

CASE REPORT

INTERMEDIATE

CLINICAL CASE

A Rare Complication of Chronic Active Epstein-Barr Virus Infection



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ABSTRACT

A 42-year-old man with a 6-month-long fever was found to have chronic active Epstein-Barr virus infection complicated by aneurysmal coronary arteries with other arteries. In adult patients with this infection, coronary aneurysms are rare but are a poor prognostic factor. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:756-9) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

HISTORY OF PRESENTATION

A 42-year-old man was admitted to our hospital because of a fever lasting 6 months, anterior uveitis, hearing loss, systemic lymphadenopathy, splenomegaly, and abdominal aortic arteritis.

MEDICAL HISTORY

Epstein-Barr virus (EBV) antibody titers were as follows: viral capsid antigen immunoglobulin G (IgG), 1:1280; viral capsid antigen IgM, <1:10; early antigen

IgG, 1:640; and EBV nuclear antigen, 1:80. The EBV-DNA load in peripheral blood was determined to be 3.7×10^3 copies/ 10^6 white blood cells. Monoclonal proliferation of EBV-infected cells was demonstrated in the peripheral blood with Southern blot analysis using EBV-terminal repeat. On the basis of these results, chronic active EBV infection (CAEBV) was diagnosed. Contrast-enhanced computed tomography (CT) showed that the coronary artery was diffusely dilated without aneurysm and that the wall of the abdominal aorta was also thickened, suggesting arteritis without aneurysm (**Figure 1A**). After CAEBV was diagnosed, prednisolone was administered at an initial dosage of 1 mg/kg/day and then slowly tapered depending on its effectiveness. The decreased wall thickness of the abdominal aorta was confirmed with CT (**Figure 1B**).

LEARNING OBJECTIVES

- To consider the rare etiology of coronary and aortic artery aneurysm in patient with chronic active Epstein-Barr virus infection.
- To identify the risk of cardiac complications such as coronary artery aneurysm in patient with chronic active Epstein-Barr virus infection.
- To appreciate the importance of monitoring the progression of coronary artery aneurysm.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis included coronary artery aneurysms associated with inflammatory disorders such as Kawasaki disease, Takayasu disease and Churg-Strauss syndrome, or connective tissue

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disorders such as Marfan syndrome and Ehlers-Danlos syndrome.

INVESTIGATIONS

Two years after the diagnosis of CAEBV, an abdominal aortic aneurysm and bilateral common iliac artery (CIA) aneurysms were discovered with CT just before allogeneic bone marrow transplantation was performed as a curative treatment for CAEBV. The maximum diameter of the aortic abdominal aorta was 34 mm (Figure 1E), and the maximum diameter of the right CIA was 26 mm (Figure 1G). Owing to prolonged fever, CT examination was performed 1 month later and demonstrated a coronary artery aneurysm from the left main trunk through the left anterior descending and right coronary arteries, with a maximum diameter of 7 mm in the left main trunk and 6 mm in the right coronary artery (Figure 1C). Regarding treatment, the decision was made for close monitoring without intervention at that time. The EBV-DNA level in peripheral blood finally decreased to beneath the detection limit. Follow-up CT 6 years after diagnosis of CAEBV showed fusiform dilatation

of the aneurysms, with a maximum diameter of 11 mm in the left main trunk, 7 mm in the right coronary artery (Figure 1D), 40 mm in the abdominal aorta (Figure 1F), and 40 mm in the right CIA (Figure 1H, Table 1). The patient has been followed on aspirin with close monitoring until the present time.

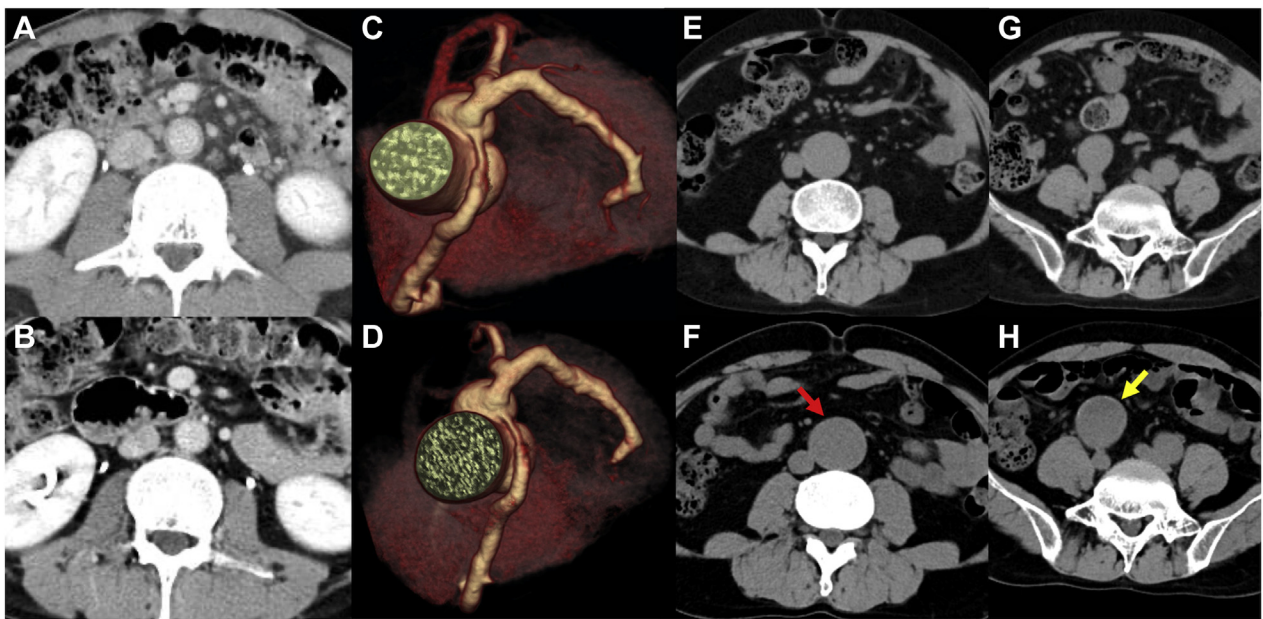
DISCUSSION

Coronary artery aneurysm (CAA) is classically defined as a focal dilatation of more than 1.5 times the diameter of an adjacent artery (1). The prevalence of CAA was reported to be 0.2% to 4.9% of patients undergoing coronary angiogram (2,3). Patients with CAA can be completely asymptomatic, as in our patient, but can present with a variety of symptoms, including chest pain, congestive heart failure, acute coronary syndrome, and sudden cardiac death (1). The Coronary Artery Aneurysm Registry, the largest multicenter registry, found in adult patients a mortality rate of 15.3% and a major adverse cardiac events rate of 31% (4). However, no reports have been

ABBREVIATIONS AND ACRONYMS

- CAA = coronary artery aneurysm
- CAEBV = chronic active Epstein-Barr virus infection
- CIA = common iliac artery
- CT = computed tomography
- EBV = Epstein-Barr virus
- Ig = immunoglobulin

FIGURE 1 Contrast-Enhanced Computed Tomography of the Coronary Artery, Abdominal Aorta, and Iliac Artery



Cross-sectional view of the contrast-enhanced computed tomography (A) at first admission and (B) after prednisolone was administered. (C) Three-dimensional reconstruction of the coronary computed tomographic image 1 month after the allogeneic bone marrow transplantation. (D) The coronary artery aneurysm had further expanded by 4 years after it had first been confirmed. The (E) abdominal aortic aneurysm and (G) the common iliac artery aneurysm 2 years after the diagnosis of CAEBV. Four years later, both the (F) abdominal aorta (red arrow) and (H) right common iliac artery aneurysm (yellow arrow) had expanded.

TABLE 1 Timeline	
Time	Event
2 months before the diagnosis (first admission to our institution)	Coronary artery was diffusely dilated without aneurysm and that the wall of an abdominal aorta was thickened without aneurysm.
Diagnosis of CAEBV	After prednisolone was administered, the wall thickness of an abdominal aorta was decreased.
2 yrs after the diagnosis (allogenic bone marrow transplantation)	An abdominal aortic aneurysm and CIA aneurysm with maximum diameter of 34 mm in the abdominal aorta, and that of 26 mm in the right CIA.
1 month after allogenic bone marrow transplantation	A coronary artery aneurysm from LMT through left anterior descending and RCA with maximum diameter of 7 mm in the LMT, and that of 6 mm in the RCA.
5 yrs after the diagnosis	The EBV-DNA level in peripheral blood decreased to beneath the detection limit.
6 yrs after the diagnosis	Dilation of the aneurysms, with a maximum diameter of 11 mm in the LMT, that of 7 mm in the RCA, and that of 40 mm in the right CIA.

CAEBV = chronic active EBV; CIA = common iliac artery; EBV = Epstein-Barr virus; LMT = left main trunk; RCA = right coronary artery.

published with respect to specific prognosis of patients with CAEBV complicated by CAA.

Cases of CAEBV have various symptoms, including fever, lymphadenopathy, hepatosplenomegaly, and cytopenia, which can lead to such cardiovascular complications as CAA. According to previous studies, of patients with CAEBV, a CAA develops in approximately 9% (5). Pathological studies have revealed that lymphoid infiltration is present in CAA and that these aneurysms result from lymphoid vasculitis (6).

In the present case, an abdominal aortic aneurysm and a CIA aneurysm had already been detected in addition to a CAA at the time of bone marrow transplantation, 2.5 years after disease onset. Furthermore, the aneurysms had gradually enlarged despite successful eradication of EBV-infected cells. Because coronary artery lesions, including dilation, stenosis, and calcification, have been reported to regress within several years after cord blood transplantation, allogeneic hematopoietic stem cell transplantation being performed soon after CAEBV is diagnosed might prevent aneurysms from developing (7). Although the relationships of the size of aneurysms with disease activity or prognosis remain uncertain, high EBV load, fever, and cytopenia are reported to be involved in the cardiovascular complications (7). The present case was considered to be of high risk of development of cardiac complications because of the presence of high EBV load and fever.

With respect to medical treatment for CAAs, the decision was made to administer aspirin alone to

prevent coronary artery disease, because the main etiology of CAA is atherosclerosis (1). In addition, the Coronary Artery Aneurysm Registry has reported that aspirin is the preventative agent most often prescribed (4). Moreover, although a previous report has shown the efficacy of anticoagulation therapy in a specific patient with the complication of thrombus (8), the present patient had no evidence of thrombus of the coronary artery.

FOLLOW-UP

The current practice guideline does not recommend a specific approach to monitoring CAA (9). In the present case, greater attention should have been paid to monitor the size of the CAA by performing serial contrast-enhanced CT.

CONCLUSIONS

Despite the scarce evidence of CAAs in cases of CAEBV, carefully investigating cardiovascular complications, including CAAs, is important because they are poor prognostic factors.

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KEY WORDS aortic artery aneurysm, chronic active Epstein-Barr virus infection, computed tomography, coronary artery aneurysm