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Anterolateral thigh free flaps for the reconstruction of scalp angiosarcoma – 18-year experience in Chang Gung memorial hospital

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KEYWORDS
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Angiosarcoma;
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Cortical curettage

Summary *Background:* Scalp angiosarcoma is a rare and highly aggressive cutaneous malignancy with poor prognosis and high recurrence rate. Multimodality approach is currently the treatment protocol for resectable angiosarcoma, including wide local excision and postoperative radiation. This single-institution study reviews the 18-year experience of the surgical treatment of scalp angiosarcomas.
Methods: A retrospective chart review was performed on patients with scalp angiosarcoma who received wide local excision and free flap reconstruction from 2001 to 2018. The type of free flap, safety margin, outer cortex burring, and dose for radiation were recorded. Kaplan-Meier plots were computed.

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Results: Eight male patients (mean age of 74.4 years old) were enrolled in the series. Tumor sizes ranged from 3×3 to 8×13 cm. All patients underwent wide local excision and outer cortex burring (cortical curettage). Seven (87.5%) scalp defects were reconstructed with anterolateral thigh free flap. All patients received adjuvant radiation therapy for tumor bed and margins. Chemotherapy was adopted for the management of local recurrence (37.5%) or distant metastasis (37.5%). The 2-year and 5-year survival rates are 72.9% and 38.9%, respectively, and 1-year and 2-year disease-free rates are 37.5% each.
Conclusion: Scalp angiosarcoma is a rare and highly aggressive cutaneous malignancy with poor prognosis. Anterolateral thigh free flap is a good reconstructive option due to its ability to cover large cutaneous defects with minimal need for skin grafting. Multimodal treatment protocol, including wide local excision with cortical curettage, and adjuvant radiation (regular basis) and chemotherapy (local recurrence or distant metastasis) may offer improved 1-year survival rate (100%).

Introduction

Angiosarcoma is a rare disease accounting for 1%–2% of soft-tissue sarcoma.[1-3] It is an aggressive malignant tumor that arises from vascular endothelial cells.[4] Although most angiosarcomas arise spontaneously, there are reports suggesting areas of chronic lymphedema or previous radiotherapy leading to the development of these tumors.[1,5] Angiosarcoma can arise from any soft tissue, with the cutaneous form typically involving the head and neck region, particularly the scalp[6,7].

Scalp angiosarcoma is more commonly found in the elderly, with higher incidence in men than women.[8] The location of scalp angiosarcoma in the hair-bearing area typically delays diagnosis due to late detection of the lesion. The clinical presentation may also vary, some manifesting as pink or blue papules, whereas others appear as a bruise with or without nodular elevation or ulceration.[9]

The treatment is challenging, with poor prognosis. Scalp angiosarcoma carries a 5-year survival rate of only 10%–15%.[6] It has a high local recurrence rate, with a tendency for early hematogenous metastasis to the lungs.[3,6,10] Despite recent adoption of aggressive treatment protocol for scalp angiosarcoma, the prognosis remains poor.

The treatment protocol for scalp angiosarcoma has yet to reach a consensus in the oncology circle. Wide local excision combined with postoperative radiotherapy is widely considered as the optimal treatment to date.[1,11,12] Taxane-based chemotherapy is used as palliative therapy in cases of metastatic tumors.[1,10,13] Choi et al. reported reconstruction following wide local excision of scalp angiosarcoma using free latissimus dorsi flap and split-thickness skin graft.[14]

This single-institution study reviews the 18-year surgical experience in managing resectable scalp angiosarcomas by using the institutional protocol, including wide local excision, outer cortex burring, anterolateral thigh (ALT) flap reconstruction, and adjuvant therapy.

Patients and methods

An Institutional Review Board–approved retrospective review was performed on patients with histologically confirmed scalp angiosarcoma who underwent wide local excision and free flap reconstruction at Chang Gung Memorial Hospital, between January 2001 and December 2018. Patients with angiosarcoma located at sites other than the scalp were excluded from the study. This study was conducted in accordance with cohort study guidelines outlined in the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.

Surgical treatment

Under general anesthesia, all scalp tumors were treated by wide local excision, with resection margin of 4–5 cm. For tumor clearance of the deep margin, the underlying periosteum was resected, and the outer cortex of the calvarium was superficially burred (cortical curettage), even though there was no clinical or radiographic evidence of bony invasion. The scalp defects were reconstructed preferentially with ALT flap. The donor site was primarily closed as long as the size of the harvested flap was smaller than 22×8 cm. If the donor site could not be primarily closed, the defect was approximated by shoelace procedure, a dermatotraction-based technique, instead of using skin graft technique.

Data analysis

Demographic (age, gender, and comorbidity status), clinical (prior surgical interventions, skull involvement, and neoadjuvant therapy), therapeutic (type of resection and reconstruction, complications, and adjuvant therapy), and outcome (local recurrence, distant metastasis, and survival time) data were extracted from the medical records.

Local recurrence was defined as new tumor growth located within 2 cm of the primary tumor excision site. Distant metastasis was defined as tumor spread to distant organs (lung, bone, brain, breast, etc.) detected by computed tomography (CT) scan, posirton emission tomography (PET) scan, or bone scan. Local recurrence, distant metastasis, and survival time were calculated starting from the time of wide local resection and flap reconstruction in our center. Kaplan-Meier survival plots were computed.

Results

Eight Taiwanese male patients (74.4 years on average) with scalp angiosarcoma were included (Table 1). Gross tumor

Table 1 Characteristics of patients with angiosarcoma receiving wide excision and free flaps.

No	Age/ Sex	Area	Stage	Comorbidity	Size (cm2)	Prior surgery to free flap	Skull involved	Local recurrence*	Distant metastasis*	Other Treatment	RT dosage (Gy/fx)	Survival time (mo)
1	86/M	Scalp	T2aN0M0 Stage3	HTN, DM	7 × 6	Biopsy	None	NE	Lung, 15 mo	RT, CT	60/30	24 mo
2	68/M	Scalp	T2N0M0 Stage3	HTN, DM	8 × 6	Local excision**	None	NE	Lung, 1.5 mo	RT, CT	42/21 52/26 (1 year after op)	26 mo
3	70/M	Scalp	T1N1M0 Stage3	None	3 × 3	Biopsy	None	3 mo (resection margin)	Lung, 6mo	RT, CT	62/31(tumor bed and margin) + 46/23(neck)	13 mo
4	77/M	Scalp	T2N0M0 Stage2b	HTN	6 × 5.5	Wide excision and STSG**	None	NE	NE	RT	66/33(tumor bed and margin)+46/23(neck)	NE(>27mo)
5	60/M	Scalp	pT1aN0M0 Stage2a	None	4 × 2	Wound de-bridement**	None	2.5 mo (resection margin)	NE	RT, CT	60/30(tumor bed) + 6/3(neck)	15 mo
6	82/M	Scalp	T2aN0M0 Stage3	DM, HTN, CAD	6 × 5	Local excision**	None	NE	NE	RT	60/30	NE (> 12mo)
7	72/M	Scalp	T1N0M0 Stage 2a	HTN	4 × 3.5	Biopsy	None	3 mo (resection margin)	NE	RT, CT	60/30	86 mo
8	80/M	scalp	T3N0M0	HTN	8 × 13	nil	None	NE	NE	Neoadjuvent RT	60/20	NE(> 15mo)

Abbreviation: RT, Radiotherapy; CT, Chemotherapy; DM, Diabetes Mellitus; HTN, Hypertension; CAD, cardiovascular disease; NE, No event; Mo, Months.

* After surgical excision and free flap reconstruction.

** Performed elsewhere.

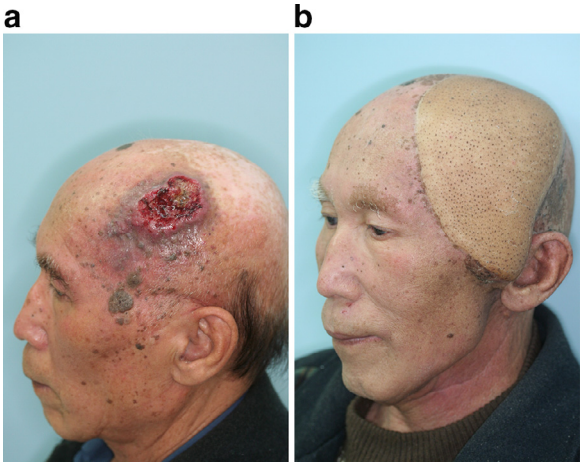

Figure 1 (a) A 70-year-old male patient presented with 1-year history of an ulcerative nodule on his left scalp (patient no. 3, Table 1). A 3 cm angiosarcoma was diagnosed, with left-sided parotid lymph node metastasis and without another systemic metastasis. After a shared decision making between patient, his family, and clinicians, (b) he underwent a wide surgical excision (4 cm resection margin plus cortical curettage) associated with left total parotidectomy with supraomohyoid neck dissection. Instead of ALT flap, tensor fascia lata perforator flap was used due to intraoperative finding of vascular pedicle variant. Postoperative pathology showed deep margin clearance of <1 cm. He received postoperative radiotherapy (62 Gy). He developed left face and lung metastasis within 6 months, and paclitaxel was initiated. He survived for 13 months after surgery.

size ranged from 3×3 cm to 13×8 cm. The cancer staging ranged from stage 2a to stage 4. All patients underwent preoperative imaging, including head and neck MRI or whole-body CT scan, PET scan, or bone scan, which showed no calvarial bony involvement. One (12.5%) patient had parotid lymph node metastasis and without other systemic metastasis at presentation (Figure 1). One (12.5%) patient presented with a recurrent scalp tumor after treatment performed elsewhere (Figure 2). One (12.5%) patient underwent neoadjuvant radiotherapy, with reduction in tumor size from 10×15 cm to 8×13 cm (Fig. 3). No neoadjuvant chemotherapy was performed.

All patients were surgically treated by wide excision (margin of 4–5 cm plus bone curettage) **(Electronic Supplementary Material 1)**. Negative surgical margins were achieved in all patients. Seven (87.5%) defects were covered with free tissue transfer using ALT flap with sizes ranging from 12×15 cm to 20×25 cm. One (12.5%) defect was reconstructed using tensor fascia lata perforator flap due to vascular pedicle variation (Figure 1). All vascular anastomoses were performed utilizing the ipsilateral superficial temporal artery and its concomitant vein, with no requirement for vein graft. Two (25%) patients presented with flap-related complications (venous congestion). Reoperation was performed in two (25%) patients; one of them underwent local flap transferring, and the other one underwent another ALT flap transferring.

Adjuvant radiotherapy was performed in all cases. The median postoperative follow-up time was 86 months. Three

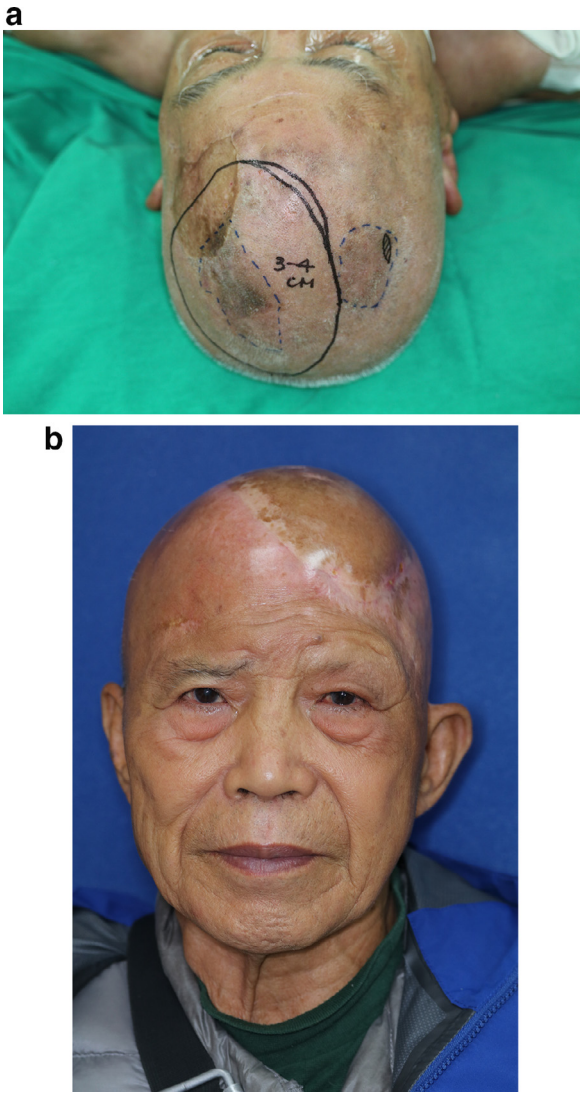

Figure 2 (a) A 77-year-old man presented with a recurrent left frontal scalp angiosarcoma after wide excision and split-thickness skin graft reconstruction performed at a local hospital (patient no. 4, Table 1). The recurrent tumor measured 6 cm in maximal diameter. (b) The defect created by the wide local excision (4 cm resection margin plus cortical curettage) was resurfaced by ALT flap. He received postoperative radiation (66 Gy). He is currently disease free at 27 months postoperatively.

(37.5%) patients developed local recurrence (ranging from 2 to 3 months). Three (37.5%) patients had distant metastasis (ranging from 1.5 to 15 months) (Table 1). Chemotherapy (taxanes such as paclitaxel or docetaxel) was used for the management of these local recurrences and distant metastasis. The median survival time after surgery was 19 months (ranging from 12 to 86 months). The Kaplan-Meier survival plots were shown in Figure 4.

Discussion

Scalp angiosarcoma is an aggressive disease with poor prognosis, and the survival rate remains unsatisfactory.

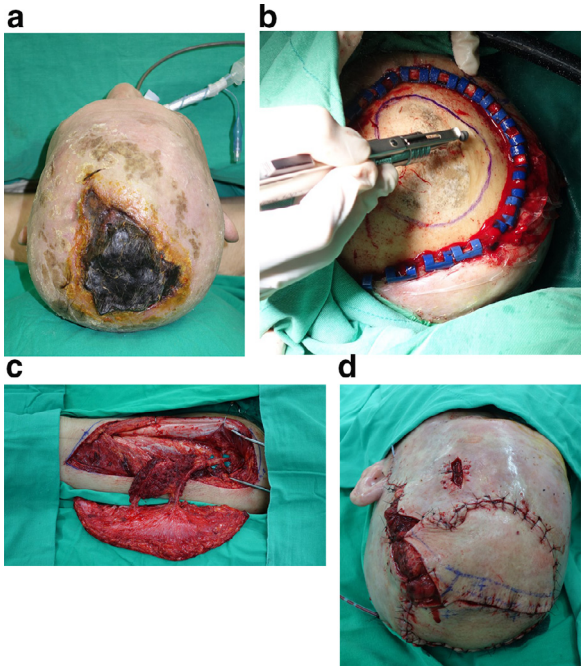

Figure 3 (a) An 80-year-old man presented with a chronic ulcerating scalp wound for 3 months (patient no. 8, Table 1). He was diagnosed with angiosarcoma (maximal diameter 13 cm) without bony invasion and distant metastasis. He received neoadjuvant radiation to reduce the tumor size, (b) followed by a wide local excision (4 cm resection margin plus cortical curettage). (c) The defect was reconstructed using a split ALT flap of 2 skin paddles based on two perforators of descending branch of lateral femoral circumflex artery. (d) Two skin paddles based on one pedicle for scalp reconstruction. He received postoperative radiation (60 Gy). He is currently disease free at 15 months postoperatively.

The treatment options for scalp angiosarcoma discussed in the literature included surgical resection and radiotherapy for local treatment, and chemotherapy for metastatic tumors.[1] Surgical excision with wide margins, followed by radiotherapy, is currently the most popular approach for treating primary scalp angiosarcoma.[7,15] However, the appropriate surgical resection margin remains controversial. Lim et al. reported they performed radical tumor resection or the scalp with a minimum of 5-cm resection margins, combined with burring of the outer cortex of the cranium, ipsilateral superficial parotidectomy, and ipsilateral upper neck dissection.[16] In contrast, Buschmann et al. advocated for a simple wide local excision, including the outer cortex and covering the defect by a split-thickness skin graft,[17] which reduces the tumor load, preserve quality of life, and minimize hospital stay. However, Dickinson et al. reported 279 patients with soft tissue sarcoma without analyzing the metastatic disease and revealed statistically significant evidence that increasing the width of resection improves local control and overall survival.[18] Nurkin concluded that relationship between margin status, local regional recurrence, and survival seems to be correlated as opposed to causation in his study of soft-tissue sarcoma.[19] At our institution, we performed wide surgical excision, but without routine superficial parotidectomy or ipsilateral upper neck dissection. We also advocate adjuvant radiation with 60 Gy RT dose, which had previously been reported to significantly lower local recurrence rate.[10]

As previously described by other group treating two patients with scalp angiosarcoma and concomitant parotid lymph node metastases,[16] we adopted our regular indication therapeutic criteria for the patient who presented with symptomatic scalp angiosarcoma (bleeding and foul smell) and parotid lymph node metastasis but without other systemic metastasis. Furthermore, the final therapeutic choice was based on a shared decision-making process between the patient, family members, and our team. This resulted in a combined therapy (wide surgical excision, microvascular-based reconstruction, and adjuvant radiotherapy) instead of adopting only radiotherapy, chemotherapy, or resection with skin grafting reconstruction.

Multiple series involving the treatment of scalp angiosarcoma have demonstrated improved local control, disease-specific survival, and overall survival in patients treated with combined-modality therapy, which included both surgical resection and radiation compared to those treated with surgery alone or radiation alone.[11,12,20] In terms of radiation dose, several studies recommended 60 Gy in 30 fractions for the treatment of a primary tumor postoperatively.[6,10,12] Higher doses (70 Gy) in 30 fractions was recommend as the only treatment for those who could not tolerate surgery due to poor health status.[10]

Chemotherapy was the primary treatment option for distant metastases, although evidences are limited. Several studies have suggested higher efficacy of taxane-based chemotherapy in the treatment of cutaneous angiosarcoma in the head and neck region.[1,21,22] Paclitaxel has been recommended as the first-line treatment as paclitaxel has been evaluated in different phase-2 studies.[23,24] Moreover, docetaxel still has a role as a second-line therapy in patients refractory to paclitaxel.[25,26] However, in cases without distant metastasis, there was no clear benefit of neoadjuvant or adjuvant chemotherapy use, when combined with wide local excision and postoperative radiation.[26] Shin mentioned that several studies have found postoperative radiation and chemotherapy to be effective in patients with metastasis.[3] Thus, we used chemotherapy when local recurrence or distant metastasis is detected.

Owing to the aggressive nature of scalp angiosarcoma, wide local excision leads to a large defect with exposed bone. This makes microsurgical free tissue transfer play an important reconstructive role[27] (Table 2). Previous studies have recommended latissimus dorsiflap, ALT flap, and radial forearm flap as the three main reconstructive options for large scalp defects.[27,28] Latissimus dorsi flap was the most commonly used flap in scalp defect reconstruction because of its large size, but ALT flap is becoming increasingly popular due to its low donor site morbidity, versatile design, and ease of harvest.[29] Radial forearm flap has the main drawback of limited flap size available on the donor site. In Lin's series, the use of customized free ALT flaps achieved functionally and cosmetically superior results in scalp reconstruction, especially with bone exposure.[30,31] Similarly, Philandrianos et al. investigated the functional donor-site outcome and esthetic outcomes (both donor and recipient sites) and concluded that reconstruction using ALT flap was

Table 2 Review of literatures of free flap reconstruction for scalp angiosarcoma.

	Age/ Sex	Etiology	Free flap	Safety margin	Defect (cm^2)	Recipient artery	Donor site repair	Other treatment	Complication	Survival time (mo)
Choi et al., 2015	52 M	Angiosarcoma	LD,STSG	1 cm, G	NR	STA	NR	-	RC,MT	85
	70 M		LD,STSG	2 cm, B				RT	RC,MT	30
	61 M		LD,STSG	3 cm, P				-	RC,MT	23
	64 F		LD,STSG	2 cm, P				NR	RC	FL
	76 M		LD,STSG	5 cm, B				-	MT	48
	71 M		LD,STSG	5 cm, P				RT	RC,MT	NE
	70 M		LD,STSG	5 cm, B				-	RC,MT	37
	75 M		LD,STSG	NR, B				-	RC	FL
	64 M		LD,STSG	3 cm, B				RT	RC,MT	32
	81 M		Local flap	1 cm, G				-	RC,MT	12
	58 M		LD,STSG	2 cm, P				RT	RC,MT	NE
	75 M		LD,STSG	3 cm, P				RT	RC	NE
	81 M		LD,STSG	3 cm, B				RT	RC	NE
	68 M		LD,STSG	3 cm, B				RT	NE	NE
Barbera S. Lutz 2002	61 M	Angiosarcoma	LD +STSG	NR	600	STA	Primary closure	NR	RC 3 mo	>10
	59 F	Angiosarcoma	ALT	NR	228	STA	Primary closure	Brachytherapy before op	RC 7 mo	>18
Lim et al., 2010	8 pts, 71 M on average	Angiosarcoma	LD, STSG	5 cm,burring of external table, parotidectomy, neck dissection	210 in median	STA	NR	RT	NE in 20 mo	>20
Gudewer et al., 2009	67 M	Angiosarcoma	LD + SA + STSG	Radical excision	900	STA	NR	RT	NE	Follow-up 16
Lin and Miguel et al., 2013	56 M	Angiosarcoma	ALT	NR, wide excision	130	STA	STSG	RT, CT	RC	Follow-up 4
Davison and Capone, 2011	82 F	Angiosarcoma	Inverted LD + STSG + mesh	Radical excision	150	STA	Primary close	RT	NE	Follow-up 12
Labow et al., 2009	82 F	Angiosarcoma	LD + STSG	NR	625	NR	NR	NR	NR	NR
Nagasao et al., 2011	68 M	Angiosarcoma	LD	Radical excision	124	STA	NR	RT	RC	NR

Abbreviation: M, Male; F, Female; NR, Not recorded; G, Galea; P, Periosteum; B, Bone; RT, Radiotherapy; C, Chemotherapy; Gy, Grays; NR, No record; NE, No event; FL, Follow-up loss; STSG, Splitting thickness skin graft; STA, Superficial temporal artery; ALT, Anterior lateral thigh; LD, Latissimus dorsi; RC, Regional recurrence; SA, Serratus anterior; MT, Metastasis.

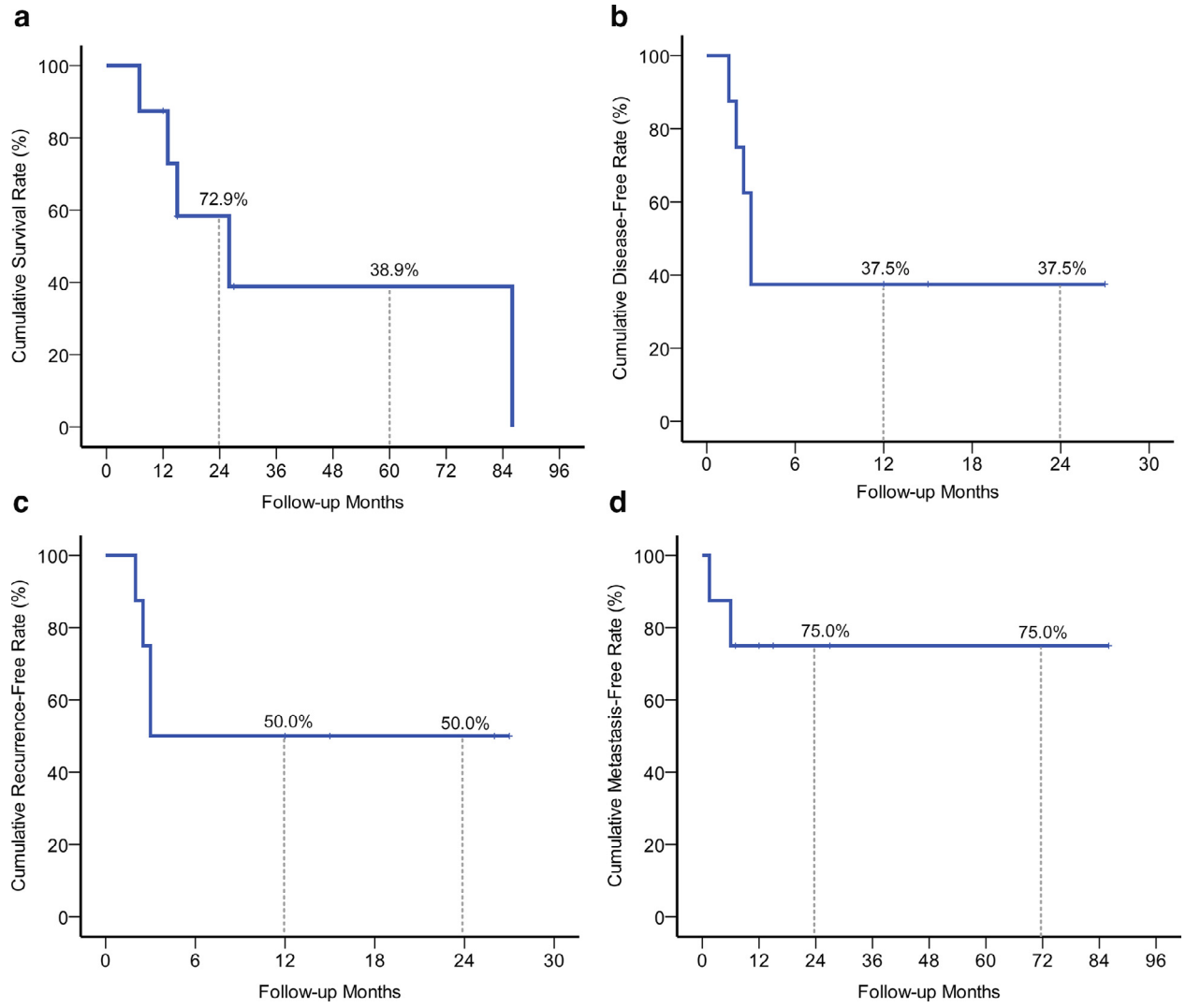

Figure 4 Kaplan-Meier survival plots. (a) The overall 5- and 2-year cumulative survival rates were 38.9% and 72.9%, respectively. (b) The two- and one-year cumulative disease-free rates were 37.5% each. (c) The two- and one-year cumulative recurrence-free rates were 50% each. (d) The 6- and 2-year cumulative metastasis-free rates were 75% each.

significantly better than latissimus dorsi flap.[32] Horn et al. also compared the outcome of latissimus dorsi and ALT flap reconstructions and found similar success and complication rates.[33] At our institution, ALT flap was more frequently used for scalp reconstruction after angiosarcoma excision for several reasons. First, the size of ALT flaps was large enough for scalp reconstruction in this series. Second, ALT flap harvesting and tumor excision allowed a simultaneous two-team approach with the patient in supine position, which translated into shorter operating time without the need for patient repositioning. Third, there was often only one donor site when using ALT flap (donor site often could be closed primarily), whereas using latissimus dorsi flap with split-thickness skin graft would result in two donor sites.

With regard to the deep margin of resection, Choi et al. reviewed 14 cases of scalp angiosarcoma that underwent wide excision and latissimus dorsi flap reconstruction and found that the deep margin played a significant role in the rate and speed of local recurrence.[14] Lim et al. performed 8 cases of scalp angiosarcoma resection combined with burring of calvarium, with survival rate of at least 20 months without local recurrence.[16] Based on these published results, our institution established the protocol of wide surgical resection (with 4 cm of margin), combined with cortical curettage (burring the outer cortex of the calvarium), to maximize the likelihood that the deep margin would be clear of tumor cells. Such approach, in combination with postoperative radiation and initiation of chemotherapy upon detection of local recurrence or distant metastasis, has allowed us to achieve 1-year survival rate of 100%, which compares favorably to the published series in the literature.

Conclusion

Scalp angiosarcoma is a rare and highly aggressive cutaneous malignancy with poor prognosis. ALT flap is a good reconstructive option due to its ability to cover large cutaneous defects with minimal need for skin grafting. Multimodal treatment protocol, including wide local excision

with cortical curettage, adjuvant radiation, and chemotherapy (when local recurrence or distant metastasis occurs), may offer improved 1-year survival rate (100%).

Credit authorship contribution statement

PYC, CYH, and RD were responsible for data collection, data analysis, and writing of manuscript; DK and Cheng-Hung Lin instructed and supervised the data management; Chih-Hung Lin was responsible for data analysis and editing of manuscript.

Declaration of Competing Interest

No conflicting relationship exists for any author.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2019.07.024.

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