Clin Oral Invest (2004) 8:52–55
DOI 10.1007/s00784-003-0233-4

ORIGINAL ARTICLE

Satoshi Yamaguchi · Hirokazu Nagasawa · Tetsuo Suzuki · Eiji Fujii · Hiroshi Iwaki · Minoru Takagi · Teruo Amagasa

Sarcomas of the oral and maxillofacial region: a review of 32 cases in 25 years

Received: 29 November 2002 / Accepted: 17 September 2003 / Published online: 30 October 2003

Abstract Thirty-two cases of sarcomas involving the oral and maxillofacial region over a period of 25 years were reviewed. The age range was from 5 months to 77 years with a mean age of 42. The male to female ratio was 3:1. The sarcomas were located in the maxilla including the maxillary sinus (*n*=13), mandible (*n*=13), buccal mucosa (*n*=3), temporomandibular fossa (*n*=2), and submandibular region (*n*=1). Histologically sarcomas were classified as osteosarcoma (*n*=9), malignant fibrous histiocytoma (*n*=7), rhabdomyosarcoma (*n*=5), fibrosarcoma (*n*=3), plasmacytoma (*n*=2), leiomyosarcoma (*n*=2), angiosarcoma (*n*=2), liposarcoma (*n*=1), and ameloblastic fibrosarcoma (*n*=1). Surgical resection was performed in 29 cases. Local recurrence was found in 10 patients and metastasis in 11 patients. Metastases included five regional lymph node metastases and eight distant metastases. The survival of patients with local recurrence or metastasis was poor. Surgery is the most reliable treatment for sarcomas of the oral and maxillofacial region. Adequate excision with safety surgical margin as the initial therapy is important for better survival. The value of radiation therapy and/or chemotherapy is uncertain. The 5-year survival rate of primary cases was 61%.

S. Yamaguchi (✉) · H. Nagasawa · T. Suzuki · H. Iwaki · T. Amagasa
Maxillofacial Surgery, Graduate School,
Tokyo Medical and Dental University,
1-5-45 Yushima, Bunkyou-ku, 113-8549 Tokyo, Japan
e-mail: yamachan.mfs@tmd.ac.jp
Tel.: +81-3-58035503
Fax: +81-3-58035500

E. Fujii
Oral and Maxillofacial Surgery,
Kofu Municipal Hospital,
Yamanashi, Japan

M. Takagi
Molecular Pathology, Graduate School,
Tokyo Medical and Dental University,
Tokyo, Japan

Keywords Sarcoma · Oral · Treatment · Recurrence · Metastasis

Introduction

Sarcomas are malignant neoplasms derived from cells of mesenchymal origin. The originating tissue is diverse and includes bone, cartilage, muscular, fibrous, vascular, fatty, and neural tissue. Sarcomas of the head and neck are rare tumors, accounting for 4–10% of all sarcomas [1, 2, 3, 4, 5] and fewer than 1% of neoplasms in this region [3, 6]. Sarcomas of the oral and maxillofacial region are even rarer. Gorsky and Epstein [6] reviewed 11,250 head and neck malignancies, among which there were 139 cases of sarcomas (1.24%), and among these there were only 16 cases (0.14%) of intraoral soft tissue sarcoma [6]. There are some previous reports on sarcomas of the head and neck, but only few reports focus on sarcoma of the oral and maxillofacial region [7, 8, 9]. The number of patients reviewed in these references was 14 over 15 years [7], 25 over 35 years [8], and 10 over 8 years [9]. This demonstrates the rarity of sarcomas in the oral and maxillofacial region. Because of their diversity of the originating tissue and their rarity, there are many open questions about sarcomas of the oral and maxillofacial region in clinical and pathological features, treatment, and prognosis. The present study was carried out to review 32 patients for better understanding of these rare tumors.

Materials and methods

The study included 32 sarcoma patients referred to the 1st Department of Oral and Maxillofacial Surgery at Tokyo Medical and Dental University between 1974 and 1998. Patients' clinical features, modes of treatment, and survival are listed in Table 1. Of the 32 cases 26 were primary and 6 recurrent. This series included 24 males and 8 females. The mean age at first visit was 42 years, with a range from 5 months to 77 years. The primary sites of sarcomas included the maxilla including maxillary sinus (*n*=13, 41%), mandible (*n*=13, 41%), buccal mucosa (*n*=3, 9%), temporomandibular fossa (*n*=2, 6%) and submandibular region (*n*=1, 3%).

Table 1 Clinical data (*Rec* recurrence, *Met* metastasis, *Pr* primary, *Tmf* temporomandibular fossa, *Smr* submandibular region, *S* surgery, *R* radiation therapy, *C* chemotherapy, *UR* primary site of tumor unresectable, *L* regional lymph node metastasis, *D* distant metastasis, *Ao* alive without disease, *Ac* alive with disease, *Dc* died of disease)

Case no.	Diagnosis	Case	Sex	Age (years)	Site	Treatment	Rec	Met	Follow-up	Status
1	Osteosarcoma	Pr	M	25	Tmf	S+R+C	–	–	7 years 1 month	Ao
2	Osteosarcoma	Pr	F	34	Maxilla	S	–	–	9 years 6 months	Ao
3	Osteosarcoma	Pr	F	40	Mandible	S	+	–	6 years 4 months	Ao
4	Osteosarcoma	Pr	M	46	Mandible	S	–	D	5 years	Dc
5	Osteosarcoma	Pr	M	50	Mandible	S	+	D	13 years 7 months	Ac
6	Osteosarcoma	Pr	M	50	Maxilla	S+C	–	–	3 years 2 months	Ao
7	Osteosarcoma	Rec	M	56	Maxillary sinus	S+R+C	+	–	4 years 1 month	Dc
8	Osteosarcoma	Rec	F	63	Maxilla	S+R+C	–	D	3 years 3 months	Dc
9	Osteosarcoma	Rec	M	67	Mandible	S	–	–	9 years 3 months	Ao
10	MFH	Pr	M	29	Maxillary sinus	S+C	+	–	1 year 4 months	Dc
11	MFH	Pr	M	43	Mandible	S	+	L	2 years	Dc
12	MFH	Pr	M	45	Smr	S+R	–	–	8 years 1 month	Ao
13	MFH	Rec	M	48	Mandible	S	–	–	4 years 6 months	Ao
14	MFH	Pr	M	56	Maxilla	S+R+C	–	–	11 years 8 months	Ao
15	MFH	Pr	M	57	Maxillary sinus	S	+	L	9 months	Dc
16	MFH	Pr	M	63	Maxillary sinus	S+R+C	–	–	5 years	Ao
17	Rhabdomyosarcoma	Pr	M	11	Buccal mucosa	S	+	–	17 years 3 months	Ao
18	Rhabdomyosarcoma	Pr	F	27	Buccal mucosa	S+R+C	–	D	1 year 6 months	Dc
19	Rhabdomyosarcoma	Pr	M	55	Maxilla	S+C	–	D	2 years 3 months	Dc
20	Rhabdomyosarcoma	Pr	M	58	Maxilla	C+R	UR	L+D	4 months	Dc
21	Rhabdomyosarcoma	Pr	M	77	Mandible	S	–	–	2 years 9 months	Ao
22	Fibrosarcoma	Pr	F	5m	Mandible	S+C	–	–	9 years 9 months	Ao
23	Fibrosarcoma	Pr	F	10	Mandible	S	–	–	11 years 6 months	Ao
24	Fibrosarcoma	Pr	F	16	Mandible	S	–	–	19 years	Ao
25	Plasmacytoma	Pr	M	53	Mandible	S+R	–	–	14 years	Ao
26	Plasmacytoma	Pr	M	59	Maxillary sinus	S+R	–	–	5 years 1 month	Ao
27	Leiomyosarcoma	Rec	M	25	Maxilla	C+R	UR	L+D	2 months	Dc
28	Leiomyosarcoma	Pr	M	43	Mandible	S	–	D	8 years	Ac
29	Angiosarcoma	Pr	M	34	Tmf	C+R	UR	–	4 years	Dc
30	Angiosarcoma	Pr	M	53	Maxilla	S+R	+	L	8 months	Dc
31	Liposarcoma	Pr	F	33	Buccal mucosa	S	+	–	2 years 10 months	Dc
32	Ameloblastic fibrosarcoma	Rec	M	31	Mandible	S	+	–	5 months	Dc

The most common histological type was osteosarcoma (n=9; 28%), followed by malignant fibrous histiocytoma (MFH;(n=7, 22%), rhabdomyosarcoma (n=5, 16%), fibrosarcoma (n=3, 9%), plasmacytoma (n=2, 6%), leiomyosarcoma (n=2, 6%), angiosarcoma (n=2, 6%), and liposarcoma (n=1, 3%), ameloblastic fibrosarcoma (n=1, 3%). The histological subtypes of osteosarcoma were chondroblastic (n=5; Table 1, nos. 1, 2, 6, 8, 9), osteoblastic (n=3, nos. 3, 4, 7), and telangiectatic (n=1, no. 5). In rhabdomyosarcoma, the histological subtypes were alveolar (n=3, nos. 17, 18, 20) and pleomorphic (n=2, nos. 19, 21). Patients with malignant lymphoma were excluded from this study because malignant lymphoma is a systemic disease. Two cases of plasmacytoma were both of the solitary type, therefore these cases were included.

Surgical resection (S) alone was carried out in 15 patients. Triple modality of S, radiation therapy (R) and chemotherapy (C) was performed in 6, combined therapy of S/C in 4, and S/R was in 4. We judged that the primary tumors were unresectable in three cases; therefore combined therapy of R and C was given to these 3 patients. Radiation therapy was given preoperatively in 6 cases, postoperatively in 3 and both in 1. The doses used varied from 18 to 80 Gy, with an average of 48 Gy. All radiation therapy was external irradiation. The fraction sizes were 2.5 Gy, treating 4 days in a week. Chemotherapy was given preoperatively in 8 cases and postoperatively in 2. The chemotherapy regimens were varied.

Treatment was determined according to the experience of the surgeon. This resulted in a lack of unity in the treatment protocol. The common agents were cisplatin (n=5), 5-fluorouracil (n=4), and doxorubicin (n=4). The regional intra-arterial infusion chemotherapy administered via the superficial temporal artery was given in 9 of 11 patients who had sarcoma of the maxilla, maxillary sinus, or the temporomandibular fossa. The survival rate and survival curve were calculated by the Kaplan-Meier method using SPSS for Windows, version 10.

Results

Fourteen patients of 32 were making satisfactory progress without local recurrence or metastasis at a mean follow-up period of 8.5 years, ranging from 2 years 3 months to 19 years. Local recurrence was found in 10 cases (31%) and metastasis in 11 (34%). Among 10 patients with local recurrence, 3 are alive after 6–17 years, and 7 died of their tumors after 5 months to 4 years. Among the 3 patients alive, one (no. 3) was treated by surgery and the other (no. 17) by surgery and postoperative radiation therapy (50 Gy) after local recurrence was found. These two patients are alive without evidence of disease over 3 years and 7 years after salvage treatment. Another patient (no. 5) was treated by preoperative radiation therapy (45 Gy) and surgery for local recurrence. The local recurrence was controlled, but this patient developed distant metastasis to the lung.

The 5-year survival rate of patient with local recurrence was 30% (Fig. 1). Among 11 patients with metastases 9 died

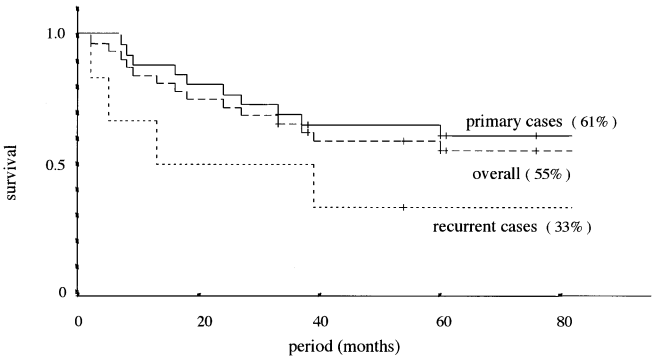

Fig. 1 Survival rate of patients with sarcomas in the oral and maxillofacial region (n=32) using the Kaplan-Meier method

of tumors, and 2 (nos. 5, 28) are alive with tumor. The 5-year survival rate of the patient with metastases was 18%.

Five out of 9 patients with osteosarcoma developed local recurrence and/or metastasis. The patients with MFH developed local recurrence frequently (3/7, 43%). In neither of the patients with angiosarcoma could the primary site of tumor be controlled. Metastases occurred frequently in patients with rhabdomyosarcoma (3/5), and leiomyosarcoma (2/2). All metastases in patients with osteosarcoma were distant, but in patients with MFH only regional lymph node metastases occurred. The patients with rhabdomyosarcoma or leiomyosarcoma showed both types of metastases, but distant metastases (5/7) were predominant.

The number of cases of maxillary including the maxillary sinus equaled that of mandible, but survival after 5 years for maxillary cases (36%) was clearly lower than that in the mandible (75%), even though 2 patients alive with mandibular sarcoma live with their tumors. In 6 out of 13 patients (46 %) with maxillary sarcoma, the primary site of tumor was not controlled, and 6 patients (46 %) with maxillary sarcoma developed metastases. Local recurrence was less common in patients with adjuvant therapy (radiation therapy and/or chemotherapy) than in patients treated by surgery alone, but the overall survival rate in patients with adjuvant therapy (56%) was lower than that in patients treated by surgery alone (65%). There was no clear difference in the rate of metastases between patients with adjuvant therapy and patients treated by surgery alone. The overall 5-year cumulative survival rate was 55%. The 5-year cumulative survival rates of primary cases and recurrent cases were 61% and 33%, respectively.

Discussion

Sarcomas are rare disease, and therefore it is difficult to establish a standard treatment. We can be fairly certain, however, that surgical resection is the best treatment for sarcomas of the oral and maxillofacial region. Wide resection with clear margins is very important for a favorable survival. We should ascertain that the resection margins are tumor free in frozen section taken during operation. Important advances in reconstructive surgery have recently been made, and these advances enable wide resections. However, the oral and maxillofacial regions include complex and vital structures, and therefore wide resection is difficult at some sites, especially at the maxilla. This may be one of the reasons why the prognosis of maxillary sarcoma was poor in our series.

The effect of radiation therapy or chemotherapy on sarcomas is debatable. Eeles et al. [10] showed that combined therapy of surgery and radiotherapy achieves longer local recurrence-free survival, but not in overall survival. Wanebo et al. [11] reported that patients who received adjuvant therapy had lower survival rates than those who did not. These results were similar to our own and may reflect the advanced nature of the disease treated by surgery and adjuvant therapy. In our series there were two cases in which chemotherapy was obviously effective: in a 5-month-old girl with fibrosarcoma (no. 22) receiving preoperative chemotherapy with vincristine, actinomycin D, and cyclophosphamide, and in a 50-year-old man with osteosarcoma (no. 6) receiving combined chemotherapy with methotrexate, bleomycin, cyclophosphamide, and actinomycin D. Combined therapy of irradiation (35 Gy) and chemotherapy (5-fluorouracil, 3000 mg) given preoperatively to the patient with MFH (no. 16) showed good results. Also, preoperative radiotherapy (45 Gy) to the patient with plasmacytoma (no. 26) had sufficient effects.

Outcome of treatment according to tumor type showed that patients with fibrosarcoma and plasmacytoma had good survival, but survival in patients with rhabdomyosarcoma, angiosarcoma, and liposarcoma was poor. Patients with osteosarcoma, rhabdomyosarcoma, and leiomyosarcoma had distant metastases at a relatively high rate (8/16, 50%) in our series, which seems to influence the survival of these patients (Table 2). The relationship of survival according to age showed that 5-year survival was 100% in patients under the age of 19 years (Table 2). Other reports have also shown that younger patients have better survival [8, 10]. One of the reasons for this is that young patients respond better to radiation therapy or chemotherapy. However, it must be noted that children treated for soft tissue sarcomas of the head and neck with combined therapy showed late treatment-related effects on dentition, vision, hearing, growth, and cosmetic appearance [12, 13]. Rao et al. [14] suggested that surgery alone is a sufficient initial therapy for patients in whom complete resection is achieved. Our data also show that the prognosis of patients under 19 years of age treated by surgery alone is good, and therefore we also recommend surgery alone as the initial treatment for young patients, if the tumor is resectable.

Survival in patients with local recurrence was poor. Therefore complete resection of the tumor by surgery as the initial therapy is very important to achieve a favorable prognosis. When local recurrence occurs, surgical resection should be carried out if the recurrent tumor is resectable. Survival was also poor in patients with metastasis (Table 3). The control of metastatic tumors is very difficult. The metastasis is related to tumor size, surgical margins, presence of tumor necrosis, and the adequacy of excision [5]. Complete resection by initial

Table 2 Outcome of treatment according to histological type, age, site, and modality (*Tmf* temporomandibular fossa, *Smr* submandibular region, *S* surgery, *R* radiation therapy, *C* chemotherapy)

	n	Recurrence	Metastasis	5-year survival rate (%)
Histological type				
Osteosarcoma	9	3	3	63
MFH	7	3	2	57
Rhabdomyosarcoma	5	1 (1)[a]	3	40
Fibrosarcoma	3	0	0	100
Plasmacytoma	2	0	0	100
Leiomyosarcoma	2	0 (1)[a]	2	50
Angiosarcoma	2	1 (1)[a]	1	0
Liposarcoma	1	1	0	0
Ameloblastic fibrosarcoma	1	1	0	0
Age (years)				
0–19	4	1	0	100
20–29	4	1 (1)[a]	2	25
30–39	4	2 (1)[a]	0	25
40–49	6	2	3	63
50–59	10	4 (1)[a]	5	48
60–79	4	0	1	67
Site				
Maxilla[b]	13	4 (2)[a]	6	36
Mandible	13	4	4	75
Buccal	3	2	1	33
Tmf	2	0 (1)[a]	0	50
Smr	1	0	0	100
Modality				
S	15	7	5	65
S+ R+C	6	1	2	50
S+C	4	1	1	50
S+R	4	1	1	75
S+(R and/or C)	14	3	4	56
R+C	3	0 (3)[a]	2	0

[a] Tumor was unresectable
[b] Includes maxillary sinus

Table 3 Outcome in patients with recurrence or metastasis

	n	Alive	Dead	5-year survival rate (%)
Recurrence	10	3	7	30
Metastasis	11	2	9	18

surgery is also important in this respect. Sarcomas in the oral and maxillofacial region are rare diseases, and the number of cases is limited at single institutions. Therefore there is a need for joint studies at multiple institutions.

References

1. Yang JC, Glatstein EJ, Rosenberg SA, Antman KH (1993) Sarcoma of soft tissue. In: DeVita VT Jr, Helleman S, Rosenburg SA (eds) Cancer, principles and practice of oncology, 4th edn. Lippincott, Philadelphia, pp 1436–1508
2. Tsujimoto M, Aozasa K, Ueda T, Sakurai M, Ishiguro S, Kurata A, Ono K, Matsumoto K (1998) Soft tissue sarcomas in Osaka, Japan (1962–1985), review of 290 cases. Jpn J Clin Oncol 18:231–234
3. Figueiredo MTA, Marques LA, Campos-Filho N (1988) Soft-tissue sarcomas of the head and neck in adults and children: experience at a single institution with a review of literature. Int J Cancer 41:198–200
4. Torosian MH, Friedrich C, Godbold J, Hajds SI, Brenna MF (1988) Soft-tissue sarcomas, initial characteristics and prognostic factors in patients with and without metastatic disease. Semin Surg Oncol 4:13–19
5. Mandard AM, Petiot JF, Marnay J, Mandard JC, Chasle J, Ranień E, Dupin P, Herlin P, Ranień J, Tanguy A, Boulier N, Abbatucci JS (1989) Prognostic factors in soft tissue sarcomas. Cancer 63:1437–1451
6. Gorsky M, Epstein JB (1998) Head and neck and intra-oral soft tissue sarcomas. Oral Oncology 34:292–296
7. Sanroman JF, Hoyo JRA, Diaz FJ, Gil-Diez L, Monje F, Naval L, Alamillos FJ, Rubio ADP (1992) Sarcomas of the head and neck. Br J Oral Maxillofac Surg 30:115–118
8. Nagler RM, Malkin L, Ben-Arieh Y, Laufer D (2000) Sarcoma of the maxillofacial region, follow-up of 25 cases. Anticancer Res 20:3735–3742
9. Pandey M, Thomas G, Mathew A, Abraham EK, Somanathan T, Ramadas K, type EM, Ahamed IM, Sebastain P, Nair MK (2000) Sarcoma of the oral and maxillofacial soft tissue in adults. Eur J Surg Oncol 26:145–148
10. Eeles RA, Fisher C, A' Hern RP, Robinson M, Rhys-Evans P, Henk JM, Archer D, Harmer CL (1993) Head and neck sarcomas, prognostic factors and implications for treatment. Br J Cancer 68:201–207
11. Wanebo HJ, Koness JR, MacFarlane JK, Eliber FR, Byers RM, Elias EG, Spiro RH (1992) Head and neck sarcoma, report of the head and neck sarcoma registry. Head Neck 14:1–7
12. Freedman AM, Reiman HM, Woods JE (1989) Soft-tissue sarcomas of the head and neck. Am J Surg 158:367–372
13. Fromm M, Littman P, Raney RB, Nelson L, Handler S, Diamond G, Stanley C (1986) Late effect after treatment of twenty children with soft-tissue sarcomas of the head and neck. Cancer 57:2070–2076
14. Rao BN, Santana VM, Fleming ID, Pratt CB, Shapiro D, Fontanesi J, Kumar APM, Austin BA (1989) Management and prognosis of head and neck sarcomas. Am J Surg 158:373–377