Maxillary Sinus Sarcomas: Epidemiological and Clinicopathological Experience of 25 Years in a National Reference Cancer Center

Rosa Angélica Salcedo-Hernández ·
Leonardo Saúl Lino-Silva · Kuauhyama Luna-Ortiz

Received: 26 October 2011 / Accepted: 10 February 2012 / Published online: 22 February 2012
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Abstract The aim of this study was to report our experience with malignant soft tissue tumors of the maxillary sinus in the period between 1985 to 2010. This is a retrospective case study in a tertiary cancer center setting. Review of patient's records and new evaluation of pathological specimens were made for 20 patients (14 men and 6 women) still met present criteria. After review the most common histological diagnoses were malignant peripheral nerve sheath tumor and malignant fibrous histiocytoma. There are male sex predilection, the median age was 38.9 years; 95% of tumors were >5 cm, 80% were high grade, 0% have metastatic disease at the diagnosis and the tumors were initially treated by surgical resection had better survival ($p = 0.02$). We present the results of a one of the larger series published to date in maxillary sinus sarcomas where analyzed the clinicopathological characteristics of 20 cases.

Keywords Sarcoma · Head and neck · Cancer · Paranasal sinuses · Rhabdomyosarcoma · Synovial sarcoma

Introduction

Sarcomas are rare mesenchymal neoplasms that constitute 1% of all malignancies in the body and in the head and neck area accounts 4–10% of all [1]. Soft tissue sarcomas comprise more than 50 different histological subtypes with a wide spectrum of biological behavior, most are slow growing, locally aggressive, but lymph node metastases occur only in 3–10% and distant metastases in 28% (most commonly in lung, bone, liver and central nervous system). The metastasis are more common in high grade sarcomas [2].

In the maxillary sinus the sarcomas are very rare in most series, and as much as 25% of head and neck sarcomas occur in this location; but there are only isolated reports of tumors in this region [3, 14].

Surgery is the cornerstone of treatment and resection margin status and extent of surgical resection are the most important predictors of persistence, recurrence and overall survival. However, these tumors invade areas of difficult surgical access, making it difficult to achieve adequate surgical margins in head and neck area where there are no compartments as in the extremities, resulting in a high risk of local recurrence [4, 5]. In head and neck the most common site of involvement is the scalp, followed by the sinonasal tract and the most common histological types are unclassifiable sarcoma, angiosarcoma and Malignant fibrous histiocytoma (MFH) [6].

The knowledge that we currently have in head and neck sarcomas is based in classic series that began decades ago in which there are misclassification in up to 39% of the population [1, 7] and there are not series published to date of maxillary sinus sarcomas.

We present a series of sarcomas of the maxillary sinus in a Hispanic population in order to evaluate clinical and pathological data and demographics to better understand of these rare tumors in this location.

R. A. Salcedo-Hernández
Departamento de Cirugía Oncológica, Instituto Nacional de
Cancerología, México, DF, Mexico

L. S. Lino-Silva (✉)
Departamento de Patología Oncológica, Instituto Nacional de
Cancerología, Avenida San Fernando No. 22, Colonia Sección
XVI, 14080 México, DF, Mexico
e-mail: saul.lino.sil@gmail.com

K. Luna-Ortiz
Departamento de Cirugía de Cabeza y Cuello, Instituto Nacional
de Cancerología, México, DF, Mexico

Materials and Methods

We reviewed the medical records of patients with sarcomas in our institution between 1985 and 2010, we excluded those with bone sarcomas, odontogenic sarcomas, cutaneous sarcomas as Kaposi's sarcoma and cases that represent metastases of other sites (generally soft tissues of extremities). In all, 108 (6.5%) patients met the criteria for inclusion of sarcomas of the head and neck, of these 20 (1.2%) occurred in the maxillary sinus. The documented data were age, sex, tumor location, histological type, histological grade, tumor size, deep or superficial status, nodal status, presence or absence of metastasis, surgical resection and clinical stage. We used the American Joint Committee on Cancer (AJCC) staging system at its seventh revision (2010), taking into account the clinical, radiological and pathological data (including surgical limits) in addition to those established by the College of American Pathologists (CAP) [9] in the same year; In summary, R2 is considered when grossly visible tumor is in the limit section, R1 is the presence of microscopic tumor at the edge section and R0 means surgical margin free of neoplasia. The histological gradification system used was the French system FNCLCC (Fédération Nationale de Centres de Lutte Contre le Cancer) based on 3 grades [2] for which use the criteria established by Trojani [10] that evaluates necrosis, nuclear pleomorphism and mitosis. All surgical specimens or biopsies were reviewed

histologically to determine the margin status, confirm the histological diagnosis and grading tumors.

To compare differences between qualitative variables studied (nominal or ordinal), we used a nonparametric Pearson's χ^2 statistically significant for $p < 0.05$. To analyze the distributions of the survival curves were used the Kaplan–Meier and Log Rank test.

Results

Demographic and Pathological Findings

The clinicopathologic features of 20 cases analyzed are summarized in Tables 1 and 2. The average age at diagnosis was 38.9 years (range 17–79). Fourteen cases were in males (70%) and six cases in women (30%). The most common histological types were Malignant Tumor of Peripheral Nerve Sheath (MPNST) and MFH with 4 (20%) cases each, followed by Rhabdomyosarcoma with 3 cases (15%) (Table 3). No sarcoma was shown to be more prevalent in any age group. Of the 4 cases of MPNST ages of presentation were 22, 41, 47 and 49 years for the MFH were 17, 24, 33 and 76 years for the presentation rhabdomyosarcoma ages were 19.26 and 60. With respect to gender, tumor size, was obtained in 101 patients (93.5%) and in 37 cases (38%) was <5 cm, whereas 64 (63%) cases was >5 cm. In terms of

Table 1 Clinico-pathological features of 20 maxillary sinus sarcomas

Case	Sex	Age (year)	Diagnosis	Size (cm)	Metastases	Clinical stage	Status	Survival (months)
1	Male	48	Angiosarcoma	>5	No	IIA	DOD	21
2	Male	90	Angiosarcoma	>5	No	III	DOD	13
3	Male	26	SS	>5	No	IIA	DFD	119
4	Female	25	Fibrosarcoma	>5	No	IB	AFD	51
5	Female	47	Fibrosarcoma	>5	No	IIB	AWD	25
6	Male	22	MPNST	>5	No	III	DWD	128
7	Female	41	MPNST	>5	No	IB	AWD	57
8	Female	47	MPNST	<5	No	IB	AFD	102
9	Male	49	MPNST	>5	No	III	DOD	2
10	Male	17	MFH	>5	No	III	DOD	104
11	Male	24	MFH	>5	No	IA	DFD	19
12	Male	33	MFH	>5	No	IIB	AFD	48
13	Male	76	MFH	>5	No	IIB	AFD	11
14	Female	53	HE	>5	No	III	DOD	27
15	Male	38	HE	>5	No	III	AFD	22
16	Male	20	Liposarcoma	>5	No	III	DOD	13
17	Male	17	MFS	>5	No	IIB	AWD	6
18	Male	19	RMS	>5	No	IIB	AFD	6
19	Male	26	RMS	>5	No	IIB	DOD	24
20	Female	60	RMS	>5	No	IIA	AWD	59

Table 2 Comparison of Clinico-pathological features of 20 maxillary sinus sarcomas

Feature	Number	%	<i>p</i> *
Sex			0.074
Male	14	70	
Female	6	30	
Pathological T			0.022
T1b	6	30	
T2b	14	70	
Histologic grade			0.387
G1	4	20	
G2	7	35	
G3	9	45	
Clinical stage			0.199
IA	1	5	
IB	3	15	
IIA	3	15	
IIB	6	30	
III	7	35	
IV	0	0	
Initial treatment			0.035
Surgery	12	60	
Chemotherapy	3	15	
Radiotherapy + chemotherapy	5	25	
Resection (13 patients)			0.166+
R0	9	69	
R1	4	31	
Reconstruction	8	61	
Recurrence	6		
Adjuvant therapy		46	
No	7	35	
Radiotherapy	12	60	
Chemotherapy	1	5	

* Pearson's χ^2 + Only R0 versus R1

depth, 10 cases (10%) were superficial to the underlying fascia, the 91 (90%) remaining cases were deep to this fascia. Histologic grade was high (grade 3) in 9 (45%) cases, grade 2 in 7 (35%) cases and grade 1 in 4 (20%) cases (Table 2). As for sex, the two cases of fibrosarcoma were females as well as 2 of 4 (50%) of MFH. The remaining lesions were exclusively or predominantly in men.

Clinical Stage and Surgical Margins

Clustering, 20% occur in localized stage with low metastatic potential (stage I) and 80% with high-grade tumors with high metastatic potential (stages II and III) and 0% in metastatic disease. Underwent surgery 13 patients who obtained a complete R0 resection in 9 (69%) cases and R1 resection in 4 (31%) cases, no have cases marked as R2 as

Table 3 Histological subtypes

Subtype	Number	%
Malignant peripheral nerve sheath tumor	4	20
Malignant fibrous histiocytoma	4	20
Rhabdomyosarcoma	3	15
Angiosarcoma	2	10
Fibrosarcoma	2	10
Hemangioendothelioma	2	10
Synovial sarcoma	1	5
Myofibroblastic sarcoma	1	5
Liposarcoma	1	5

Table 4 Overall survival analysis (univariate)

Variable	<i>p</i>
Sex	0.111
Histological subtype	0.987
Pathological tumor size and deep	0.267
Histologic grade	0.473
Clinical stage	0.457
Initial treatment	0.020
Resection (R0 or R1)	0.351

is shown in Table 2. G1 tumors were resected with R0 in 22% and G2–G3 by 80%. With respect to tumor size and depth, T1b tumors were taken to R0 50% of cases, T1b in 52.9%, T2a in 50 and 85.7% in T2b. Reconstruction was performed in 8 patients undergoing surgery (2 patients with T1b, T2a patients 2 and 4 patients with T2b). In terms of recurrence, no patients with R0 recur while 2 of 4 patients (50%) with R1 resection recur ($\chi^2 p = 0.02$).

Of the seven patients not treated surgically, two were treated with chemotherapy as single modality and the remaining 5 with concomitant chemotherapy and radiation. Chemotherapy was based on platinum and adriamycin. The average dose of radiotherapy was 19.8 Gy. Of all patients who underwent surgery 12 (92%) received radiation therapy, either by close margins, positive margins or high grade tumor, and one patient received adjuvant chemotherapy.

In the survival analysis (Table 4) only patients who underwent surgery as initial treatment had better survival than those who received another treatment modality ($p = 0.020$). None of the other factors shown to be associated with improved survival, including histological grade and clinical stage.

Discussion

The head and neck sarcomas are rare and heterogeneous neoplasms, constitute only 1% of all cancers and account

for 2–15% of cases of sarcomas in adults. They show a wide spectrum of clinical behavioral ranging from slow growing lesions to aggressive lesions with recurrent and metastatic capacity, which affect lymph nodes in 3–10% and distant sites in 28%, being the most affected site the lung, followed by bone, central nervous system and liver [14–22]. In the maxillary sinus there are not large series about this and experience is low and based on isolated case reports and by application of the knowledge derived from the soft tissues of the extremities. Then the discussion we will make it based on the studies published to date of head and neck sarcomas in general [11–22].

Analysis of the sarcomas in this location poses specific problems. First, it is very difficult due to their rarity achieve an adequate sample for statistical analysis. Second, the evaluation and monitoring of patients was based on radiographic studies with technology (hardware and software) continuously changed over the years, improving the assessment of patients. Third, the classification of sarcomas has evolved, are a heterogeneous group of at least 50 histological subtypes, each with its own histological variants classified according to their supposed origin tissue [2], but today we know that sarcomas originate from a pluripotent stem cell can differentiate into any mesenchymal component, so that today the classification is based on the phenotype of the tumor. With advances in the field of immunohistochemistry (IHC) and molecular biology: now, we can classify more properly these tumors even in small samples [3]. However up to 20% of sarcomas are not classified [14]. Fourth, advances in the field of surgical oncology, especially the use of microvascular free flap reconstruction and advanced techniques have changed the surgical approach, allowing more and better resections achieving higher rates of resections R0. Fifth, we must mention that there are series that are excluded tumors such as rhabdomyosarcoma and primitive neuroectodermal tumor, since its natural history is different (respond well to chemotherapy) other authors also exclude the angiosarcoma, it is a highly malignant neoplasm.

Risk Factors

The cause of most sarcomas in any location remains unknown. There are genetic and environmental factors are clearly associated with these neoplasms. Patients with hereditary retinoblastoma, neurofibromatosis, and Lynch syndrome are at increased risk of sarcomas. Also, prior radiation to the head and neck is a risk factor. Makimoto et al. [23] found only 6 cases (0.14%) in 4184 patients with previous history of radiation in this area, I et al. [24] found it in 0.38% of their patients and the most common subtype is the MFH. It has been speculated that trauma and chronic

infection plays a role in the development of sarcomas, but a real cause–effect relationship has not been proven.

Clinical Features and Presentation

Most sarcomas of the maxillary sinus presents with non-specific signs and symptoms. Most appear as a tumor with progressive growth without pain, although it is reported that 14–25% may have pain [8] and can occur a variety of other symptoms such as runny nose and nasal obstruction.

The relationship between man and woman ranges from 1:1 to 2.8:1 [10–12] predominating in men. The most common age of presentation is between 50 and 60 years, ranging from 15 to 93 years, only the study of Eeles et al. [7] shows age of onset below 40 years, although their series included patients from 3 years old, decreasing the average age; the series of Kraus et al. [18] and Chen et al. [22] demonstrated mean age of onset <50 years and the rest we see that the average age is 50 years. In our series the proportion of male–female condition is 2.3 – 1 and the average age of presentation is 38.9 years. The explanation for this is unclear, because we know that is not due to early detection, because 61% of tumors are in advanced stage.

Histologic Subtypes

In past decades the most common sarcomas were the Unclassified sarcoma, MFH and fibrosarcoma. Today, the majority of sarcomas can be classified and the latter two are considered diagnoses of exclusion only diagnosable if not demonstrated by IHC, cytogenetics, molecular and/or electron microscopy differentiation to a clearly recognizable histological subtype. Thus, in most of the series we see that the most prevalent subtype is MFH (20–34%), followed by fibrosarcoma (17–38%) and angiosarcoma (19–22%). As the series are more contemporary, diagnoses of fibrosarcoma, MFH, and unclassifiable sarcoma often are lost, for the reasons outlined above. In recent years the most common sarcomas are angiosarcoma, leiomyosarcoma and MPNST. In our series, in the maxillary sinus the most common subtypes were the MFH and MPNST (20% each) and rhabdomyosarcoma (15%), note that the percentages of different tumors in our series (Table 2) are very similar to each other, the difference between the first and last are 15% points and are 9 different tumors.

Sarcomas may be misdiagnosed or misclassified by the general pathologist. In recent works reviewing the sarcomas there are a change in diagnosis in 33–48% of cases, for example, in the study of Bree et al. [25] a histopathological review of 41 patients treated for head and neck sarcomas revealed that 7% of the cases studied revealed not to be sarcomas and 39% of the subtypes were diagnosed in another way, in particular, the original diagnosis of

fibrosarcoma and MFH changed. Because these findings may have obvious implications, an expert pathology review and supported by additional studies is essential before starting treatment and also when reviewing historical retrospective material.

One of the main determinants of the biological behavior of these sarcomas is tumor grade, which correlates with lymph node metastasis, distant metastasis, recurrence, positive margins and overall survival [2, 5, 22]. Gradificación systems based on histological parameters were introduced in the eighties to provide more precise information on the degree of malignancy of tumors. Many and various systems were devised in order to discriminate between tumors of low grade and high grade. Generally, MFH, angiosarcoma, synovial sarcoma and alveolar sarcoma are by definition high-grade lesions. Dermatofibrosarcoma protuberans and well-differentiated liposarcoma are low-grade lesions. Other subtypes are gradified based on individual morphological parameters such as necrosis, nuclear pleomorphism and mitosis [10]. In the published series the proportion of low-grade tumors (G1) and high grade (G2 and G3) is close to 1:1, the G1 numbers varies from 22 to 45%, the G2 from 15 to 53% and G3 from 16 to 58%. In series where high-grade is unified combined G2 and G3 tumors, high grade tumors predominate slightly over the low grade, although there are series like Le Vay et al. [19] and Chen et al. [22] which correspond to 71 and 74% of cases. Our series is not far from the latter, adding grades 2 and 3 have 80% of high-grade tumors and 20% of low grade.

Tumor size and depth are important factors in evaluating the tumor resection. In the seven series in which data are available, the ratio of tumors smaller than 5 cm and >5 cm is similar in 2 of them and on the other 5 is dominated by <5 cm in 55–72%. Data from our series are different, as 30% of cases are <5 cm and the rest over 5 cm. This reflects the culture of our population, where the patient seeks medical attention when the tumor becomes a problem (e.g. very large lesion). Regarding the depth of the tumor, this finding is difficult to find in the different series analyzed, only the series of Chen et al. [22] reported 36 cases (92%) as deep and 3 (8%) superficial. Data from our series are similar for the superficial lesions were 10–90% deep.

Clinical Stage

Based on these clinical stages defined by the staging system of the seventh edition of the AJCC in 2010 [the disease can be divided into three groups, namely, an early stage with low-grade malignancy that has little or no metastatic potential (stages IA, IB), a locally advanced stage and aggressive high-grade tumors with high metastatic potential (stage IIA and IIB) and a stage with metastatic disease, whether lymph nodes (stage III) or other sites (stage IV)].

In published series are few data to stage and there are series like Colville et al. [5] in that missing data in 47% of cases did not allow staging. In our series we have in stage I a 20% of the study population, in stage II 45%, 35% in stage III and 0% in stage IV. This again is related to tumor size, lesion depth and histological type, as in our population predominated tumors larger than 5 cm, located deep to the underlying fascia and are high grade.

Treatment

Management of sarcomas of the maxillary sinus from any location is primarily surgical. The type of surgery is determined by several factors such as depth and location of the tumor, involvement of adjacent structures, need for reconstruction and functional status of the patient. Advances in the reconstructions (e.g., microvascular free flaps) allow wider excision, with potential improvement in cancer outcomes, aesthetic and functional. Due to the low prevalence of lymph node metastases elective lymph node dissection is not justified. In our series of 13 patients who underwent surgery, 92% of them received adjuvant radiotherapy, 69% were carried to complete resection (R0) and none of them recur. Of the cases with R1 (31%) only two recur in the follow-up.

The most important prognostic factors in sarcoma are tumor grade and clinical stage; both have shown over the years to be the best predictors of survival. In our study only patients who underwent surgery as initial treatment had better survival than those who received another treatment modality ($p = 0.020$). None of the other factors shown to be associated with improved survival, including histological grade and clinical stage. Perhaps these findings are due to sample size but we know that there are no published series and our knowledge is based on isolated reports.

Conclusions

Sarcomas of the maxillary sinus are rare tumors and represent a heterogeneous group of tumors with different histologic variants. The most frequent tumors were MPNST, MFH and rhabdomyosarcoma. The histological subtype is becoming more important due to the development of new treatment modalities and advances in immunohistochemistry and molecular biology have made more precise classification of sarcomas. We present the results of the first series of the maxillary sinus sarcomas, they predominated in men, the average age at diagnosis was 38.9 years, 90% of the tumors are deep, 80% are high grade and 70% are larger than 5 cm. Surgery is the mainstay of therapy and showed improved survival when it was the initial treatment.

Conflicts of interest None.

References

- Huber GK, Matthews TW, Dort JC (2006) Soft-tissue sarcomas of the head and neck: a retrospective analysis of the Alberta experience 1974 to 1999. *Laryngoscope* 116:780–785
- de Bree R, van der Waal I, de Bree E, Leemans CR (2010) Management of adult soft tissue sarcomas of the head and neck. *Oral Oncol* 46:786–790
- Sun JJ, Rasgon BM, Wild TW, Hilsinger RL Jr (2003) Synovial cell sarcoma of the maxillary sinus: a first reported case. *Otolaryngol Head Neck Surg* 129(5):587–590
- Hoffman HT, Robinson RA, Spiess JL, Buatti J (2004) Update in management of head and neck sarcoma. *Curr Opin Oncol* 16:333–341
- Colville RJ, Charlton F, Kelly CG, Nicoll JJ, McLean NR (2005) Multidisciplinary management of head and neck sarcomas. *Head Neck* 27:814–824
- Guillou L, Coindre JM, Bonichon F, Nguyen BB, Terrier P, Collin F et al (1997) Comparative study of the National Cancer Institute and French Federation of Cancer Centers Sarcoma Group grading systems in a population of 410 adult patients with soft tissue sarcoma. *J Clin Oncol* 15:350
- Eeles RA, Fisher C, A'Hern RP, Robinson M, Rhys-Evans P, Henk JM et al (1993) Head and neck sarcomas: prognostic factors and implications. *Br J Cancer* 68:201–207
- AJCC Staging system 7th edition. Available at: <http://www.cancerstaging.org/>
- College of the American Pathologist's Cancer Protocols, available at: http://www.cap.org/apps/docs/committees/cancer/cancer_protocols/2011/SoftTissue_11protocol.pdf
- Coindre JM, Trojani M, Contessa G, David M, Rouesse J, Bui NB et al (1986) Reproducibility of a histological grading system for adult soft tissue sarcomas. *Cancer* 58:306
- Freedman AM, Reinman HM, Woods JE (1989) Soft-tissue sarcomas of the head and neck. *Am J Surg* 158:367–372
- Farhood AI, Hadju SI, Shiu MH, Strong EW (1990) Soft tissue sarcoma of the head and neck in adults. *Am J Surg* 160:365–369
- Tran LM, Mark R, Meier R et al (1992) Sarcomas of the head and neck. Prognostic factors and treatment strategies. *Cancer* 70:169–177
- Sturgis EM, Potter BO (2003) Sarcoma of the head and neck. *Curr Opinion Oncol* 15(3):239–252
- Willers H, Hug EB, Spiro JJ, Efrid JT, Rosenberg AE, Wang CC (1995) Adult soft tissue sarcomas of the head and neck treated by radiation and surgery or radiation alone: patterns of failure and prognostic factors. *Int J Radiat Oncol Biol Phys* 33:585–593
- Barker JL, Paulino AC, Feeney S, McCulloch T, Hoffman H (2003) Locoregional treatment for adult soft tissue sarcomas of the head and neck: an institutional review. *Cancer J* 9:49–57
- Dudhat SB, Mistry RC, Varughese T, Fakih AR, Chinoy RF (2000) Prognostic factors in head and neck soft tissue sarcomas. *Cancer* 89:868–872
- Kraus DH, Dubner S, Harrison LB, Strong EW, Hajdu SI, Kher U et al (1994) Prognostic factors for recurrence and survival in head and neck soft tissue sarcomas. *Cancer* 74:697–702
- Le Vay J, O'Sullivan B, Catton C, Cummings B, Fornasier V, Gullane P, Simm J (1994) An assessment of prognostic factors in soft-tissue sarcoma of the head and neck. *Arch Otolaryngol Head Neck Surg* 120:981–986
- Le QT, Fu KK, Kroll S, Fitts L, Massullo V, Ferrell L et al (1997) Prognostic factors in adult soft-tissue sarcomas of the head and neck. *Int J Radiat Oncol Biol Phys* 37:975–984
- Dijkstra MD, Balm AJ, Coevorden FV, Gregor RT, Hart AA, Hilgers FJ et al (1996) Survival of adult patients with head and neck soft tissue sarcomas. *Clin Otolaryngol* 21:66–71
- Chen SA, Morris CG, Amdur RJ, Werning JW, Villaret DB, Mendenhall WM (2005) Adult head and neck soft tissue sarcomas. *Am J Clin Oncol* 28:259–263
- Makimoto Y, Yamamoto S, Takano H, Motoori K, Ueda T, Kazama T et al (2007) Imaging findings of radiation induced sarcoma of the head and neck. *Br J Radiol* 80:790–797
- Ko JY, Chen CL, Lui LT, Hsu MM (1996) Radiation induced malignant fibrous histiocytoma in patients with nasopharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg* 122:535–538
- De Bree R, van der Valk P, Kuik DJ, van Diest PJ, Doornaert P, Buter J et al (2006) Prognostic factors in adult soft tissue sarcomas of the head and neck: a single centre experience. *Oral Oncol* 42:703–709