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Synovial sarcomas of the head and neck: Comparative analysis with synovial sarcoma of the extremities

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ABSTRACT

Objective: This study analyzed synovial sarcoma (SS) of the head and neck in order to identify features associated with survival improvement and compared them with the survival of SS of limbs.
Methods: Clinical charts and histopathologic material with analysis for SYT/SSX gene rearrangement of 16 patients were reviewed. The clinicopathologic features and their association with survival were analyzed and compared with 174 SS of limbs.
Results: The average age was 24.2 years (range 21–86). Eight cases occurred in each sex. The most frequent site was the parapharyngeal space (PPS). The mean tumor size was 5.38 cm. Sixty-nine percent occurred in Stages II–III and 9% in Stage IV. Fifteen cases were excised: R0 resection in seven (46.7%) cases and R1 resection in eight (53.3%) cases. No patient with R0 resection has recurred, and three patients (37.5%) with R1 resection have recurred ($p = 0.035$). Patients with R0 surgery had better survival rates compared to those who received other treatments ($p = 0.045$). SS of head and neck showed a 5-year survival rate of 58% compared to 44.6% of the limbs ($p = 0.450$).
Conclusion: The most prevalent location was the PPS. Surgical resection with clear margins correlated with low recurrence. Head and neck sarcomas had similar survival rates compared to sarcomas of limbs.

1. Introduction

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

Synovial sarcoma (SS) is a spindle-cell tumor that has variable epithelial differentiation and is associated with the fusion gene *SYT–SSX*. SS usually occurs in the limbs and is rare in other locations. The head and neck develop 1.9–3.5% of all SS, and the vast majority arise in the neck, especially in the hypopharynx, parapharynx and paravertebral soft tissues [1,2]. In the head, there are only occasional case reports with limited long-term follow-up [3–9,2,10–12]. In 2009, a study was published detailing a series of 36 cases where the more common affected sites were parotid gland and temporal region; however, these series exclude the cases located in the maxillary sinus, nasal cavity and oral cavity [13]. In this series, we present clinicopathologic data of 16 FISH (fluorescence in situ hybridization) confirmed SS of the head and neck, including the oral region and sinonasal tract. We analyze the clinicopathologic characteristics of SS of the head and neck for identification of features associated with better survival and compare them with survival of 174 SS of the limbs.

2. Materials and methods

We review the medical charts of patients with sarcoma diagnosed in our institution between 1985 and 2010, excluding those with bone sarcomas, odontogenic sarcomas, cutaneous sarcomas as Kaposi's sarcoma, and cases that represent metastases (generally from limbs). What remains is a pool of 1662 soft tissue sarcomas. In all, 108 (6.5%) patients met the criteria for inclusion of sarcomas of the head and neck and of these, 16 (0.96%) were SS, 15 corresponded to new cases and one was a previously published case (case 16, Table 1) [22]. The documented data were age, sex, tumor location, tumor size, location respect fascia, nodal status, presence or absence of metastasis, surgical resection and clinical

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Table 1
Analysis of 16 cases of synovial sarcomas of the head and neck.

Case	Sex	Age (years)	Size (cm)	Metastases	Clinical stage	Status	Initial treatment	Adjuvant therapy	Survival (months)	Site
1	Female	86	7	No	III	DOD	Surgery, R1	Yes, CRT	19	Mouth floor
2	Male	23	3	No	IIA	DOD	Surgery, R1	No	20	Lateral neck
3	Male	31	9	No	III	AWD	Surgery, R0	No	16	Lateral neck
4	Female	40	3.5	No	IIA	AFD	Surgery, R1	No	24	Orbit
5	Female	62	4.5	No	IIA	DFD	Surgery, R1	Yes, CRT	193	Parotid gland
6	Male	39	6.5	No	III	DOD	Surgery, R1	Yes, CRT	61	Parotid gland
7	Male	50	9	Lung	IV	DOD	Radiotherapy	No	50	Soft palate
8	Female	27	11	Node	III	DOD	Surgery, R1	No	49	Soft palate
9	Male	26	4	No	IIA	DOD	Surgery, R0	No	119	Maxillary sinus
10	Male	29	4.5	No	IIA	AFD	CT + surgery, R0	No	16	Parapharyngeal space
11	Female	49	8	No	III	DOD	CRT + surgery, R0	No	20	Parapharyngeal space
12	Female	39	9	No	III	AWD	Surgery, R1	Yes, CT	117	Parapharyngeal space
13	Female	21	1.2	No	IB	DOD	Surgery, R0	No	12	Larynx
14	Male	28	3	No	IB	AFD	Surgery, R0	No	120	Hyoid
15	Female	55	2	No	IA	AWD	Surgery, R1	No	30	Hard palate
16	Male	26	1	No	IA	AFD	Surgery, R0	No	18	Tongue

DFD, dead free of disease; DOD, dead of disease; AWD, alive with disease; AFD, alive free of disease; CT, chemotherapy; CRT, chemoradiotherapy.

stage. For staging we used the American Join Committee on Cancer (AJCC) staging system, seventh revision (2010), in addition to those established by the College of American Pathologists (CAP) [14]. With regards to surgical resection, R2 is considered when a grossly visible tumor is in the surgical margin, R1 is the presence of a microscopic tumor in the surgical margin, and R0 is the surgical margin free of tumor. The histologic grading system used is the French system FNCLCC (*Fédération Nationale de Centres de Lutte Contre le Cancer*), based on three grades established by Trojani [15,16] that evaluate necrosis, nuclear pleomorphism and mitosis. By definition, SS are grade 3. All surgical specimens or biopsies were reviewed histologically to determine the margin status, confirm the histological diagnosis and search the *SYT*/*SSX* translocation. The clinical data and follow-up information were obtained from the referring clinician, patient charts and, in some cases, from the patients themselves. Literature research about synovial sarcomas involving the head and neck were reviewed from the PubMed literature from 1950 to 2011.

Immunohistochemical stains were performed with a Ventana automatic stainer (Ventana Medical Systems, Tucson, AZ), using the avidin–biotin complex-based with the i-View DAB kit (Ventana Medical Systems, Tucson, AZ) detection system with appropriate controls. The following primary antigens were studied: Vimentin (V9, Dako Cytomation, Carpintera, CA, 1:200, heat-induced epitope retrieval, pH 8.0 for 30 min), Epithelial membrane antigen (E29, Dako Cytomation, 1:200, protease digestion), Keratin cocktail (AE1/AE3, Chemicon, Temecula, CA, 1:400), BCL2 (Clone 124, monoclonal, Dako, Carpintera, CA, 1:20) and TLE-1 (sc-9121, Santa Cruz Biotechnology, CA, 1:20).

Fluorescence in situ hybridization (FISH) studies were performed to identify the SS-specific translocation *t*(X;18), using the SS18 (SYT) locus-specific, dual-color, break-apart rearrangement probe (Abbott Molecular, Des Plaines, IL). The standard 4–5 mm sections of formalin-fixed, paraffin-embedded tumor tissue were subjected to pretreatment and proteinase K digestion using Spot-Light Tissue Pretreatment Kit (Zymed, San Francisco, CA) according to the manufacturer's instructions. The FISH conditions were those recommended by the manufacturer (Abbott Molecular) for the SS18 probe. Color images were obtained by using an Olympus BX60 epifluorescence microscope. For each case, non-overlapping nuclei with well-defined nuclear outlines were evaluated for fluorescent signals, and cases with split signals in over 50% of the cells were considered positive for translocation.

Additionally, from the pool of 1662 patients, we identified 174 patients with SS of the limbs, and compared some clinicopathological characteristics and overall survival with the 16 patients with SS of head and neck. To compare differences between qualitative variables studied (nominal or ordinal), we used a nonparametric Pearson's Chi-square test statistically significant for p less than 0.05 comparing proportions between strata for each variable. To analyze the distributions of the survival curves, we used the Kaplan–Meier and Log Rank test.

This study was approved by the Institutional review Board of Instituto Nacional del Cancerología de México.

Table 2
Comparison of clinico-pathologic features of 16 synovial sarcomas.

Feature	Number	%	p^*
Sex			
Male	8	50	0.154
Female	8	50	
Pathological T			
T1a	2	12.5	0.179
T1b	7	43.7	
T2b	7	43.7	
Clinical stage			
IA	2	12.5	0.189
IB	2	12.5	
IIA	5	31.3	
IIB	0	0	
III	6	37.5	
IV	1	6.2	
Initial treatment			
Surgery alone	12	75	0.035
Chemotherapy	1	6.25	
Radiotherapy + chemotherapy	2	12.5	
Radiotherapy	1	6.25	
Resection (15 patients)			
R0	7	46.7	0.166*
R1	8	53.3	
Reconstruction	2	18	
Recurrence	4	36	
Adjuvant therapy			
No	12	75	0.236
Chemo-Radiotherapy	3	18.75	
Chemotherapy	1	6.25	

* Pearson's Chi square test p-values were obtained comparing proportion differences between strata of each variable (e.g. male vs. female, T1a vs. T1b vs. T2b; surgery alone vs. chemotherapy vs. radiotherapy + chemotherapy + radiotherapy, etc.)

+ Only R0 vs. R1.