Endovascular therapy for intracranial infectious aneurysms associated with a left ventricular assist device: illustrative case

Tomohiro Okuda, MD,1 Ataru Nishimura, MD, PhD,1 Koichi Arimura, MD, PhD,1 Katsuma Iwaki, MD,1 Takeo Fujino, MD, PhD,2 Tomoki Ushijima, MD, PhD,3 Hiromichi Sonoda, MD, PhD,3 Yoshihisa Tanoue, MD, PhD,3 Akira Shiose, MD, PhD,3 and Koji Yoshimoto, MD, PhD1

Departments of 1Neurosurgery, 2Cardiovascular Medicine, and 3Cardiovascular Surgery, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

BACKGROUND Cerebrovascular events and infection are among the most common complications of left ventricular assist device (LVAD) therapy. The authors reported on a patient with an infectious intracranial aneurysm (IIA) associated with LVAD infection that was successfully occluded by endovascular therapy.

OBSERVATIONS A 37-year-old man with severe heart failure received an implantable LVAD. He was diagnosed with candidemia due to driveline infection 44 months after LVAD implantation, and empirical antibiotic therapy was started. After 4 days of antibiotic treatment, the patient experienced sudden dizziness. Computed tomography (CT) revealed subarachnoid hemorrhage in the right frontal lobe, and CT angiography revealed multiple aneurysms in the peripheral lesion of the anterior cerebral artery (ACA) and middle cerebral artery. Two weeks and 4 days after the first bleeding, aneurysms on the ACA ruptured. Each aneurysm was treated with endovascular embolization using n-butyl cyanoacrylate. Subsequently, the patient had no rebleeding of IIAs. The LVAD was replaced, and bloodstream infection was controlled. He received a heart transplant and was independent 2 years after the heart transplant.

LESSONS LVAD-associated IIAs have high mortality and an increased risk of surgical complications. However, endovascular obliteration may be safe and thus improve prognosis.

https://thejns.org/doi/abs/10.3171/CASE21559

KEYWORDS infectious aneurysm; endovascular therapy; left ventricular assist device

Left ventricular assist devices (LVADs) are mechanical pumps used to bridge heart transplantation or destination therapy in patients with severe heart failure. Despite the progress of LVAD design and treatment protocols, neurological complications involving ischemic and hemorrhagic strokes remain major causes of morbidity and mortality in patients with LVAD. There are few reports on intracranial hemorrhage or subarachnoid hemorrhage (SAH) due to intracranial infectious aneurysms (IIAs) in patients with bloodstream infections associated with LVAD. To date, there have been no controlled trials for the management and treatment of IIAs. We present the extremely rare case of a patient with an LVAD and a ruptured IIA, which was successfully treated with endovascular embolization. The patient had a good postoperative course.

Illustrative Case

A 37-year-old man with severe heart failure due to congenital transposition of the great arteries type I received an implantable LVAD, a Jarvik 2000 pump (Jarvik Heart, Inc.), as a bridge to transplantation. He received appropriate anticoagulation therapy with warfarin for LVAD. He was treated with antibiotic therapy for repeated

ABBREVIATIONS ACA = anterior cerebral artery; CI = confidence interval; CT = computed tomography; CVA = cerebrovascular accident; IIA = infection intracranial aneurysm; LVAD = left ventricular assist device; MIFA = middle internal frontal artery; NBCA = n-butyl cyanoacrylate; RR = relative risk; SAH = subarachnoid hemorrhage.

INCLUDE WHEN CITING Published March 14, 2021; DOI: 10.3171/CASE21559.

SUBMITTED September 29, 2021. ACCEPTED December 9, 2021.

© 2022 The authors, CC BY-NC-ND 4.0 (http://creativecommons.org/licenses/by-nc-nd/4.0/)
driveline infection, and surgical debridement of the driveline exit site was performed twice when the infection deteriorated.

The patient was febrile (38.6°C) 44 months after LVAD implantation. Laboratory studies revealed an elevated white blood cell count (9,800/mm³), neutrophil left shift (neutrophil 90.3%, lymphocyte 5.1%, monocyte 2.5%, eosinophil 1.1%, basophil 0.2%), and elevated C-reactive protein (5.08 mg/dl) and β-D glucan (74.7 pg/ml) levels. His blood cultures were negative, *Candida albicans* grew in the pus culture from driveline at the exit site, and the β-D glucan level was elevated. The patient was subsequently diagnosed with candidemia due to driveline infection, and empirical antibiotic therapy with intravenous micafungin and amphotericin B was initiated.

He experienced dizziness 4 days after the onset of fever. A computed tomography (CT) scan of his head revealed a small SAH in the right frontal lobe (Fig. 1A). Cranial CT angiography revealed 2-mm aneurysms on the peripheral segment of the right anterior cerebral artery (ACA) (Fig. 1B and C) and middle cerebral artery (MCA). However, there was no evidence of an aneurysm around the SAH. The patient was diagnosed with IIAs due to candidemia and continued his medical therapy.

Four days after the first onset of SAH, he had a headache, and a CT scan revealed SAH in different lesions of the right frontal lobe with previous bleeding (Fig. 1D). CT angiography and digital subtraction angiography revealed an aneurysm in the middle internal frontal artery (MIFA) (Fig. 1E and F). The aneurysm was considered the source of bleeding, and we performed endovascular embolization to prevent rebleeding. A microcatheter was navigated to the proximal portion of the aneurysm on the MIFA. A provocative test with superselective injection of intraarterial xylocaine (10 mg) to confirm the safety of occlusion of the artery produced negative results. Subsequently, 0.07 ml of 20% n-butyl cyanoacrylate (NBCA) was injected until the aneurysm was completely occluded (Fig. 2A–C). No postoperative neurological complications were observed, and a CT scan obtained the day after the treatment revealed no evidence of cerebral infarction (Fig. 2D).
Ten days after the first treatment, a follow-up CT scan and CT angiography revealed new intracerebral hemorrhage inside the right frontal lobe and enlargement of the aneurysm on the anterior internal frontal artery inside the hematoma. Endovascular embolization of the aneurysms was performed using the same strategy (Fig. 3). After the treatments, the patient had no neurological symptoms or rebleeding of IIAs. Antibiotic therapy was changed to intravenous amphotericin B and voriconazole and continued for approximately 4 weeks.

One month after the endovascular therapy, the implantable LVAD was removed, and extracorporeal LVAD was temporarily inserted. After the bloodstream infection was controlled, he underwent implantation of Jarvik 2000 PA again. Finally, he received a heart transplant 11 months after LVAD replacement. He was free from neurological symptoms and was independent 2 years after the heart transplant.

Discussion

LVAD-supported patients are at high risk of bloodstream infection associated with the implantation of an LVAD (~60%), and bloodstream infection is a common cause of morbidity and mortality. Persistent bloodstream infections may increase the risk of all-cause stroke 7-fold, with the most common source being driveline infections (57%). A recent meta-analysis has suggested an association between bloodstream infection and cerebrovascular accident (CVA) in patients with LVAD. In this meta-analysis, there was an association between bloodstream infection and increased incidence of hemorrhagic CVA after LVAD (relative risk [RR] 5.28, 95% confidence interval [CI] 2.65–10.53) with minimal heterogeneity ($I^2 = 30$).

Participants with bloodstream infections were more likely to develop ischemic CVA (RR 2.18, 95% CI 1.23–3.84) than patients without bloodstream infections. Treatment of such driveline infections can be difficult, with severely complicated cases requiring device exchange. IIAs are rare aneurysms reported in 0.7%–5.4% of all cerebral aneurysms with high mortality. These complications are typically associated with infective endocarditis, with a rate of 2%–4%. They could arise from bacterial invasion into the vascular walls in the presence of vascular injury, atherosclerotic plaque, or preexisting aneurysms. Treatment strategies for IIAs, including antibiotic therapy, surgery, and endovascular therapy, are controversial because there are no randomized trials for the management of IIAs. However, it is generally supported by antibiotic therapy for the causative pathogen for $\geq 2$ weeks to unruptured IIAs. Surgery with or without bypass and endovascular embolization may be indicated if IIAs rupture or enlarge under medical treatment. Surgical treatment for patients with LVAD is associated with a high risk of hemorrhagic complications due to anticoagulation therapy with warfarin. Furthermore, LVAD-supported patients have been reported to have coagulopathy induced by von Willebrand factor defects caused by LVAD-driven circulation. Moreover, if general anesthesia is needed for surgery with craniotomy, patients with LVADs are at a high risk of cardiopulmonary complications, probably because of altered hemodynamics due to continuous blood flow. Consecutively, LVAD-supported patients potentially have a higher risk of complications associated with surgical therapy than patients without LVAD. Therefore, we selected endovascular treatment after medical treatment. Endovascular therapy for IIAs has a high success rate and safety of endovascular embolization with NBCA for IIAs in patients.
undergoing open-heart surgery and exposed to anticoagulants. Theoretically, placing foreign materials, including coils and liquid embolization agents, into an infected vessel could extend the infection and result in brain abscess or meningitis. Moreover, it is a concern that neurointerventional treatment using embolization substance for IAAs of patients with an LVAD has a higher risk of the focal infection of the cerebral vessel persisting or worsening than patients without LVAD because an infected LVAD remains in the body. However, a review article reported no evidence suggesting continued infection due to the presence of coils and stents in IIAs, and endovascular treatment of IIAs has become more favored recently. Therefore, we performed endovascular embolization for IIA after rerupture after endovascular repair, the patient recovered to the point of receiving a heart transplant without suffering from brain abscess or meningitis.

**Observations**

Only one study reported an IIA associated with LVAD infection successfully treated with endovascular therapy. In a previous report, a ruptured MCA aneurysm due to Klebsiella rhinoscleromatis was embolized with an ethylene-vinyl alcohol copolymer (Onyx, Covidien). In our case, an IIA in the ACA due to candidemia associated with LVAD infection was successfully treated with NBCA without neurological complications. We first reported a good long-term postoperative course in a patient with IIAs associated with LVAD and treated with endovascular therapy.

**Lessons**

LVAD-supported patients have a risk of cerebrovascular events, and LVAD-associated cerebrovascular events in the IIA setting are associated with high mortality. Surgical treatment for patients with LVAD has a higher hemorrhagic complications risk than for patients without LVAD because of coagulopathy. However, endovascular embolization with NBCA against IAAs in patients with LVAD may be as safe as for patients without LVAD, improving prognosis.

**Acknowledgments**

We thank the individuals who contributed to the study or manuscript preparation but did not meet all criteria for authorship.

**References**

1. Kirkin JK, Naftel DC, Kormos RL, et al. Fifth INTERMACS annual report: risk factor analysis from more than 6,000 mechanical circulatory support patients. *J Heart Lung Transplant*. 2013;32(2):141–156.
2. Izzy S, Rubin DB, Ahmed FS, et al. Cerebrovascular accidents during mechanical circulatory support. *Stroke*. 2018;49(5):1197–1203.
3. Remirez JM, Sabey Y, Baca M, et al. Mycotic intracranial aneurysm secondary to left ventricular assist device infection. *J Vasc Interv Neurol*. 2017;9(3):23–25.
4. Ducruet AF, Hickman ZL, Zacharia BE, et al. Intracranial infectious aneurysms: a comprehensive review. *Neurosurv Rev*. 2010;33(1):37–46.
5. Koval CE, Rakita R. Ventricular assist device related infections and solid organ transplantation. *Am J Transplant*. 2013;13(suppl 4):348–354.
6. Trachtenberg BH, Cordero-Reyes AM, Aldeiri M, et al. Persistent blood stream infection in patients supported with a continuous-flow left ventricular assist device is associated with an increased risk of cerebrovascular accidents. *J Card Fail*. 2015;21(2):119–125.
7. Kanjanahattakij N, Horn B, Abdulhadi B, Wongjarupong N, Mezue K, Rattanawong P. Blood stream infection is associated with cerebrovascular accident in patients with left ventricular assist device: a systematic review and meta-analysis. *J Artif Organs*. 2018;21(3):271–277.
8. Nakahara I, Taha MM, Higashi T, et al. Different modalities of treatment of intracranial mycotic aneurysms: report of 4 cases. *Surg Neurol*. 2006;66(4):405–410.
9. Bennett JE, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett’s Principles and Practice of Infectious Diseases. Elsevier; 2014.
10. Esenkaya A, Duzgun F, Cinar C, et al. Endovascular treatment of intracranial infectious aneurysms. *Neuroradiology*. 2016;58(3):277–284.
11. Nascimbene A, Neelamegham S, Frazier OH, Moake JL, Dong JF. Acquired von Willebrand syndrome associated with left ventricular assist device. *Blood*. 2016;127(25):3133–3141.
12. Cheng-Ching E, John S, Bain M, et al. Endovascular embolization of intracranial infectious aneurysms in patients undergoing open heart surgery using n-butyl cyanoacrylate. *Intervent Neurol*. 2017;6(1-2):82–89.

**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Nishimura, Okuda, Arimura. Acquisition of data: Okuda, Fujino, Sonoda. Analysis and interpretation of data: Okuda, Fujino. Drafting the article: Okuda. Critically revising the article: Nishimura, Tanoue. Reviewed submitted version of manuscript: Nishimura, Iwaki, Fujino, Sonoda, Shiose. Approved the final version of the manuscript on behalf of all authors: Nishimura. Administrative/technical/material support: Ushijima, Sonoda, Shiose. Study supervision: Arimura, Iwaki, Yoshimoto.

**Correspondence**

Ataru Nishimura: Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan. nataru@ns.med.kyushu-u.ac.jp.