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CASE REPORT

Extracorporeal Membrane Oxygenation with rituximab-combined chemotherapy in AIDS-associated primary cardiac lymphoma: A case report

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Abstract

Although effective combination of antiretroviral medications is being developed, the incidence of non-Hodgkin lymphoma (NHL) with human immunodeficiency/acquired immunodeficiency syndrome (HIV/AIDS) still remains significantly higher than that in individuals without infection. Primary cardiac lymphoma (PCL) is an NHL that involves the heart and/or the pericardium. PCL is very rare and often causes serious complications, which can be a diagnostic challenge. To our knowledge, no study has reported the measurement of rituximab concentration under venoarterial extracorporeal membrane oxygenation (VA-ECMO). Herein, we report the case of a 54-year-old male patient with AIDS-associated primary cardiac NHL who developed right ventricular outflow tract obstruction. The patient experienced fatigue and dyspnea on exertion. Contrast-enhanced computed tomography showed a bulky tumor mass in his right atrium and ventricle, and an echocardiogram revealed severe hypokinesis of his heart and poor cardiac output. A biopsy was performed, and immunohistochemistry revealed diffuse large B-cell lymphoma. Therefore, he was treated with rituximab-combined chemotherapy under VA-ECMO. Blood levels of rituximab were measured during chemotherapy with VA-ECMO. Thereafter, he was temporarily discharged from the hospital. This clinical case suggests that VA-ECMO and rituximab-combined chemotherapy are useful in rescuing patients with severe cardiopulmonary failure due to AIDS-associated PCL.

KEYWORDS

acquired immune deficiency syndrome (AIDS), diffuse large B-cell lymphoma (DLBCL), extracorporeal membrane oxygenation (ECMO), primary cardiac lymphoma (PCL), rituximab

1 | INTRODUCTION

Despite the existence of effective combinations of antiretroviral medications, the incidence of non-Hodgkin lymphoma (NHL) with human immunodeficiency/acquired immunodeficiency syndrome (HIV/AIDS) remains significantly higher than that in individuals without infection. Kaposi's sarcoma that develops in patients with HIV invades the epicardium and pericardium. However, NHLs, such as high-grade B-cell lymphoma, are the second most common tumors involving the heart in patients with HIV. Primary cardiac lymphoma (PCL) is an NHL that involves the heart and/or the pericardium. PCL is very rare and often presents with nonspecific clinical and imaging features, posing a diagnostic challenge [1]. Patients with hematological malignancy undergoing venoarterial extracorporeal membrane oxygenation (VA-ECMO) are at a high risk of developing severe complications such as bleeding and infection. However, no study has reported measuring rituximab blood levels during chemotherapy with VA-ECMO. To the best of our knowledge, this is the first report of a patient with AIDS-associated PCL accompanied with direct cardiac muscle infiltration and treated with rituximab-combined chemotherapy under VA-ECMO.

2 | CASE REPORT

A 54-year-old man with AIDS received an initial antiretroviral therapy 1 month after diagnosis. Six months later, he experienced fatigue and dyspnea on exertion. Transthoracic echocardiography revealed a tumor in the right chamber from around the tricuspid valve annulus, which excluded the tricuspid valve and caused passage obstruction, with a mean pressure gradient of 17 mmHg. Contrast-enhanced computed tomography showed a bulky tumor (11 cm ×9.0 cm ×8.5 cm) in his right atrium, outside the right atrial wall and ventricle, and an echocardiogram revealed severe hypokinesis of the heart and poor cardiac output (Figure 1A-C).

His laboratory data were as follows: white blood cells, 10,880/μL; lymphoid cells, 1447/μL; CD4, 80/μL; platelets, 215,000/μL; aspartate aminotransferase, 1703 U/L; alanine aminotransferase, 860 U/L; lactic dehydrogenase, 659 U/l; blood urea nitrogen, 41.4 mg/dL; Cre 1.99 mg/dL; uric acid, 14.9 mg/dL; N-terminal-pro hormone-brain natriuretic peptide, 4450 ng/L; and sIL-2R, 1443 U/L. He had exacerbated general malaise and low cardiac output syndrome. Under oxygen therapy of 10 L/min via a reservoir mask, blood gas analysis indicated pH of 7.4, PCO2 of 13.3 mmHg, PO2 of 71.8 mmHg, and lactic acid of

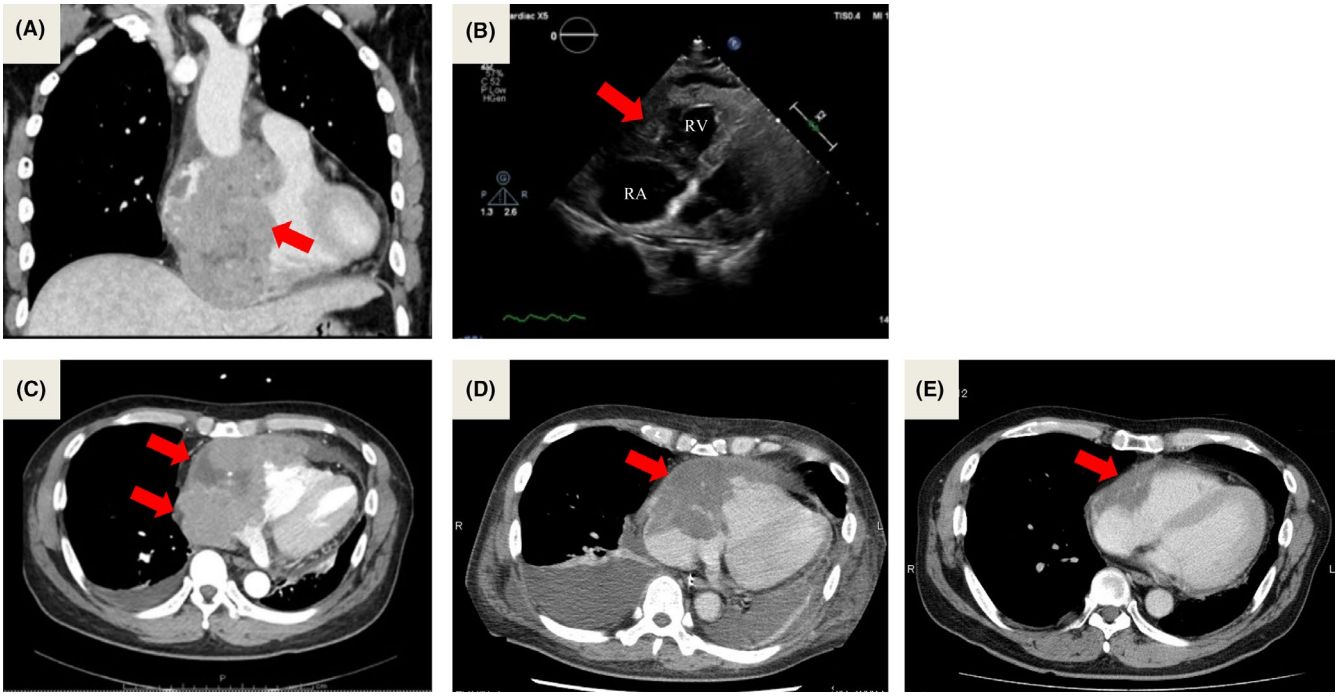

FIGURE 1 A, The reconstructed coronal view of the chest CT revealed a right atrial mass. B, Echocardiography showed a mass in his right atrium and ventricle. C, Contrast-enhanced CT revealed heterogeneous enhancement in his right atrium and ventricle (arrow). D, Contrast-enhanced CT showed a tumor in his right atrium and ventricle decreased by 30–40% after the first chemotherapy. E, Contrast-enhanced CT revealed a tumor in his right atrium and ventricle decreased by 70–80% after the first chemotherapy after the rituximab-combined CHOP therapy six times. RA, right atrium; RV, right ventricle

84 mg/dl. This situation required urgent cardiac tumor biopsy to determine treatment strategy. During cardiac tumor biopsy, the tumor obstructed the right ventricular outflow tract. Thus, for hemodynamics, VA-ECMO (HPO-23WH-C, Senko, Tokyo, Japan), artificial ventilation, and continuous hemodialysis were started. The initial blood gas analyses indicated pH of 7.01, PaO2 of 520 mmHg, PaCO2 of 40.3 mmHg, and SvO2 of 46% due to low cardiac output. To relieve tumor obstruction, prednisolone of 100 mg per day was administered for 1 week; however, this treatment neither improved the right ventricular outflow tract obstruction nor decreased the bulk of the tumors.

Histopathological immunostaining of the cardiac tumor biopsy revealed that CD20, bcl-2, bcl-6, and MUM-1 were all positive, and CD10, EBER, and c-myc were negative. He was then diagnosed with diffuse large B-cell lymphoma (non-GCB type) 7 days after intensive care (Figure 2). All findings pointed to AIDS-associated PCL. Rituximab was administered once under VA-ECMO and continuous hemodialysis, but it did not improve his circulatory dynamics. Blood concentration of rituximab after 48 h of its administration was below sensitivity; therefore, he was treated with reduced-dose CHOP therapy 9 days after the initiation of VA-ECMO. As his circulatory dynamics gradually improved, full-dose CHOP therapy was started. His circulatory dynamics gradually improved, and his tumor size decreased by 30%–40% (Figure 1D). Finally, he was successfully withdrawn from VA-ECMO 18 days after the start of treatment. Thereafter, he was temporarily discharged from the hospital. He had got rituximab-combined CHOP therapy six times as an outpatient, and however, he relapsed a neurological exacerbation of his brain. For reduction of recurrent lesions, he received high-dose methotrexate-based chemotherapy and whole brain irradiation. In spite of such as these treatments, he died from progression disease at six months after diagnosis.

3 | DISCUSSION

The clinical course of this case provides two important insights. First, VA-ECMO and multiagent chemotherapy are useful in rescuing patients with severe cardiopulmonary failure due to AIDS-associated PCL. Second, blood levels of rituximab were measured during chemotherapy with VA-ECMO.

PCL is rare and accounts for 2% of primary cardiac tumors [1]. It often presents with nonspecific clinical course and echocardiographic finding, posing a diagnostic challenge. Recently, ECMO as cardiac or respiratory support is increasingly used in different disorders associated with hypoxia, severe respiratory acidosis, and cardiac failure [2]. The Survival After Venoarterial ECMO (SAVE) score is used to predict survival after ECMO [2]. The SAVE score of this case was −4 points, which was classified as risk group III, and the survival rate was 42%. However, the SAVE score could not be useful for PCL because there was no information indicating an oncologic emergency. Providing ECMO in patients with hematologic malignancy and acute heart failure is a controversial issue because of its risks of high mortality and high complication rate; however, successful ECMO weaning in patients with newly diagnosed malignant lymphoma have been

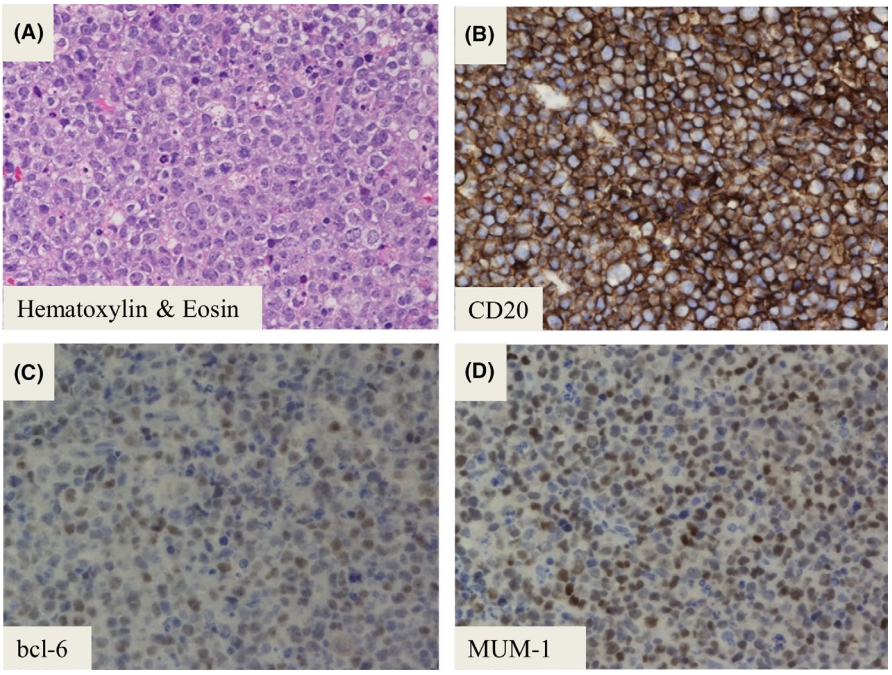

FIGURE 2 (A-D) Histopathological examination of the myocardium. (A) Biopsy showed a diffuse proliferation of large-sized lymphoid cells, which exhibited clear nucleoli and scanty cytoplasm by hematoxylin-eosin (HE) stain. (B) Neoplastic cells were positive for CD20, (C) bcl-6, and (D) MUM-1

TABLE 1 Individual patient characteristics and outcomes

No.	Sex/Age	Malignancy	Type of ECMO	ECMO duration days	ECMO weaning	Outcome	References
1	M/54	DLBCL	VA	18 days	yes	alive	Our case
2	Sex (-)/ median age 32, range (22–55)	DLBCL	VV	4 days	-	died	wohlfarth P, et al. [8]
3		ALL	VV	3 days	yes	alive	
4		ATL	VV	25 days	yes	alive	
5		DLBCL	VA	3 days	yes	alive	
6		DLBCL	VV	4 days	yes	alive	
7	M/51	DLBCL	VV	8 days	no	died	Park TS, et al. [9]
8	M/65	PBL	VA	11 days	yes	alive	Allain G, et al. [10]
9	M/24	BL	VA	8 days	yes	alive	Lau V, et al. [6]
10	M/40	T-LBL	VV	8 days	yes	alive	Oto M, et al. [4]
11	F/40	DLBCL	VA	3 days	no	died	Ellen CM, et al. [11]
12	(-) /20	T-ALL	VA	7 days	yes	alive	Lueck C, et al. [5]
13	M/43	HGBCL	VV	6 days	yes	alive	Aboud A, et al. [3]

Abbreviations: ALL, acute lymphoblastic leukemia; BL, burkitt lymphoma; DLBCL, diffuse large B-cell lymphoma; ECMO, extracorporeal membrane oxygenation; F, female; HGBCL, high-grade B-cell lymphoma; M, male; PBL, plasmablastic lymphoma; T-ALL, T-cell acute lymphoblastic leukemia; T-LBL, T-cell lymphoblastic lymphoma; VA, venoarterial; VV, venovenous.

reported [3-6]. If ECMO is used, such as bridging from diagnosis to chemotherapy, patients could be weaned from ECMO [3-5]. Studies have proven that these patients benefit from early admission in the intensive care unit [7,8]. We also present some previously reported cases of hematological malignancies treated with induction chemotherapy using ECMO (Table 1). Table 1 shows patients with hematological malignancies receiving combined use of ECMO and induction chemotherapy. The present case demonstrates the successful removal of ECMO after 18 days through immunochemotherapy and the effectiveness of introducing VA-ECMO into AIDS-associated PCL.

Changes in pharmacokinetics under ECMO make it challenging to predict the relationship between drug dose and side effects [12]. The half-life of 375 mg/m^2 of rituximab was 76.3 hours [13], but the blood concentration of rituximab under VA-ECMO has not been reported. Herein, we measured the patient's blood concentration of rituximab after 48 hours of VA-ECMO, and the result was below the sensitivity of detection. In addition, the cardiac tumor size was not reduced clinically after rituximab monotherapy. Rituximab was possibly adsorbed on to the VA-ECMO membrane. Elahi et al. reported that ECMO with rituximab was effective in a rare case of fulminant infectious mononucleosis complicated with an X-linked lymphoproliferative disorder [14]. We had not been able to find another report on the use of rituximab with VA-ECMO, measurement of rituximab concentration, and its effect under VA-ECMO. Our study suggested that rituximab was not effective, though at least CHOP therapy under VA-ECMO was very useful. However, ECMO is not widely available or easily accessible, so patients with hemodynamic instability due to right ventricular outflow tract obstruction tumors should be transferred to a facility with ECMO capability.

In a life-threatening airway, heart, and vessel compression by a treatable hematological malignant tumor, VA-ECMO can be a temporary treatment option and should be well considered for use in patients with life-threatening AIDS-associated PCL requiring rituximab-combined chemotherapies.

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CONFLICT OF INTERESTS

Not applicable.

AUTHOR CONTRIBUTIONS

Hoyuri Fuseya: conceived presented idea and wrote the manuscript with support from coauthors. Takuro Yoshimura: made substantial contributions to conception of idea and drafting of manuscript. Minako Tsutsumi, Yosuke Nakaya, Mirei Horiuchi, Masahiro Yoshida, Yoshiki Hayashi, and Takafumi Nakao: encouraged primary author to investigate cardiovascular and hematological diseases. Takeshi Inoue: made substantial contributions to diagnose cardiac biopsies. Takahisa Yamane: made substantial contributions to supervise of this work. All authors provided critical feedback and contributed to the final manuscript.

ETHICAL APPROVAL

The use of clinical information was approved by the Research Ethics Committee of Osaka City General Hospital.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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