CONCISE COMMUNICATION

Prognostic value of $^{18}$F-FDG PET/CT in patients with cutaneous angiosarcoma: a retrospective study of 18 cases

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ABSTRACT

Cutaneous angiosarcoma (CAS) is a rare soft tissue sarcoma with rapid growth and poor prognosis. We retrospectively analyzed the data of 18 patients with CAS who underwent $^{18}$F-fluorodeoxyglucose positron emission tomography/computed tomography ($^{18}$F-FDG PET/CT) at the initial visit to the Department of Dermatology, Okayama University Hospital from September 2006 to March 2016. In the univariate survival analysis, patients with high standardized uptake values (SUVmax) of the primary tumor showed significantly poorer prognosis than those with low SUVmax. Early assessment of prognosis using PET/CT may predict patient survival and is useful in the selection of therapeutic strategies.

Key words: angiosarcoma, PET/CT, positron emission tomography, SUVmax, prognostic factor
INTRODUCTION

Cutaneous angiosarcoma (CAS) is a rare and severe soft tissue sarcoma with a 5-year survival rate of 30%–35%. Recent studies have shown the effectiveness of taxane chemotherapy in the treatment of CAS. In addition, new anti-cancer or molecular-targeted agents, such as eribulin, trabectedin, and pazopanib have shown potential in improving the prognosis of patients with soft tissue sarcomas including CAS. However, useful prognostic factors for CAS have not yet been identified. Therefore, early indicators of prognosis may improve patient survival. 18F-fluorodeoxyglucose (18F-FDG) parallels glucose metabolism in the human body and is widely used in the imaging of malignant tumors. 18F-FDG positron emission tomography/computed tomography (PET/CT) has been increasingly used in the diagnosis, staging, and management of malignancies such as soft tissue sarcomas. Several studies showed that a high standardized uptake value (SUVmax) during PET/CT is predictive of poor prognosis in patients with sarcomas. In a similar manner, PET/CT could be used to predict prognosis in CAS.

Here we describe 18 patients with CAS in whom PET/CT was performed at the initial hospital visit. The prognostic values of four factors (age, sex, stage, and SUVmax) were analyzed.

CASE REPORTS

We examined patient records of the Department of Dermatology, Okayama University Hospital,
and identified 18 consecutive CAS patients who underwent PET/CT at the initial hospital visit from September 2006 to March 2016 (Table 1). PET/CT was performed at the Okayama Diagnostic Imaging Center. Skin biopsy confirmed the diagnosis of CAS in all patients. The mean age was 74 years and 12 patients were males. The median length of follow-up was 18.0 months (range, 4.8−60.8). Two female patients had primary CAS of the leg or hip arising from chronic leg edema and were diagnosed with Stewart–Treves syndrome. The remaining 16 patients had CAS of the scalp. The patients were classified into three stages: stage I for those with limited, local cutaneous tumors; II for those with regional lymph node metastases; and III for those with distant metastases. In Figure 1, representative image of PET/CT in patient 18 is shown. PET/CT detected primary tumor of CAS on his scalp with SUVmax of 12.01, and metastatic lesion on the middle lobe of the right lung with SUVmax of 4.30. He was diagnosed as stage III. All primary tumors were treated with radiation therapy. Taxane monotherapy was also initiated around the same time as radiation therapy. The standard chemotherapy regimen used was either paclitaxel (PTX) 80 mg/m² on days 1, 8, and 15 of a 35-day cycle for two courses followed by 210 mg/m² on day 1 of a 28-day cycle until disease progression or docetaxel (DTX) 30 mg/m² on days 1, 8, and 15 of a 35-day cycle for two courses followed by 60 mg/m² on day 1 of a 28-day cycle until disease progression. Eleven patients received PTX and four patients received DTX. The remaining three patients did not receive taxane because of advanced age or interstitial pneumonia.
Eleven patients died due to CAS during the observation period. No death occurred due to other causes.

**STATISTICAL ANALYSIS**

All statistical analyses were performed using IBM SPSS Statistics, version 20.0 (Chicago, IL, USA). Kaplan–Meier analysis was performed for age, sex, stage, and SUVmax of the primary tumor to evaluate patient survival. SUVmax of the metastatic lesion in stage II and III patients was not used in this analysis. A log-rank test was used to compare survival curves. A $P$-value of $<0.05$ was considered statistically significant.

**ETHICS**

The ethics committee of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, and Okayama University Hospital approved this study (Epidemiologic study No. 954).

**RESULTS**

We performed univariate analysis of all 18 patients for age, sex, stage, and SUVmax of the primary tumor using Kaplan–Meier curves. Median age (77 years) and SUVmax (7.96) were used
as cut-off values. As shown in Figure 2, age and sex showed no significant differences in the log-
rank test. Patients with metastases (stages II and III) had significantly poorer prognosis than those
without (stage I) (Figs. 2a–c). Furthermore, patients with high SUVmax had significantly poorer
prognosis (Fig. 2d) than those with low SUVmax.

**DISCUSSION**

In this study, we showed that SUVmax of angiosarcoma primary lesions could potentially predict
prognosis. There are several case reports on the use of PET/CT in angiosarcoma, 11-14 but to the
best of our knowledge, this is the first reported case series in which PET/CT use for CAS was
systematically reviewed.

PET/CT is a combined imaging modality in which PET scans generate functional information
while CT scans generate morphological information. It has the advantage of generating
quantitative information (SUVmax) compared with conventional CT. In Kaplan–Meier analysis,
patients with high SUVmax were observed to have poorer prognosis than those with low SUVmax.
In recent years, the SUVmax of the primary tumor has been shown to be predictive of prognosis
in sarcomas. 7-9 In two studies, multivariate analysis showed that SUVmax was a statistically
significant independent predictor of prognosis. 7,9 Kubo et al. performed a meta-analysis of six
studies, totaling 514 patients with bone and soft tissue sarcomas. In their analysis, they
demonstrated that higher SUVmax is predictive of a significantly shorter overall survival period compared with a lower SUVmax. However, in this present study, multivariate analysis could not be performed because of the insufficient number of cases examined. The results of our study did however show that the SUVmax of primary CAS is predictive of prognosis, which was similar to that for other sarcomas.

In recent years, novel therapeutic agents, such as eribulin, trabectedin, and pazopanib have been shown to potentially improve the prognosis of patients with soft tissue sarcomas. However, Kitamura et al. have reported that pazopanib does not bring remarkable improvement in patients with CAS. Thus, the benefits of novel agents for CAS are still controversial. An early assessment of prognosis using SUVmax at the initial visit might be helpful for the selection of therapies among conventional taxane chemotherapy and newly developed therapies.

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CONFLICT OF INTEREST: None declared.
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**LEGENDS**

Figure 1. Representative image of the PET/CT in patient 18 is shown. (a) PET/CT detected primary tumor (yellow arrow) of CAS on his scalp with 12.01 SUVmax. (b) PET/CT also detected metastatic lesion (yellow arrow) on the middle lobe of the right lung with 4.30 SUVmax. He was diagnosed as stage III CAS.

Figure 2. Kaplan–Meier analysis of four factors (age, sex, stage, and SUVmax of the primary tumor) in all 18 patients. (a) The cut-off value for age is defined as a median age of 77 years. Using the log-rank test, no significant differences between older and younger patients were observed. (b) Sex differences were found to be not significant. (c) Patients with metastases (stages II and III) have poorer prognoses than stage I patients ($P = 0.010$). (d) The cut-off value for
SUVmax is defined as a median of 7.96. Patients with high SUVmax have poorer prognosis ($P = 0.015$) than those with low SUVmax.