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Cutaneous Angiosarcoma of Head and Neck – A Single-Centre Analysis

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Abstract

BACKGROUND: Cutaneous angiosarcoma of the head and neck region is a subtype of cutaneous angiosarcoma with an unfavourable prognosis. Diagnosis is often delayed.

PATENTS AND METHODS: The setting is an Academic Teaching Hospital Skin Cancer Center. Eight Caucasian patients could be identified, 5 men and 3 women. Delay to diagnosis was between 12 to 4 months (mean 7.8 ± 2.9 months). The diagnosis was confirmed in all cases by histopathology and immunohistochemistry. Hematoxylin-eosin, Giemsa, PAS, iron and reticulin stains were performed. Endothelial markers such as CD31, CD34, and Ki67 for proliferation assessment were used in all tumours. Other markers used included pan-cytokeratin (CK), CK7, CK20, ERG, CD 40 and c-MYC. Tumours were classified as localised versus multifocal or diffuse form. Tumour staging was performed according to the 8th edition of the AJCC. The mean age of patients was 79 years ± 26.4 years. The male to female ratio was 1.7. Tumour classification was diffuse in 2 patients, multilocular in one and localised in 5 patients. In 5 of 8 patients, a multimodal treatment was performed, one had radiotherapy alone, in another patient surgery was performed, and radiotherapy is planned. The mean OS was 26.4 months ± 24.5 months.

CONCLUSION: Cutaneous angiosarcoma of the head and neck is an aggressive tumour with a poor prognosis. Although surgery remains a cornerstone of treatment, the tumour size at first presentation may be too large, and the elderly patients maybe not suitable for extensive surgery. Therefore, multimodal treatment with adjuvant radiotherapy and/ or chemotherapy is necessary. Multimodal treatment offers a better outcome than radiotherapy or chemotherapy alone. Stealth liposomal encapsulated doxorubicin is a therapeutic option for elderly patients with improved safety compared to conventional doxorubicin.

Introduction

Cutaneous angiosarcoma of the head and neck is a rare tumour entity of vascular origin. It comprises about half of all angiosarcomas and accounts for 1% of all soft tissue sarcomas. This tumour is notorious for its aggressive and relentless progression with frequent local recurrence and distant metastasis. It affects mainly older people with a mean age of 73 years. Due to its scarcity and innocuous appearance at an early stage diagnosis is often delayed for months. Bleeding is one of the leading symptoms that is responsible for the first consultation. However, bleeding is not an early sign [1].

A study of the National Cancer Institute's Surveillance, Epidemiology, and End Results Program recorded 434 cases of cutaneous angiosarcoma from 1973 to 2007 with a comparable incidence in men and women. Caucasians represented the majority of patients compared to patients with Asian or African descent. Survival rates are dependent on age, anatomical site, and stage of the disease. In this study, patients < 50 years had a 10-year relative

survival rate of 71.7%, whereas patients ≥ 50 years had a 36.8% 10-year survival rate. Tumours of the scalp and neck had a poor survival rate (13.8% 10-year relative survival rate) compared to tumours on the trunk (75.3% 10-year survival rate). Tumours localised to the skin had a better prognosis (53.6% 10-year relative survival rate) than those with the regional or distant stage (19.0% and 6.2%) [2].

Scalp sarcoma tends to be larger at the time of diagnosis. That is responsible for a poorer prognosis than facial angiosarcoma. An analysis on 50 patients with cutaneous head and neck angiosarcomas from the Princess Margaret Cancer Centre, Toronto / Ontario, Canada, estimated a 5-year overall survival (OS) rate of 9% for scalp tumours and 26% for tumours of the face. In multivariate Cox proportional hazards analysis of their data, scalp location was independently prognostic for mortality (hazard ratio [HR], 2.10; 95% CI, 1.03-4.28; p = .04) [3].

Patients and Methods

Patients were seen and treated at the Department of Dermatology and Allergology, Skin Cancer Center. Delay to diagnosis was between 12 to 4 months (mean 7.8 ± 2.9 months). Differential diagnoses were lentigo, bruising, rosacea, squamous cell carcinoma and erysipelas.

The diagnosis was confirmed in all cases by histopathology and immunohistochemistry. Hematoxylin-eosin, Giemsa, PAS, iron and reticulin stains were performed. Endothelial markers such as CD31, CD34, and Ki67 for proliferation assessment were used in all tumours. Other markers used included pan-cytokeratin (CK), CK7, CK20, ERG, CD 40 and c-MYC.

Tumours were classified as localised versus multifocal or diffuse form. Tumour staging was performed according to the 8th edition of the AJCC [4]. The demographics are listed in Table 1.

Table 1: Demographics of head and neck cutaneous angiosarcoma

	Age	Sex	Localization	Size (cm)	Remarks	TNM
1	79 yrs	F	Scalp, temporoparietal	20	ulcerations, bleeding	pT4N0M0
2	74 yrs	M	Cheek	3.5	relapse after 6 yrs.	pT1N0M0
3	81 yrs	F	Scalp	30	ulceration, bleeding	pT4N1M0
4	85 yrs	M	Scalp	20	ulceration, bleeding	pT4N1M0
5	66 yrs	M	Cheek	4	Oedema	pT2N0M0
6	82 yrs	F	Scalp	2	multilocular, bleeding	pT2N0M0
7	66 yrs	M	Nose	6	oedema, redness	pT2N0M0
8	79 yrs	M	Scalp	12	Bleeding	pT3N0M0

The mean age was 79 years ± 26.4 years. The male to female ratio was 1.7. Tumour classification was diffuse in 2 patients, multilocular in one and localised in 5 patients (Figure 1).

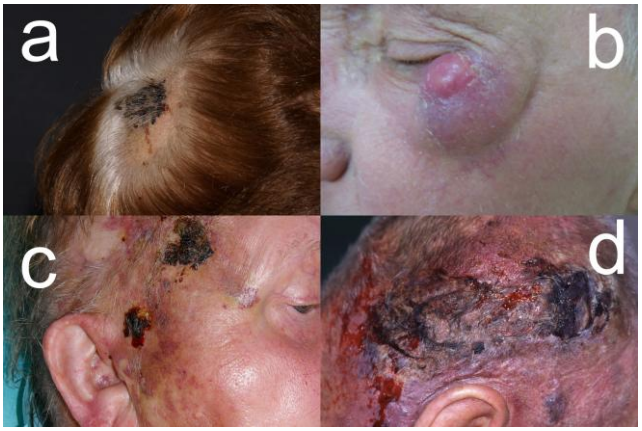

Figure 1: Cutaneous angiosarcoma of the head and neck region; A) Localized patch; B) Localized nodule; C) Multifocal tumour; D) Diffuse tumour

In 5 of 8 patients, a multimodal treatment was performed, one had radiotherapy alone, in another patient surgery was performed, and radiotherapy is planned (Figure 2). The mean OS was 26.4 months ± 24.5 months (Table 2).

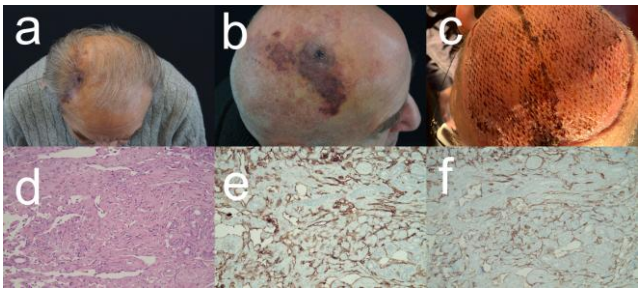

Figure 2: Cutaneous angiosarcoma, patient #8; A) Primary presentation – "bruising after local trauma"; B) Large localized scalp tumor after shaving; C) After surgery with curative intent (safety margin 2 cm), stable meshed graft transplant; D) and E) Histopathology and immunohistochemistry of the tumour; D) Irregular vascular proliferations interposed by the dermal collagen fibers. Endothelial cells with atypical nuclei, prominent toward the lumen, mitotic figures (Hematoxylin-eosin x 4); E) Immunoperoxidase staining for CD31, strongly expressed by the endothelial tumour cells (x 20); F) Immunoperoxidase staining with Ki67 demonstration a highly proliferative fraction of almost 100 % of tumour cells (x 20)

Discussion

The mainstay of treatment of cutaneous angiosarcoma of the head and neck is surgery. Surgery with curative intent as the initial treatment is significantly associated with improved overall survival [5].

However, complete excision is not always possible. In such a situation, multimodal regimens seem to improve the outcome [6]. A trial from the Mayo Clinic analysed 55 patients with angiosarcoma localised to the face or scalp. Multimodal treatment

received 73% of patients (the combination of surgery, radiation therapy, and/or chemotherapy), 15% were treated only surgically, 95 with chemotherapy, 2% with radiation alone and 2% had observation alone. The 5-year OS was 38%. On univariate analysis, the use of multimodality therapy (vs no multimodality therapy) was associated with higher 5-year OS (46% [26% vs 16%) [7].

Table 2: Treatment of head and neck cutaneous angiosarcoma and outcome

	Treatment	Safety	Overall Survival
1	Liposomal doxorubicin (20 mg/m^2) followed by electron beam (total 40 Gy)	Palmoplantar dysesthesia (CTC 0) radiation-induced erythema (CTC 2)	40 months
2	Surgery followed by electron beam (total 40 Gy)	Radiation-induced erythema (CTC 2)	80 months
3	Liposomal doxorubicin (20 mg/m^2) followed by electron beam (total 40 Gy)	Anemia & lymphopenia (CTC 2); radiation-induced erythema (CTC 2)	9 months
4	Electron beam (total 40 Gy)	Radiation-induced erythema (CTC 2)	3 months
5	Paclitaxel followed by electron beam (total 40 Gy)	Radiation-induced erythema (CTC 3)	6 months
6	Electron beam (total 40 Gy)	Radiation-induced erythema (CTC 2)	44 months
7	Surgery followed by electron beam (total 40 Gy)	Post-radiation-erythema (CTC 3)	80 months
8	Surgery, radiation is planned	-	> 4 months

Radiotherapy is most often used in combination with surgery. A meta-analysis from South Korea demonstrated that OS of the radiation therapy and chemotherapy group (37.0 ± 0.0 months) was significantly longer than that of the radiation therapy group alone (22.7 ± 7.6 months) or the chemotherapy group alone (15.1 ± 4.6 months) [8]. This is in one line with a trial from Osaka, Japan, that demonstrated patients treated with both surgery and radiotherapy (2-year OS: 45.8%) had a significantly better OS than patients treated with either surgery or radiotherapy alone (2-year OS: 11.1%) and patients treated with neither surgery nor radiotherapy (2-year OS: 0%) [9].

Considering chemotherapy in elderly patients, taxanes showed a response rate of 83.3% and a median progression-free survival of seven months, compared to non-liposomal doxorubicin with a response rate of 50% and median progression-free survival of 3months [10]. Taxanes show anti-angiogenic activity. The conventional doxorubicin therapy bears a high risk of cardiotoxicity, that leads to the cessation of the treatments. This has not been observed with stealth liposomal doxorubicin [11].

In our series, advanced tumour stages and age > 70 years was characteristic. Initial differential diagnoses were bruising, lentigo-like hyperpigmentation and rosacea. Most patients presented to the doctor because of bleeding. None of the tumours was diagnosed at outpatient cancer screenings.

In conclusion, cutaneous angiosarcoma of the head and neck is a rare but aggressive vascular malignancy with a less favourable prognosis than the counterparts on trunk or extremities. Many patients are older than 70 years of age that needs to be considered for multimodal treatment. Surgery plus radiotherapy is the treatment of choice. When chemotherapy is necessary, stealth liposomal doxorubicin offers a better safety profile for this age group that conventional doxorubicin or taxanes [11], [12], [13].

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