5.8%, $n = 3$) and a neurofibroma (1.9%, $n = 1$). Most tumours were 5 cm or more in size (36/51 or 70.5%) and displayed deep infiltration through the superficial fascia (40/51 or 78.4%). According to the FNCLCC histological criteria, grade I was diagnosed in 10 (19.6%) tumours, grade II in 11 (21.5%) tumours, and grade III in 30 (58.8%) tumours. According to the NCI criteria, grade I was diagnosed in 9 (17.6%) tumours, grade II in 11 (21.57%) tumours, and grade III in 31 (60.7%), tumours.

Treatment characteristics

Forty-eight (94.1%) patients were treated with primary surgery, of whom 35

Table 1. Distribution of HNSTS by anatomical region.

Scapula/face–head	*NC (%)	Parotid/neck	*NC (%)	Upper airway	*NC (%)
Face skin	3 (5.8)	Neck	5 (9.8)	Larynx	2 (3.9)
Frontal	2 (3.9)	Parotid	2 (3.9)	Palate	1 (1.9)
Infratemporal fossa	1 (1.9)			Pharynx	3 (5.8)
Malar region	5 (9.8)			Tongue	1 (1.9)
Mandible	6 (11.7)				
Maxilla	10 (19.6)				
Orbit	2 (3.9)				
Scalp	8 (15.6)				
Total	37 (72.5)		**7 (13.7)**		**7 (13.7)**

* Number of cases.