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Surgery with curative intent is associated with prolonged survival in patients with cutaneous angiosarcoma of the scalp and face -a retrospective study of 38 untreated cases in the Japanese population☆

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ABSTRACT

Background: In patients with cutaneous angiosarcoma of the scalp and face, the validity of surgery remains controversial, because of the potentially diffuse nature of involvement and difficulty in obtaining negative margins.
Objective: To evaluate the survival benefit of surgery as a primary treatment.
Patients and methods: Fifty-one patients with primary cutaneous angiosarcoma of the scalp and face presenting with locoregional involvement were referred to National Cancer Center Hospital, Tokyo, Japan, between May 1982 and March 2013. Data of those patients in whom the diagnosis had been confirmed histologically and the primary treatments had been initiated at our center were analysed retrospectively. Only untreated cases were selected with aim to evaluate actual survival benefit of surgery as a primary treatment.
Results: Of the 51 patients, 38 were found to be eligible for inclusion in this analysis; of these 38 patients, 29 (29/38 = 76.3%) patients had tumour diameter > 5 cm, and 29 underwent surgery with curative intent (curative-intent surgery) as the initial treatment. Histologically positive margins were found in 10 patients. Multivariate analysis identified curative-intent surgery as being significantly associated with improved overall survival (OS; HR = 0.26; 95% CI, 0.10–0.63). In the Surgery group, neither negative margins nor combined-modality treatment had any significant influence on the OS.
Conclusion: Removal of primary tumour with curative-intent surgery may be a valid treatment option even for patients with primary cutaneous angiosarcoma of the scalp and face larger than 5 cm in size, regardless of the histological surgical margin status.

Introduction

Angiosarcoma is one of the rarest forms of sarcoma, that originates from the vascular endothelial cells and accounts for 1%–2% of all soft-tissue and visceral sarcomas [1–3]. Angiosarcomas can be divided into several clinical entities, such as cutaneous angiosarcoma not associated with lymphedema (primary cutaneous angiosarcoma), cutaneous angiosarcoma associated with lymphedema, radiation-induced angiosarcoma, angiosarcoma of the deep soft tissue, and angiosarcoma of the parenchymal organs. Primary cutaneous angiosarcoma is the most common, accounting for about 28% of all cases, and is typically located in the head and neck, particularly the scalp and upper forehead [4].

Cutaneous angiosarcoma of the head and neck region carries a poor prognosis, with the reported 5-year survival rate in the range of 11%–53% [1,2,4–9]. Because of the rarity of this disease, the optimal management strategy has not yet been established.

☆ This work is attributed to the Department of Dermatologic Oncology, National Cancer Center Hospital, Tokyo, Japan.

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Especially, the survival benefit of surgery remains controversial because of the difficulty in accurately determining the extent of the lesion and obtaining negative margins [10]. Several researchers have argued that radical surgery with adjuvant radiation therapy (RT) is the optimal local treatment strategy [5,7,10–14]. Some authors have asserted that the high propensity for distant metastasis and dismal prognosis of this disease warrant only limited surgical procedures [15]. Some investigators have suggested that RT plus chemotherapy (without surgical resection) might provide sufficient local control [1,16,17] and even greater survival prolongation than surgery-based therapy [18].

A meta-analysis revealed some predisposing factors for poor prognosis and effective treatments [9]. In this meta-analysis, surgery was reported to be the most effective treatment for increasing the 5-year survival rate compared with RT or chemotherapy. This positive impact of surgery on survival warrants further discussion because this meta-analysis was based on 11 retrospective studies of small-scale.

Because of the rarity of this disease, optimal management is difficult to establish by a prospective study in the future. Hence it is valuable to further explore the efficacy of surgery with an additional single institutional retrospective analysis in a different patient population. We conducted the current analysis to retrospectively assess the survival benefit of surgery performed as a primary treatment in Japanese patients with primary cutaneous angiosarcoma of the scalp and face presenting with locoregional involvement.

Methods

Study design

We retrospectively reviewed clinical records of patients with primary cutaneous angisarcoma of the scalp and face who were referred to the National Cancer Center Hospital, Tokyo, Japan between May 1982 and March 2013. From this list of patients, we extracted those in whom the diagnosis had been established histologically and the primary treatments had been initiated at our center. Only untreated cases were selected with aim to evaluate actual survival benefit of surgery as a primary treatment. Data pertaining to the patient characteristics, treatments administered and treatment outcomes were collected from the medical records of the patients. Patients with secondary angiosarcomas (associated with lymphedema or irradiation) were excluded from this analysis. Patients with distant metastasis at presentation were also excluded, although those with regional lymph node metastasis were included as cases with locoregional disease. Every individual had undergone a full evaluation by history, physical examination, baseline imagings and laboratory tests prior to the treatment. All the surgical procedures and RT were undertaken at our center. Treatment planning was left to the discretion of the treating physicians, based on the general condition of the patient and the extent of the disease. Combined-modality therapy was defined as any two or three combination of surgery, radiation and chemotherapy. Surgical procedure was considered as curative-intent surgery when tumour was resected with clinically sufficient margins based on preoperative assessment. We did not depend on intraoperative frozen section because reliability of intraoperative frozen section is doubtful especially in highly differentiated lesion. The negative predictive value of intraoperative frozen section was reported to be only 33.3% by Pawlik et al. [10].

Statistical analysis

The Kaplan-Meier method was used to estimate the overall survival, and the log-rank test was used to compare the overall survival between two groups. The Cox proportional-hazards model was used for the multivariate analysis and estimation of the hazard ratio. Considering sample size, three independent factors that appeared to have a significant impact on survival according to the univariate analysis and had been already known as prognostic factors were entered into a Cox proportional hazards model to test for significant effects, simultaneously adjusting for confounding factors.

P values of ≤0.05 (two-sided) were considered to denote statistical significance. All statistical analyses were performed using the EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan) [19], which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient characteristics and treatments

Of the 51 patients with primary cutaneous angiosarcoma of the scalp and face referred to our institute, 38 were found to be eligible for inclusion in this study (Table 1). The remaining 13 were excluded from the study for the following reasons: received initial treatment at other institutes (n = 8), detected to have distant metastasis at presentation (n = 3), and received only recombinant interleukin (rIL)-2 immunotherapy as the initial treatment (n = 2). The 38 patients included in this study comprised 26 males and 12 females (male: female = 2.2:1), with a median age of 73.0 years old (range, 45–93 years). All the patients were Japanese. The tumour diameter was less than and equal to 5 cm in 9 patients and >5 cm in 29 patients. Twenty-six patients had multifocal disease, and 8 patients had regional lymph node metastasis (Table 1).

Surgical resection with curative intent was performed as the initial treatment in 29 of the 38 patients (76.3%; Surgery group). The surgery was performed with curative intent in all the patients, although histological margins were positive in 10 patients (7 patients had a positive deep margin, 1 had a positive lateral margin,

Table 1
Baseline characteristics of patients.

	Surgery (n = 29)	No-surgery (n = 9)	P value
	No. of patients (%)	No. of patients (%)	
Age (yr)			
Median (range)	73 (45–87)	73 (45–93)	
<70	10 (34.5)	3 (33.3)	1
≥70	19 (65.5)	6 (66.7)	
Gender			
Male	19 (65.5)	7 (77.8)	0.689
Female	10 (34.5)	2 (22.2)	
Performance status			
0-1	27 (93.1)	7 (77.8)	0.233
≥2	2 (6.9)	2 (22.2)	
Tumour Size			
≦5 cm	9 (31.0)	0 (0.0)	0.082
>5 cm	20 (69.0)	9 (100)	
Multifocal lesion			
No	11 (37.9)	1 (11.1)	0.223
Yes	18 (62.1)	8 (88.9)	
Nodal Disease			
No	26 (89.7)	4 (44.4)	**0.01**
Yes	3 (10.3)	5 (55.6)	
Chemotherapy			
No	21 (72.4)	5 (55.6)	0.423
Yes	8 (27.6)	4 (44.4)	
Radiation therapy			
No	6 (20.7)	3 (33.3)	0.655
Yes	23 (79.3)	6 (66.7)	

P-values of ≤0.05 were considered as statistically significant and highlighted in bold type.

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