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

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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 reruptured. 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.

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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.[1] 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.[2] 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.[3] To date, there have been no controlled trials for the management and treatment of IIAs.[4]

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.

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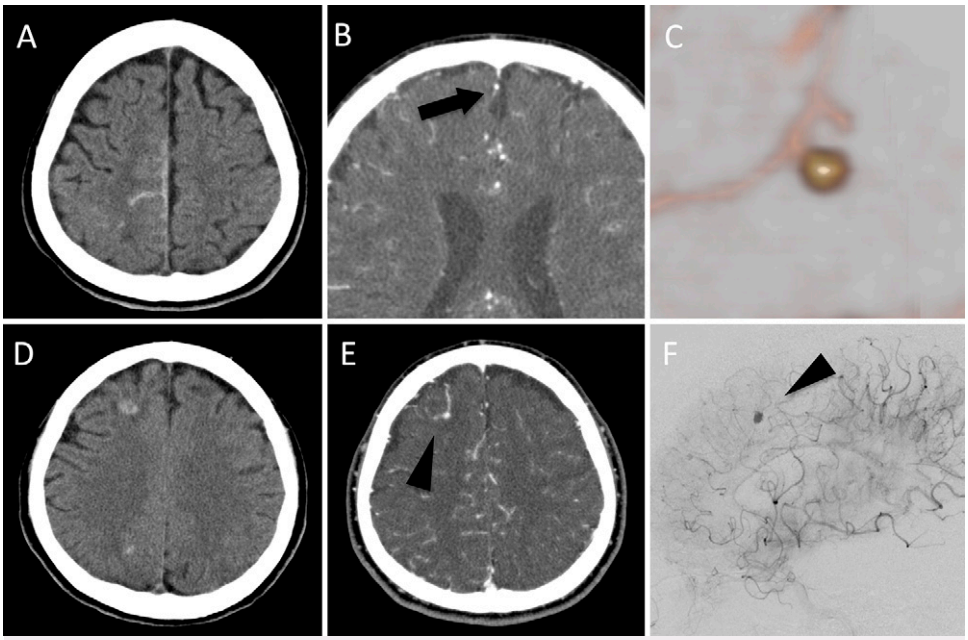

FIG. 1. A: The initial CT scan reveals small SAH in the right frontal lobe. **B and C:** CT angiography reveals a tiny aneurysm on the anterior internal cerebral artery but not near the hematoma (*arrow*). **D:** Four days after the first bleeding, CT scan demonstrates SAH and intraparenchymal hematoma on another site of the right frontal lobe. **E and F:** CT angiography and digital subtraction angiography reveal a 4-mm aneurysm on the MIFA in the hematoma (*arrowheads*).

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/mm), 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).

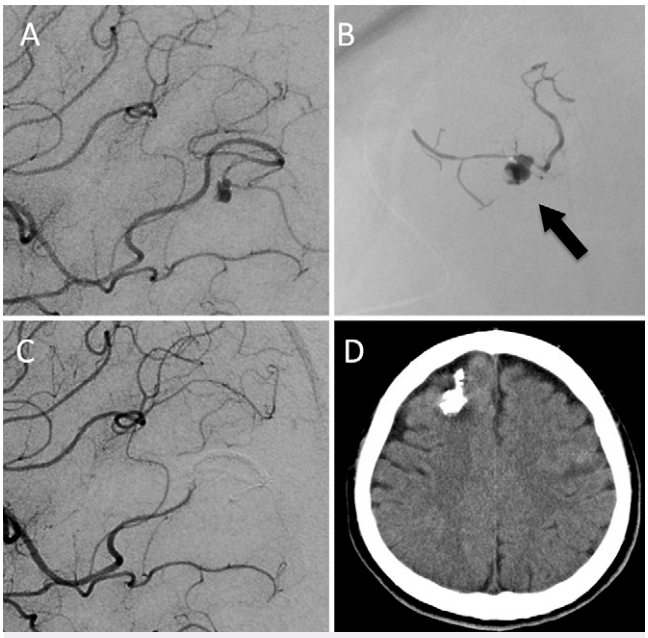

FIG. 2. A–C: The aneurysm on the MIFA is treated with endovascular embolization. NBCA was filled into the aneurysm (*arrow*). **D:** Postoperative CT scan reveals no evidence of cerebral infarction.

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.[5] Persistent bloodstream infections may increase the risk of all-cause stroke 7-fold, with the most common source being driveline infections (57%).[6] 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.[7] 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.[8] 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.[9] 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 ≥2 weeks to unruptured IIAs.[10] 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.[11] 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

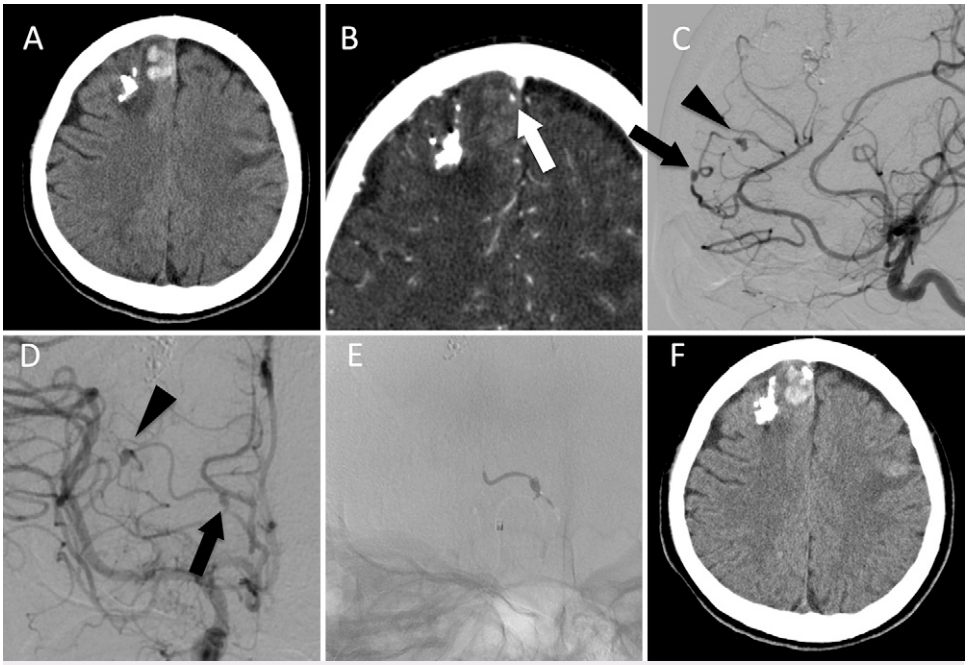

FIG. 3. A: Ten days after the first treatment, CT scan reveals another intracerebral hematoma on the medial part of the right frontal lobe. **B:** CT angiography reveals enlargement of the aneurysm on the right ACA, existing in the hematoma (*white arrow*). **C and D:** Digital subtraction angiography demonstrates the aneurysm (*black arrows*) and another distally located aneurysm (*arrowheads*) on the right anterior internal frontal artery. **E:** A microcatheter is navigated to near the proximal aneurysm. NBCA is injected and filled into the aneurysm. **F:** Postoperative CT scan demonstrates NBCA cast on the hematoma.

undergoing open-heart surgery and exposed to anticoagulants.[12] 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,[4] and endovascular treatment of IIAs has become more favored recently. Therefore, we performed endovascular embolization for IIA after rerupture after regrowth under antibiotic therapy. 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.[3] 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.

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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, Ushijima, Sonoda, Tanoue, 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.

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