

Case Report

David Slays Goliath: Exceptional Efficacy of Oral Vinorelbine in Conquering Metastatic Finger Angiosarcoma

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Abstract

Angiosarcoma (AS) is a rare and aggressive disease originating from blood or lymphatic vessel endothelium, representing <1% of soft-tissue sarcomas. The prognosis is generally poor, with a 5-year survival rate of only 30%–50%. The recurrence rate is high, and metastasis occurs in about half of the cases. The National Comprehensive Cancer Network guidelines recommend anthracycline-based, gemcitabine-based, and paclitaxel regimens as preferred first-line treatments for metastatic AS. Vinorelbine, a vinca alkaloid, is listed as supportive care in AS for patients unsuitable for intensive chemotherapy or who are heavily treated. Although the efficacy of vinorelbine is modest, some studies suggest its synergistic effect with immunotherapy. In our case report, a patient with metastatic AS received frontline paclitaxel followed by pembrolizumab, but this treatment failed. However, a complete response (CR) was achieved after oral vinorelbine. Remarkably, the patient remains in CR for 4.5 years after discontinuing vinorelbine.

Keywords: Angiosarcoma, chemotherapy, complete response, immune checkpoint inhibitor, vinorelbine

INTRODUCTION

Angiosarcoma (AS) is a rare and aggressive disease that originates from the endothelium of blood or lymphatic vessels,^[1] accounting for <1% of soft-tissue sarcomas (STS).^[1] Histologically, AS is highly vascularized, with a high mitotic activity and necrosis, with typical vascular markers such as CD34, CD31, and ERG expressed.^[1] It predominantly affects older patients (60–70 years),^[2] often originated from the cutaneous region, especially the scalp.^[3] Risk factors include

previous radiotherapy, chronic lymphedema, and exposure to certain chemicals.^[2] Treatment involves surgery for localized disease,^[2] but recurrence is common, and metastasis occurs in about half of the cases.^[3] For metastatic or locally advanced AS, the National Comprehensive Cancer Network (NCCN) recommends anthracycline, gemcitabine, or paclitaxel regimens. The 5-year survival rate is 30%–50%.^[2] Here, we

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present a case of finger AS with lung metastasis showing a complete response (CR) to oral vinorelbine therapy, with ongoing disease-free status for 4.5 years after vinorelbine discontinuation.

CASE REPORT

A 21-year-old male reported swelling and pain in his left thumb, index finger, and middle finger. Biopsy results showed spindle cells and immunohistochemistry stain revealed the tumor was positive for cytokeratin CK and ERG1 but negative for CD34, desmin, and CAMPTA1. Multiple lung nodules were detected on a computed tomography (CT) scan, leading to a diagnosis of AS with multiple lung metastases.

In December 2016, the patient underwent tumor resection of the affected fingers, followed by weekly paclitaxel treatment. Restaging evaluation in September 2017 indicated disease progression in the lung metastases [Figure 1a]. Although the programmed cell death 1-ligand 1 (PD-L1) stain for his AS came back negative, pembrolizumab was still prescribed at a fixed dose of 100 mg intravenously every 3 weeks after doctor–patient discussion. After three courses of pembrolizumab, a CT scan in November 2017 revealed a continued increase in the number and size of lung tumors, indicative of progressive disease [Figure 1b]. Concurrently, the patient experienced swelling and pain in his fingers, resembling the initial symptoms. X-ray showed an osteolytic lesion in the distal phalanx of the third finger. Amputation of the fingers was recommended, but the patient opted for conservative tumor excision in December 2017. Pathological evaluation confirmed the recurrence of AS.

Following surgery, the patient received weekly oral vinorelbine treatment at 30 mg/m² in December 2017. In May 2018,

5 months after surgery, recurrent symptoms were observed in his left hand, and a magnetic resonance image showed soft-tissue edema without evidence of recurrent tumor. Nevertheless, due to the high risk of tumor recurrence, the patient agreed to undergo amputation of his left thumb, index finger, and middle finger on May 28, 2018. Pathological analysis confirmed AS posttreatment, as atypical spindle cells positive for ERG1 were observed but not associated with vessels.

A whole-body positron emission tomography/CT scan in August 2018 revealed a CR [Figure 1c]. In December 2018, a chest CT scan showed no obvious tumors in bilateral lungs, indicating a CR [Figure 1d]. Consequently, the patient discontinued vinorelbine treatment after a 1-year course. Since then, the patient has remained disease free for 54 months.

DISCUSSION

AS is a highly aggressive neoplasm and the prognosis is generally poor. NCCN recommends anthracycline, gemcitabine, and paclitaxel regimens for metastatic disease as first-line therapy. Vinorelbine, a vinca alkaloid, inhibits microtubules in the G2 and M phases, leading to cell division failure and death.^[4] The NCCN guidelines list it as supportive care in AS for patients unsuitable for intensive chemotherapy. The evidence addressing vinorelbine in AS treatment is limited. There are only a few relevant case reports and retrospective studies, as monotherapy or in combination with other agents.^[5–7] A retrospective study evaluated vinorelbine in previously treated STS patients.^[5] A total of 58 patients were identified. The response rate was only 6%, with the best response of partial response, and the medium progression-free survival (PFS) was only 1.8 months. Notably, 26% of the patients had stable disease (SD). A Phase II study evaluated gemcitabine plus vinorelbine in patients with advanced STS.^[6] Among the 40 patients enrolled in the trial, the response rate was 12.5% (5/40), with one patient achieving CR. There were five patients having SD. The median PFS was 3.4 months for all patients and 12.6 months for responders and SD cases. Read and Williams reported a case with metastatic AS and disease-related Kasabach–Merritt syndrome.^[7] The patient had unsuccessful treatment from multiple agents, including liposomal doxorubicin, paclitaxel, bevacizumab, and pazopanib. A near CR was achieved after receiving gemcitabine plus vinorelbine. In brief, vinorelbine monotherapy provides only modest effects and a low response rate. Combination therapy with other agents improves vinorelbine efficacy. However, our patient achieved CR after vinorelbine monotherapy, with previous immune checkpoint inhibitor (ICI) treatment, which raised the question of whether vinorelbine had achieved adequate immune modulation.

Some studies reported that vinorelbine has a synergic effect with immunotherapy and induces inflammation,

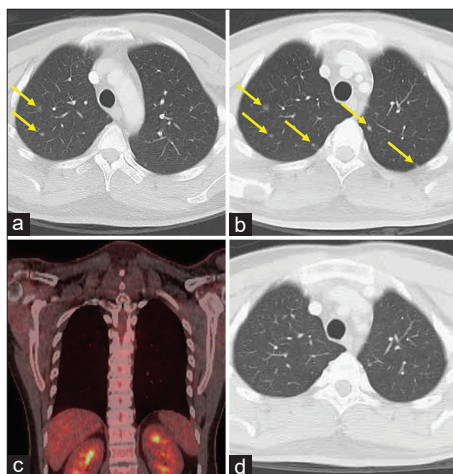


Figure 1: (a) A chest computed tomography (CT) scan before the starting of pembrolizumab, revealing multiple lung metastases (arrows). (b) A chest CT after pembrolizumab treatment, showing progressive lung metastases (arrows). (c) A whole-body positron emission tomography/CT scan 8 months after starting vinorelbine, revealing complete response (CR). (d) A chest CT before end-of-treatment of vinorelbine, showing ongoing CR

altering the tumor microenvironment.^[4] Terra *et al.* found significantly increased PD-L1 expression after vinorelbine exposure in malignant mesothelioma but not with pemetrexed.^[8] In a multicenter analysis of unresectable non-small cell lung cancer (NSCLC) patients, frontline metronomic oral vinorelbine (MOV) followed by ICIs led to an overall survival (OS) increase of 14 months.^[9] Moreover, Gebbia *et al.* conducted a retrospective study analyzing 30 advanced NSCLC patients without actionable mutations who received first-line chemotherapy, second-line ICI, and third-line MOV.^[10] They found that the disease control rate of MOV was 46.7%. The median PFS and OS were 3.9 months and 8.1 months, respectively. These preliminary findings suggest that vinorelbine may have immunostimulating effects that can enhance ICI treatment effects, which warrants further investigation and confirmation.

In summary, this case highlights the potential of oral vinorelbine in treating AS. The patient's remarkable disease-free status underscores the need for further research to understand the synergistic effects of vinorelbine with immunotherapy.

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Declaration of patient consent

The authors certify that they have obtained the patient consent form. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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