Original article

A review of adult head and neck soft tissue sarcoma in a tertiary centre: malaysia experience

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Abstract

Background: Head and neck tissue sarcoma are rare with potential high morbidity and mortality. The purpose of the present study was to present these cases and determine the optimal treatment for adult patients with head and neck soft tissue sarcomas. ***Methods:*** It is a retrospective study of adult head and neck soft tissue sarcoma conducted in the Department of Otorhinolaryngology at Universiti Kebangsaan Malaysia Medical Centre (UKMMC) which is one of the national referral center within the period of 16 years from 1998 till 2014. ***Results:*** Fourteen cases were reviewed in which7 histopathological variations of soft tissue sarcomas were identified. Local control after surgery alone or combined with radiotherapy was obtained in 50 % of the patients which is influenced by histologic grade, tumor size, and surgical margins. Patients with high-grade tumors or positive margins have improved local control if adjuvant radiotherapy is used. Distant metastases occurred in 14.2 % of patients and the 5-year survival rate was 50 %. ***Conclusions***: The optimal treatment for adult head and neck soft tissue sarcomas is surgery. Adjuvant radiotherapy improves outcomes for those with high-grade tumors or positive margins.

Keywords: Head and neck; soft tissue sarcoma ; surgery ; margin ; radiotherapy ; chemotherapy; prognosis

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Introduction:

Sarcomas are rare neoplasms, constituting only 1% of all cancers. These tumours do not commonly manifest in the head and neck region, except in the paediatric population. Head and neck sarcomas represent only 2–15% of all adult sarcoma cases [1-3].Sarcomas of the head and neck account for less than 1% of all neoplasms occurring in the head and neck [3]. They are a heterogenous group of neoplasm according to their origin site that can be bone,muscle,vessel,nerve,fat and fibrous tissue.

Adult soft tissue sarcomas display a diverse histologies and a wide spectrum of clinical activity ranging from relatively slow growing lesions to aggressive local and regionally destructive lesions with potential for systemic metastasis. Lymph node metastasis occur only in 3–10% whereas distant metastases occur in 28% of the patients at diagnosis or during follow-up and are more frequent in high grade sarcomas. The most frequently involved site is lung followed by bone, central nervous system and liver [4-5]. The sites of origin in the head and neck are also varied. However, these tumours are grouped together because of some similarities in clinical presentation, natural history and outcome [6].

The treatment of head and neck sarcoma depends on the histological type, grade, stage and operative considerations according to the site. The anatomical restrictions present in the head and neck region, where the presence of critical structures and secondary

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cosmetic deformities reduce the ability to obtain adequate surgical margins as well as the delivery of high-dose wide-field radiotherapy.This may be contribute to the higher rate of local recurrence and lower overall survival rate compared to sarcomas of other body parts.Moreover, treatment of malignancies in this area may have a substantial impact on quality of life, since they may affect swallowing, speech and cosmesis. Therefore, specialized rehabilitation after treatment head and neck sarcomas is warranted [5-6]

Because of the rarity most published series are either small or multicentre based making it difficult to establish the optimal treatment and prognosis for these tumours generally, and especially on histological sub-group level. Therefore the purpose of our study is to present our local experience of these rare head and neck soft tissue sarcomas according to their epidemiologic, clinico-radiological, histological features and the treatment management during the period of 1998 to 2014, with the additional intention of establishing a prospective database of these lesions.

Methods:

All charts of all patients with soft tissue sarcomas from 1998 until 2014 (16 years) at the Department of Otorhinolaryngology, UKMMC were reviewed. From the charts, all head and neck soft tissue sarcoma patients were extracted and included in the study.

The head and neck region in the present study was defined as any site above the clavicles with the exception of brain and eye, and only patients presenting with a primary tumour of the head and neck were included. Soft tissue sarcoma was defined as tumours of extra skeletal connective tissue origin with a predicted aggressive behaviour.

Data that was collected from the charts include patient demographics, tumour histology and staging, treatment modalities, complication of treatments,treatment outcome and recurrence and 5-year survival rate.Based on the clinical stages defined by the seventh edition of the AJCC at 2010 [7], the disease can be divided into three groups: A) Early with low-grade tumours that have little or no metastatic potential (Stages IA, IB), B) Locally advanced stage, with aggressive high-grade tumours with high metastatic potential (stage IIA and IIB) and C) Metastatic disease, whether lymph nodes (Stage III) or other sites (Stage IV).

We retrospectively analysed our center's experience with head and neck soft tissue sarcomas during the past 16 years. We characterized a series of 14 patients with respect of their clinicopathologic features and course. In general, whenever possible, patients with soft tissue sarcomas of the head and neck at our institution are treated with complete surgical resection. Recommendations for adjuvant chemotherapy or radiation are then made based on discussion at a multi-disciplinary conference which takes into account all clinical and pathologic features of a particular tumor, including histology.

Disease free survival rates was measured starting on the date of surgical resection to the point when a recurrent is detected or the last follow up date in non-recurrent cases [8]. Overall survival rates include the 5 years survival starting from the date of diagnostic biopsy until the date of last follow up[9].

Results:

Patient characteristics:

In the present study, we found 14 patients diagnosed head and neck soft tissue sarcomas
(8 males and 6 females) with age ranged from 20 to 61 years. The most common affected age range was between 40 and 50 year old. Figure 1 describe the pattern of distribution of head and neck soft tissue sarcoma in between the age and gender.

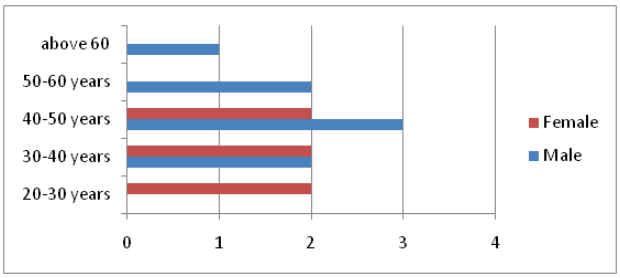


Figure 1: Age and sex distribution of head and neck soft tissue sarcoma

Tumor characteristics:

Tissue biopsy was the first step to obtain a histologic diagnosis & CT or MRI are used to evaluate the extent of the primary lesion the regional lymph nodes and distant metastases. Disease was staged according to the American Joint Committee on Cancer (AJCC). It is based on grade, tumor size, lymph node involvement and distant metastases

As far as pathology is concerned, we found 7 histopathological variations of soft tissue sarcomas and the common histologies were fibrosarcoma (3 patients), fibromyxoid sarcoma (3 patients), rhabdomyosarcoma (2 patients), hemangiopericytoma (2 patients), spindle cell sarcoma (1 patient), malignant fibrous histiocytoma (2 patient),synovial sarcoma (1 patient) as depicted in Figure 2.

Age	Sex	Site	Date	STS subtype	Size	Grade	Operation	Chemo/ RT	Stage	Recurrent	Survival years
43	Male	Left maxillary sinus	Jan-07	Hemangiopericytoma	< 5 cm	Low	Medial maxillectomy	No	1 (CT)	No	5 years
46	Male	Right pyriform fossa	Oct-05	Fibrosarcoma	> 5 cm	Low	Tracheostomy (refused pharyngectomy)	No	III (CT)	-	2 years
61	Male	Left sphenoid sinus	May-02	Fibrosarcoma	< 5 cm	Low	Sphenoidotomy& WLE	No	1 (CT)	No	12 years
41	Female	Left maxillary sinus	Nov-98	Spindle cell sarcoma	< 5 cm	Low	Medial maxillectomy	No	1 (CT)	No	9 years
41	Male	Right maxillary sinus	Sep-99	Dermatofibrosarcoma protuberan	> 5 cm	Low	Medial maxillectomy	No	II (CT)	After 5 years	5 years
53	Male	Left tonsil	Aug-06	Malignant Fibrous Histiocytoma	< 5 cm	High	Tracheostomy (inoperable)	RT	IV (CT)	-	1 year
48	Female	Frontoethmoid sinus	May-08	Hemangiopericytoma	< 5 cm	Low	Craniofacial resection	No	1 (CT+MRI)	No	1 year
33	Female	Left parapharyngeal space	Jan-07	Synovial sarcoma	< 5 cm	High	Parotidectomy& MRND	RT	III (CT+MRI)	After 5 years	7 years
20	Female	Right maxillary sinus	Oct-10	Embryonal rhabdomyosarcoma	> 5 cm	High	Subtotal maxillectomy& MRND	Chemo	III (CT)	After 2 years	3 years
25	Female	Left maxillary sinus	Dec-11	Fibromyxoid sarcoma	> 5 cm	Low	Medial maxillectomy	No	II (CT)	After 1 year	1 year
36	Male	Left posterior neck	Mar-13	Fibromyxoid sarcoma	> 5 cm	Low	Transcervical excision	No	I (CT+MRI)	No	1 year
38	Female	Left masseter	Nov-11	Alveolar rhabdomyosarcoma	< 5 cm	High	Transoral WLE	Chemo	2 (CT+MRI)	After 1 year	2 years
52	Male	Left maxillary sinus	Dec-12	Fibromyxoid sarcoma	> 5 cm	Low	Total maxillectomy	No	II (CT+MRI)	After 2 years	2 years
40	Male	Left vocal cord	Sept-13	Malignant Fibrous Histiocytoma	< 5 cm	High	Endolaryngeal surgery	Refused RT	II (CT)	After 1 year	1 year

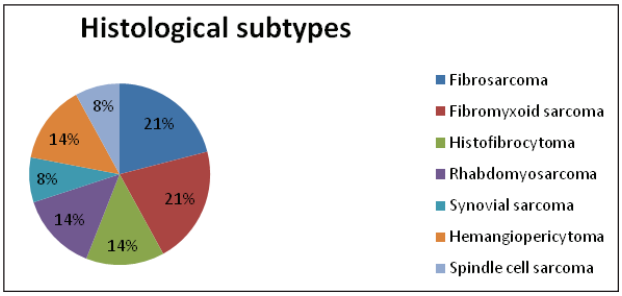
STS - Soft tissue sarcoma
WLE – Wide local excision
MRND – Modified radical neck dissection
RT – Radiotherapy
Chemo – Chemotherapy

CT – Computed tomography
MRI – Magnetic resonance imaging

Table : Head and neck soft tissue sarcoma patients in UKMMC

Site of tumor origin was grouped into the following anatomical locations: Nasal cavity and paranasal sinuses (8 patients), neck region (2 patients), larynx (2 patient), oropharynx (2 patients) as shown in Figure 3. Figure 4 showed tumour located in paranasal sinuses and neck respectively.

Figure 2: Histological subtypes of soft tissue sarcoma



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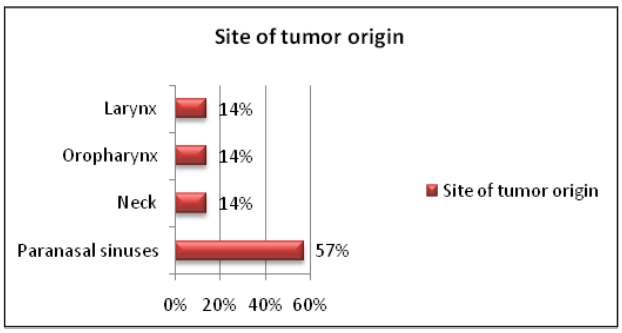

Figure 3: Site of tumor origin

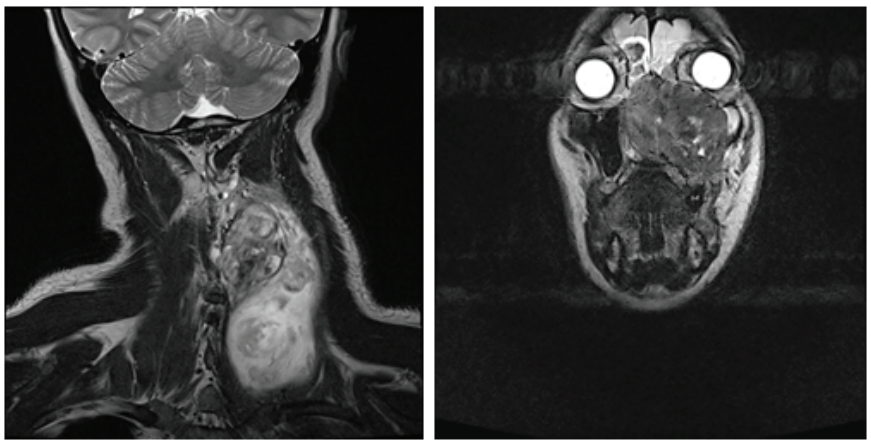

Figure 4: MRI showing the involvement of different subsites of head & neck in our cases such as deeper part of the neck and paranasal sinuses.

5 patients (35 %) had high grade disease. The majority (9 of 14) presented with locoregional disease and only threehad nodal involvement. One patient had lung metastases at diagnosis.

Treatments

Of 14 patients with localized disease, 12 underwent resection. In general, the surgeons performed the excision as wide as permitted by the nearby vital structures and functional concerns. Elective nodal dissection was not routinely performed in view of the low rate of regional node metastases in sarcomas. Two of 14 patients undergoing surgical resection also received radiation in an adjuvant (post-operative) fashion for high grade tumor. Total tumor doses ranged from 5,000 cGy to 6,600 cGy; most patients received around 6,000 cGy over 30 fractions.Chemotherapy was commenced in 2 cases of rhabdomyosarcoma which is known to be chemosensitive and standard vincristine,adriamycin, cytoxan(VAC) chemotherapy was used for rhabdomyosarcoma cases.

Recurrence and survival

The median follow-up was 4.5 years (range 1.0–12.0 years). Tumor recurrence was documented in seven patients (50 %): Two patients had locoregional and distant metastasis; and five patients had locoregional area alone. Over sixty percent of the recurrences (5 of 7) occurred within the first 3 years. 4 patients died due to advanced disease. Median disease free survival for our series was 2.5 years and median overall survival was 2 years. The 5-year survival with combined modalities were recorded in 5 out of 14 patients which represent 35.7 % of total sample.

Discussion:

Soft tissue sarcoma of head and neck (STSHN) is rare and heterogeneous malignancies that constitute 1% of all cancers and represent between 2 and 15% of cases of adult sarcomas. The clinical manifestations of soft tissue sarcomas depend of the affected site, tumor size and invasion/compression of adjacent tissues and organs. The metastasis of sarcomas affects lymph nodes in 3-10% and other distant tissues in 28%, being the most affected the lung, followed by bone, the central nervous system and liver [10-14].

The cause of most sarcomas remains unknown, but there are genetic and environmental factors that are clearly associated with these neoplasms. Patients with conditions such as hereditary retinoblastoma,

72

neurofibromatosis and Lynch syndrome are at increased risk. Radiation to the STSHN is also a risk factor. Makimoto et al. reported, only six cases (0.14%) of 4184 patients were with a history of radiation, whereas Ko et al., found sarcoma in 0.38% of patients radiated and the most frequent subtype was histiofibrocytoma [15-16]. In our study we did not find any cases of sarcoma associated with radiation.

Commonly STSHN present with nonspecific signs and symptoms. Most manifest as a progressively growing and painless mass, although it is reported that 14-25% of cases have pain. Other symptoms occur depending on the site affected (e.g. dysphagia, nasal obstruction, etc). The reported male-female ratio range from 1:1 to 2.8:1 in favour of men, and the most common age of presentation was between 50 and 60 years (range 20-61 years). Kraus et al. and Chen et al. in their case series have shown that the lowest mean age of onset was at 50 years, and in the rest of studies the average age was 50 years [11, 14]. In our series, the average age of presentation is 41.3 years with slightly higher incident in male with male-female ratio, 1.2:1.

The most frequent location of STSHN is difficult to determine because in the published series, sarcomas were grouped into "zones", for example, scalp with face, neck, parotid, paranasal sinuses and nasal cavity, etc. In most series the most common place is the scalp and face with 25-58% [11], followed by the neck/parotid with 26-53% [13] and paranasal sinuses/ nasal cavity with 5-26% [17]. In our series the most frequent site is the paranasal sinuses (57%) followed by the soft tissues of the neck (14%),the larynx (14%) and the pharynx (14%). Sarcomas located in nasal cavity, oral cavity and orbit were reported to have clear margin following resection in the majority of cases, while in soft tissues of the neck,clear resection margin can only be achieved about 45%[18].

In the past the most common sarcomas were: unclassified sarcoma, histiofibrosarcoma and fibrosarcoma. Today, most sarcomas can be diagnosed with precision using immunohistochemical, cytogenetics, molecular and electron microscopy technique that can detect a specific cell differentiation so histiofibrosarcoma and fibrosarcoma are now a diagnosis by exclusion. In most series the most prevalent subtype is histiofibrosarcoma of 20-34% [10-14] followed by fibrosarcoma [19, 20] of 17-38% and angiosarcoma [21] of 19-22%. In our series, the most common subtype is fibrosarcoma (23%), followed by fibromyxoid sarcoma (23%), rhabdomyosarcoma (15%), histofibrosarcoma (15%) synovial sarcoma (8%),hemangiopericytoma (8%) and spindle cell sarcoma (8%).

One of the main determinants of the biological behaviour of sarcomas is the histological grade which correlates with lymph node metastasis, distant metastasis, recurrence, and overall survival [22]. Grading systems based on histological parameters were introduced in the 80's to provide more accurate information on the degree of malignancy of tumours. Many different systems were designed to discriminate between tumours of low grade and high grade. Generally, histiofibrosarcoma,angiosarcoma, Kaposi's sarcoma and alveolar synovial are high-grade lesions. Dermatofibrosarcoma protuberance and well-differentiated liposarcoma are low-grade lesions. Other subtypes are individually graded, based in morphological parameters as necrosis, pleomorphism and mitosis [23]. In most published series the ratio of low-grade tumours (G1) and high-grade tumours (G2 and G3) is near of 1:1. In the series of Le Vay et al. (1994) and Chen et al. (2005) high-grade tumours correspond to 71 and 74% of cases respectively [17,24]. Our series has a high percentage of low-grade tumours (69%), which reflect in low incidence of distant metastasis and recurrent rates.

Tumour size and depth of invasion are important factors to consider the possibility of tumour resection. In the previous report, the proportion of tumours is predominately less than 5 cm in size (55-72%) [10-14]. Our series reported the same rate which is 54% of cases are less than 5 cm. This data may reflect the increased of health awareness among the community and early referral to the tertiary centre with surgery & oncology services.

In the published case series, documentation of staging is lacking and it is absent in 47% of cases [22]. Chen et al. who reported the sarcoma staging found 26% in stage I, 48% in stage II and 26% in stage III, based on the AJCC 2002 [17]. In our series, 35.7 % of the study population was in stage I, 28.5 % in stage II, 21 % in stage III and 7 % in stage IV. Thus, based on the above data, most of the present cases presented in early stage and 28 % of the population is in the metastatic stage (stage III and IV).

The treatment of head and neck sarcomas is primarily surgical.The type of surgery is determined by several factors such as depth and location of the tumour, the involved adjacent structures, the need for reconstruction and functional status of the patient. Other important considerations include the potential for morbidity related to breathing, swallowing, and speaking, and the significant cosmetic deformity

73

that may follow maxillo-facial resections. Difficulties in achieving good surgical margin due to these considerations may be the cause of local relapses and the patient succumb to it, many times without distant metastatic disease [25].Advances in the reconstruction (e.g. microvascular free-flaps) allow wider resections, with improved oncology and functional results.

Regarding adjuvant treatment, radiotherapy should be considered to decrease the risk of local recurrence and should be recommended for all high-grade tumors, tumors more than 5 cm, and in case of close or positive margin [23]. In the case of low-grade, small tumour but deep seated radiation therapy may have to be considered as good surgical margin is difficult to achieve. The other role for radiation in the management of soft-tissue sarcomas is in cases of unresectable tumors, where in it is used as a primary modality and at times with chemotherapy. But unfortunately it is more of a palliative strategy [20].

Concerning chemotherapy, it did not produce a survival benefit in the treatment of sarcomas. However, there is 10% of benefit of chemotherapy on recurrence-free survival [24]. Chemotherapy has been widely used for decades in different situations in STSHN as palliative treatment in advanced cases, for down-staging, and as adjuvant or neo-adjuvant treatment in high-grade localized disease in combination with the local treatment of the primary tumour. The most used chemotherapeutic drugs in all these situations, especially during later years, have been doxorubicin and ifosfamide[28].

The different sensitivities for different drugs or drug combinations between the most common subtypes had been observed. Table 5 depict the differences in term of tumor sensitivity to the chemotherapy therefore it is not used in histological subtypes known to be insensitive to chemotherapy[29].

Table 5: Sensitivity of soft tissue sarcoma subtype to chemotherapy

Chemoresistant	Low chemosensitive	Intermediate chemosensitive	Chemosensitive
(1) Gastrointestinal stromal tumours	(1) Epithelioid cell sarcoma	(1) Liposarcoma	(1)Rhabdomyosarcoma of embryonal and alveolar types
(2) Extraskeletalmyxoid chondrosarcoma	(2) Adult fibrosarcoma	(2) Leiomyosarcoma	(2) Desmoplastic small round cell tumour
(3) Clear cell sarcoma	(3)Haemangio-pericytoma	(3) Synovial sarcoma	
(4) Alveolar soft part sarcoma	(4) Malignant peripheral nerve sheet tumour	(4) Undifferentiated pleomorphic sarcoma	
		(5) Angiosarcoma	

Conclusion:

Sarcomas of the head and neck are rare tumours and represent a heterogeneous group of tumours with different histologic variants. The most affected sites are paranasal sinuses in which fibrosarcoma and fibromyxoid sarcoma are the most common types.Here,results of a case series showed that the optimal treatment for adult head and neck soft tissue sarcomas is surgery with adjuvant radiotherapy that may improve outcomes of those with high-grade tumors or positive margins.

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Conflict of interest: None.

74

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75

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