Case Reports in Oncology

Case Rep Oncol 2023;16:1490–1493
DOI: 10.1159/000534657
Received: September 20, 2023
Accepted: September 30, 2023
Published online: November 28, 2023

Case Report

Recurrent, Tumor Mutation Burden-High, Cutaneous Angiosarcoma of the Scalp Treated with Pembrolizumab

Ryo Amagai Taku Fujimura Yumi Kambayashi Kentaro Ohuchi
Emi Yamazaki Akira Hashimoto Yoshihide Asano

Department of Dermatology, Tohoku University Graduate School of Medicine, Sendai, Japan

Keywords
Recurrent cutaneous angiosarcoma · Taxane resistant · Foundation one liquid · Tumor mutation burden · Pembrolizumab

Abstract
Introduction: Chemoradiotherapy with taxanes is well-recognized as a first-line therapy for cutaneous angiosarcoma (CAS), but second-line therapy for CAS is still controversial. ***Case Presentation:*** In this report, we described a 75-year-old Japanese case of recurrent, tumor mutation burden-high CAS on the scalp treated with pembrolizumab. Our present case survived for 1 year despite of taxane refractory CAS with mediastinal lymph node metastasis, though the administration of anti-PD-1 Abs alone could not fully suppress the tumor progression of CAS. ***Conclusion:*** Since various factors such as pro-angiogenic molecules are correlated with the tumor progression in CAS, the administration of anti-PD-1 Abs alone could not fully suppress the tumor progression of CAS. Further novel anticancer drugs are needed in the future for the treatment of CAS.

Introduction

Cutaneous angiosarcoma (CAS) is a rare and highly aggressive type of vascular tumor [1–3]. Previous clinical studies have suggested the importance of taxane-derived agents such as paclitaxel and docetaxel in the maintenance therapy for CAS [1, 3], but a second line or beyond chemotherapy for taxane-resistant CAS is still controversial [2].

Correspondence to:
Taku Fujimura, tfujimura1@mac.com

Case Rep Oncol 2023;16:1490–1493
DOI: 10.1159/000534657

Case Report

A 75-year-old Japanese man visited our outpatient clinic with a 4-year history of angiosarcoma of scalp treated with chemoradiotherapy. He had been treated with paclitaxel for 3 years, then followed by docetaxel (2 months) and pazopanib (1 month). His tumor was resistant to paclitaxel and docetaxel, and pazopanib was not tolerable due to grade 3 nausea and anorexia as adverse events. Physical examination revealed the extended purpura on the scalp (Fig. 1a). A biopsy specimen from purpura showed atypical endothelial cells. Positron emission tomography (PET)-computed tomography (CT) showed multiple mediastinal lymph node of metastases (Fig. 1d). Since there was no standard systemic therapy for this case, we performed liquid biopsies for evaluating genome alteration using Foundation One liquid to seek the possible systemic treatment. Nonsense mutation of BRCA2 and high levels of tumor mutation burden (TMB) (10.12 Muts/Mb) were found. These results suggested the usefulness of platinum-based anticancer agents (cisplatin, carboplatin) and pembrolizumab, and we selected pembrolizumab (200 mg/body/3 weeks) because of age-related decline in renal disfunction and his performance status (PS2). The administration of pembrolizumab was well tolerable and efficacy at 3 months (Fig. 1b), 6 months was stable disease, but 9 months later, the purpuric lesion as well as other nodules were detected around the scalp (Fig. 1c), and lung metastasis and pleural lesion were detected by follow-up PET-CT. One year after the initial treatment with pembrolizumab, the patient died from hemopneumothorax. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534657).

Discussion

Several previous retrospective studies suggested importance of a taxane-switch (change paclitaxel to docetaxel or vise) regimen, eribulin methylate regimen, and pazopanib regimen [2, 4, 5], but a second line or beyond chemotherapy for taxane-resistant CAS is still controversial [2, 3]. Indeed, a multicenter retrospective study suggested that there is no significant difference of progress-free survival and overall survival (OS) between these chemotherapy regimens [2], suggesting the importance of novel anticancer drugs for the treatment of CAS.

Since there have been sporadic cases with high TMB in angiosarcoma [6], recently, immune checkpoints inhibitors are reported as one of the promising therapies for CAS. Indeed, the overall response rate of nivolumab plus ipilimumab combined therapy is 60% in CAS on the head and neck [6]. Pembrolizumab is effective for TMB-high tumors regardless of the types of primary tumor [7]. Notably, TMB is higher in ultraviolet-induced skin tumors (e.g., squamous cell carcinoma, basal cell carcinoma, and cutaneous melanoma) than that in other cancer species [8]. Therefore, since most of CAS located on the head and neck, CAS might possess high levels of TMB [6].

Indeed, our present case showed high levels of TMB and survived for 1 year despite of taxane refractory CAS with mediastinal lymph node metastasis. Notably, although progress-free survival and OS are comparable to those of taxane-switch regimen, eribulin methylate regimen, and pazopanib regimen [2], safety profile of pembrolizumab was superior to these regimens, and we could continue pembrolizumab regimen in spite of his age-related decline in renal disfunction. Notably, the OS for CAS patients in stage IV was 6–8 months in Japanese population [9], suggesting that pembrolizumab might be suitable for the treatment of advanced CAS with high levels of TMB. Since various factors such as pro-angiogenic molecules are correlated with the tumor progression in CAS [10], the administration of anti-PD-1 Abs alone could not fully suppress the tumor progression of CAS. Further novel anticancer drugs are needed in the future for the treatment of CAS.

Case Rep Oncol 2023;16:1490–1493
DOI: 10.1159/000534657

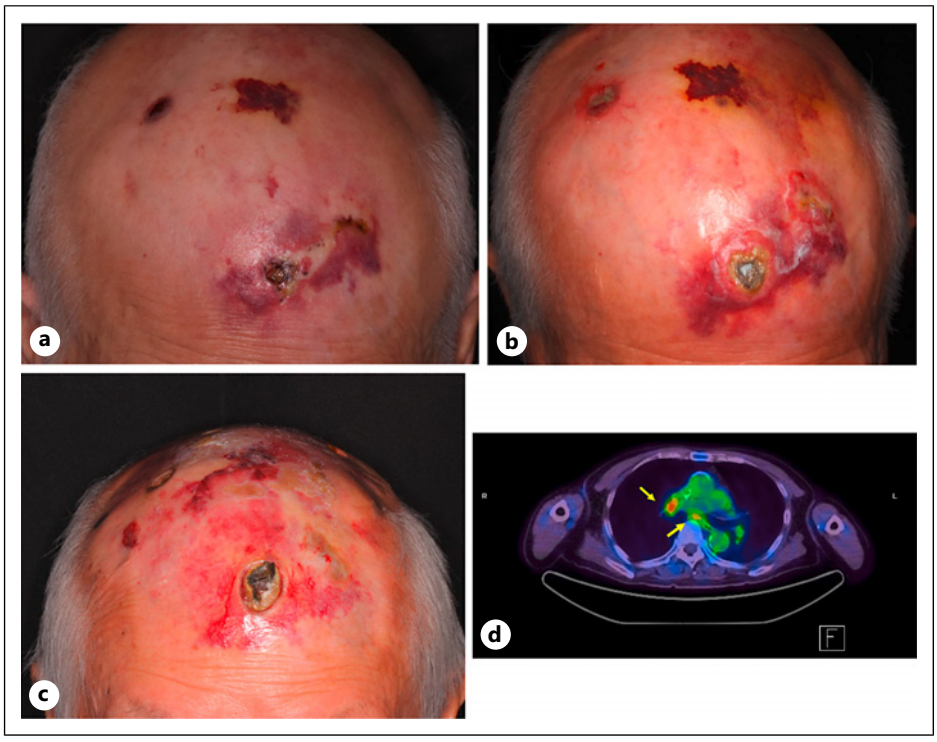

Fig. 1. Physical examination revealed the extended purpura on the scalp at the baseline (**a**), 3 months (**b**) and 9 months (**c**) after the administration pembrolizumab. PET-CT showed multiple mediastinal lymph nodes (arrowhead) of metastases (**d**).

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images prior to their passing away. The protocol for this human study was approved by the Ethics Committee of Tohoku University Graduate School of Medicine, Sendai, Japan (permit No. 2021-1-1213).

Conflict of Interest Statement

The authors have no conflicting interests to declare.

Funding Sources

There is no funding source to declare for this study.

Author Contributions

Amagai R, Fujimura T, Kambayashi Y, Ohuchi K, Yamazaki E, and Hasimoto A treated the patient and acquired the clinical data. Amagai R and Fujimura T wrote the manuscript. Fujimura T and Asano Y supervised the study.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

References

1 Fujisawa Y, Yoshino K, Kadono T, Miyagawa T, Nakamura Y, Fujimoto M. Chemoradiotherapy with taxane is superior to conventional surgery and radiotherapy in the management of cutaneous angiosarcoma: a multicentre, retrospective study. Br J Dermatol. 2014;171(6):1493–500.
2 Fujimura T, Maekawa T, Kato H, Ito T, Matsushita S, Yoshino K, et al. Treatment for taxane-resistant cutaneous angiosarcoma: a multicenter study of 50 Japanese cases. J Dermatol. 2023;50(7):912–6.
3 Fujimura T, Furudate S, Maekawa T, Kato H, Ito T, Matsushita S, et al. Cutaneous angiosarcoma treated with taxane-based chemoradiotherapy: a multicenter study of 90 Japanese cases. Skin Health Dis. 2023;3(1):e180.
4 Ogata D, Yanagisawa H, Suzuki K, Oashi K, Yamazaki N, Tsuchida T. Pazopanib treatment slows progression and stabilizes disease in patients with taxane-resistant cutaneous angiosarcoma. Med Oncol. 2016;33(10):116.
5 Fujisawa Y, Fujimura T, Matsushita S, Yamamoto Y, Uchi H, Otsuka A, et al. The efficacy of eribulin mesylate for patients with cutaneous angiosarcoma previously treated with taxane: a multicentre prospective observational study. Br J Dermatol. 2020;183(5):831–9.
6 Florou V, Rosenberg AE, Wieder E, Komanduri KV, Kolonias D, Uduman M, et al. Angiosarcoma patients treated with immune checkpoint inhibitors: a case series of seven patients from a single institution. J Immunother Cancer. 2019;7(1):213.
7 Maio M, Ascierto PA, Manzyuk L, Motola-Kuba D, Penel N, Cassier PA, et al. Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study. Ann Oncol. 2022;33(9):929–38.
8 Chan TA, Yarchoan M, Jaffee E, Swanton C, Quezada SA, Stenzinger A, et al. Development of tumor mutation burden as an immunotherapy biomarker: utility for the oncology clinic. Ann Oncol. 2019;30(1):44–56.
9 Fujisawa Y, Asagoe K, Masuzawa M, Otsuka A, Uchi H, Matsushita S, et al. Japanese dermatological association guidelines: outlines of guidelines for cutaneous angiosarcoma 2021. Jpn J Dermatol. 2021;131:245–77.
10 Ohuchi K, Amagai R, Ikawa T, Muto Y, Roh Y, Endo J, et al. Plasminogen activating inhibitor-1 promotes angiogenesis in cutaneous angiosarcomas. Exp Dermatol. 2023;32(1):50–9.