Successful Clot Retrieval Therapy of Cerebral Embolism in a Pediatric Patient with Ventricular Assist Device: A Case Report

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Objective: We describe a successful clot retrieval therapy of cerebral embolism while on a ventricular assist device (VAD) in a pediatric patient.

Case Presentations: A 15-year-old boy underwent an intracorporeal type left VAD placement as a bridge to heart transplantation for severe heart failure related to dilated cardiomyopathy. Eight months later, he suddenly presented with right hemiparesis and dysarthria. A head computed tomography (CT) scan demonstrated a hyperdense sign in the left middle cerebral artery (MCA), and cerebral angiography revealed occlusion of the left MCA M1 distal segment. Mechanical thrombectomy with a stent clot retrieval device achieved complete recanalization. His symptoms rapidly improved and disappeared.

Conclusion: Clot retrieval therapy may be useful for treating a pediatric patient with cerebral embolism related to VAD therapy.

Keywords ▶ acute clot retrieval therapy, mechanical thrombectomy, cerebral embolism, pediatric patient, ventricular assist device

Introduction

A ventricular assist device (VAD) is an intracorporeal or extracorporeal type instrument used to support the pump function of the heart. Recently, it has been commonly used as the standard of care for patients with end-stage severe heart failure, showing a rapid increase.1,2) In Japan, this device is used as a bridge to transplantation (BTT) in patients waiting for heart transplantation in addition to its temporary use for acute severe heart failure. With the enforcement of the Revised Organ Transplant Law in Japan, the number of VAD-implanted children waiting for heart transplantation will increase. Embolic stroke is a known chronic complication in VAD patients; however, only a few cases have been reported on acute revascularization therapy.3–6)

Here, we describe a pediatric patient implanted intracorporeal type left VAD in whom clot retrieval therapy was effective for occlusion of the left middle cerebral artery (MCA), and discuss with a review of the literature.

Case Presentation

Case: A 15-year-old boy; right-handed; height, 183 cm; body weight, 56 kg.
Complaint: Right hemiparesis and dysarthria.
Medical history: He was registered as a recipient for heart transplantation due to severe heart failure related to dilated cardiomyopathy 8 months before. As a BTT, an intracorporeal type left VAD (HeartMate II, Thoratec, Pleasanton, CA, USA) was implanted in the Department of Cardiovascular Surgery in our hospital. Subsequently, antithrombotic therapy with warfarin (3.25 mg/day) and aspirin (100 mg/day) was continued at the VAD Outpatient Clinic.
of the Department of Cardiology in our hospital. The medications had been administrated so that the prothrombin international normalized ratio (PT-INR) was 2.0 to 2.5.

**Present illness**
He presented with headache followed by right hemiparesis and dysarthria at home at 1:00 a.m., and was transferred to our hospital by ambulance at 2:18 a.m.

**Findings on admission**
Concerning consciousness, the Glasgow Coma Scale (GCS) score was 14 points. Aphasia was not observed, but dysarthria and severe right hemiparesis were noted. The National Institute of Health Stroke Scale (NIHSS) score was 11 points. A coagulation function test on arrival showed a PT-INR of 2.31.

**Neuroradiological findings**
Head computed tomography (CT) revealed a hyperdense MCA sign in the horizontal (M1) segment of the left MCA (Fig. 1). However, there was no early ischemic change in the cerebral parenchyma, and the Alberta Stroke Program Early CT Score (ASPECTS) was 10 points. Under a tentative diagnosis of acute cerebral embolism, emergency cerebral angiography was carried out, as the intravenous therapy of a recombinant tissue-type plasminogen activator (rt-PA) (alteplase) could not be indicated due to antithrombotic therapy. The right femoral artery had been surgically treated for a pseudoaneurysm, which had developed after intra-aortic balloon pumping removal on heart failure treatment. Therefore, the left femoral artery was punctured under local anesthesia 3 hours after onset, at 4:00 a.m. A continuous-flow VAD was used, but palpation showed relatively favorable self-beats of the left femoral artery, facilitating puncture. Cerebral angiography revealed incomplete occlusion at the distal M1 segment of the left MCA (Fig. 2). Anterograde blood flow to the left MCA territory was observed but was delayed. Under a diagnosis of VAD-derived acute cerebral embolism, clot retrieval therapy was carried out.

**Endovascular treatment**
An 8-Fr OPTIMO balloon guide catheter (Tokai Medical Products, Inc., Kasugai, Aichi, Japan) was advanced to the left internal carotid artery, and a microcatheter (Trevo Pro18, Stryker, Kalamazoo, MI, USA) was guided into the left M2 ascending branch. A stent retriever (Trevo ProVue 4 × 20 mm, Stryker) was deployed across the affected segment. Fluoroscopy confirmed that stent dilation was insufficient after 5-minute deployment, but the stent and microcatheter were withdrawn while proximal occlusion using the guide catheter with a balloon and aspiration from the guide using a 60 mL syringe. Consequently, the retrieval clot volume was very small. Cerebral angiography did not show any marked improvement, suggesting occlusion related to a hard thrombus formed in the VAD over a long period. The microcatheter was switched to a Marksman (Medtronic, Minneapolis, MN, USA), and approached in the left M2 ascending branch. A 6 × 30 mm Solitaire FR revascularization device (Medtronic) was deployed across the affected segment. After 5 minutes of the deployment, the stent retriever was withdrawn with a same manipulation. In the stent, the thrombi had been retrieved. Cerebral angiography (3 hours and 45 minutes after onset, 45 minutes after puncture) confirmed the complete recanalization of the left MCA. In addition, the lateral lenticulostriate artery originating from the distal M1 segment was visible (Fig. 2), and there were no delayed flow and distal emboli in the left MCA territory. The retrieved thrombi were black and hard, suggesting typical fibrin thrombi (Fig. 3). Immediately after clot retrieval therapy, CT shows neither any new cerebral infarction and hemorrhagic transformation nor contrast-medium leakage. The symptoms rapidly improved
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and obtained favorable outcome. Recent marked technical advances have improved the long-term durability of VADs, minimizing their size and improving the results of treatment. Currently, extracorporeal type VADs for temporary heart-function assistance and intracorporeal type VADs, which facilitate home care, are commercially available. In Europe and the United States, the latter has been increasingly used as a BTT for patients with severe heart failure and standard treatment for long-term home care (destination therapy (DT)).

On the other hand, in Japan, intracorporeal type VADs can be indicated, as a BTT, for patients waiting for heart transplantation only. With the enforcement of the Revised Organ Transplant Law, the number of organ transplants after brain death has slightly increased, and, in the future, the number of intracorporeal type VAD patients living at home/with a social life may increase. However, the 1- and 2-year survival rates in adults implanted intracorporeal type, continuous-flow VADs, which are commonly used in Europe and the United States, are reportedly 80% and 70%, respectively. The frequent causes of death include stroke, multiple organ failure, and infectious disease. In particular, stroke develops in approximately 20% of VAD patients. Ischemic cerebrovascular disease is a limitation of VADs, which are set in systemic circulation as a prosthesis, and such devices may cause cerebral hemorrhage related to antithrombotic

Discussion

We achieved clot retrieval therapy to treat cerebral embolism in a boy implanted an intracorporeal type left VAD, after recanalization, leading to complete disappearance after 1 hour. After intervention, the dose of warfarin was increased, establishing a target PT-INR of 2.5 to 3.0. After 1 week, CT did not reveal any cerebral infarction or hemorrhagic transformation, and the modified Rankin Scale score was 0 at discharge to home.

Fig. 2  (A) Initial frontal projection of the left ICA angiogram showing incomplete occlusion of the left MCA with delayed flow in the distal branches of MCA. (B) Final left ICA angiogram confirming complete recanalization of the left MCA, including lateral lenticulostriate arteries (black arrowheads). ICA: internal cerebral artery; MCA: middle cerebral artery

Fig. 3  Three black clots retrieved from the left MCA. MCA: middle cerebral artery
therapy. In patients with VAD-related stroke, the incidence of ischemic cerebrovascular disease is estimated to be 2 to 6 times higher than that of cerebral hemorrhage. To prevent thromboembolic complications in VAD patients, anticoagulant therapy with warfarin and antiplatelet therapy with aspirin are routinely combined. An optimal PT-INR for anticoagulant therapy slightly varies among devices, but a target PT-INR was established as 1.5 to 2.0 with respect to the device used in the present case. However, the coagulation-fibrinolysis system and responses to anticoagulants differ between children and adults; a consensus regarding appropriate anticoagulant therapy for VAD-implanted children has been controversial. In the present case, the physical status was similar to that of adult males, but the dose of warfarin had been regulated, targeting a higher PT-INR, 2.0 to 2.5, in the field of pediatrics. However, cerebral embolism occurred although the PT-INR was within the target range. A recent study reported that the incidence of stroke in VAD-implanted children was 29%, emphasizing the necessity of adequate anticoagulant therapy matched to individual patients.

The incidence of ischemic cerebrovascular disease in pediatrics is estimated 1.2 to 13.0 per 100,000 per year. However, its etiologies vary, and the states of occluded blood vessels or the coagulation-fibrinolysis system differ among conditions such as age. Therefore, no guidelines for the treatment of childhood cerebral infarction have been established. For adults, thrombolytic therapy by intravenous rt-PA administration for acute cerebral ischemia is strongly recommended, but its efficacy in children remains to be clarified. In the International Pediatric Stroke Study, the results were less favorable than in adults. Mechanical thrombectomy with stent retriever for acute cerebral infarction is also recommended for patients aged 18 years or older based on the results of several clinical studies, but there have been only several reports in pediatrics. For patients with VAD-related cerebral embolism, intravenous rt-PA therapy may not be indicated due to the anticoagulant therapy-related prolongation of the PT-INR, as demonstrated in the present case; mechanical thrombectomy is an important treatment option. However, anticoagulant therapy may deteriorate the neurological symptoms related to hemorrhagic transformation after recanalization; the indication of mechanical thrombectomy must be carefully discussed.

There have been four case reports of endovascular treatment for cerebral embolism during VAD support in the literature. Of these, three consisted of intra-arterial fibrinolytic therapy with rt-PA in a 2-year-old girl and mechanical thrombectomy with a Solitaire FR revascularization device (Medtronic) in 8- and 9-year-old boys. These three children showed favorable outcome. In these, cerebral embolism might occur during hospitalization; prompt diagnosis and treatment may have contributed to a favorable prognosis. In endovascular treatment for VAD patients, the following points must be considered: the femoral artery may not be palpable in non-pulsatile continuous-flow VAD-implanted patients, and echo-guided puncture is useful; and catheter procedures must be carefully conducted because VAD outflow connects to the ascending aorta. Furthermore, Madaelil et al. retrospectively reviewed 22 children who underwent mechanical thrombectomy for acute ischemic stroke, and reported a high recanalization rate and favorable outcome, suggesting the efficacy of this intervention in children. The child-specific limitations of cerebral endovascular treatment include the necessity of general anesthesia, restrictions for contrast-medium or radiation use, physical status-related difficulty in vascular puncture, and restrictions for the selection of devices/procedures. Fortunately, the physical status of our 15-year-old patient was similar to that of adult males, and it was possible to perform mechanical thrombectomy with stent retriever under local anesthesia through proximal occlusion using a guide catheter with a balloon and blood suction. In the above 8-year-old boy, blood suction alone without proximal occlusion using a 6-Fr guide catheter during withdrawal of stent was performed under general anesthesia. In a 2-year-old boy, who may be the youngest patient in the literature, thrombectomy with a 4-Fr guide catheter and 3- and 4 × 20 mm Trevo XP ProVue Retriever stents (Stryker) was performed under general anesthesia. There is no description regarding blood suction, but sufficient blood suction may have been difficult, considering the physical status. Even in pediatrics, mechanical thrombectomy using stent retriever may be facilitated under the selection of an adequate device on the basis of physical condition and blood suction in accordance with the circumstances. On the other hand, concerning the use of drugs/devices, the safety of many products in children has not been established. In particular, devices for mechanical thrombectomy, for which indications are frequent in elderly persons, were developed, assuming their use in adults; the safety in children has not been established. In the package inserts of the Solitaire FR retriever (Medtronic) used in the present case, it is described that neither the efficacy nor safety in patients under 22 years old has been confirmed. We adopted this device after obtaining...
informed consent from the patient’s family through conferences with the Department of Neurosurgery, Department of Emergency and Critical Care Medicine, and Department of Cardiology. Subsequently, we considered it necessary to review the use of a stent retriever for acute cerebral infarction in children at the Ethics Review Board, and obtained retrospective approval.

When performing intravenous rt-PA therapy or mechanical thrombectomy for patients with acute cerebral infarction, the interval from onset until the start of treatment is an important factor associated with the prognosis, and a reduction in the interval is strongly recommended. On the other hand, intravenous rt-PA injection therapy for childhood cerebral infarction was less effective than in adults. As the reason for this, a prolonged interval until diagnosis/treatment initiation was indicated. According to a study regarding mechanical thrombectomy in children published by Madaelil et al., 5.35 and 13.5 hours (mean) were required until recanalization for anterior and posterior circulation, respectively. In the present case, recanalization was achieved in a short period, that is, 3 hours and 45 minutes after onset. This was possibly because the cooperative management of cerebral embolism, involving examinations by the Department of Emergency and Critical Care Medicine and Department of Cardiology and a request to the Neuroendovascular Therapy Team, in the intracorporeal type VAD-implanted patient at home, was promptly conducted based on a close collaboration with the two departments. In endovascular therapy for pediatric acute ischemic stroke, its necessity should be reviewed by several departments, including the Department of Pediatrics and Department of Neurology. It is more important to establish an in-hospital system from prompt diagnosis to treatment than achieving the efficacy of cerebral endovascular therapies such as mechanical thrombectomy. In particular, recently, VAD for infants/children became commercially available although they are extracorporeal type products. To bridge to heart transplantation in VAD-implanted children, who may further increase in the future, it is important to establish a management system considering the onset of cerebral embolism.

Conclusion

We performed mechanical thrombectomy using a stent retriever for cerebral embolism while on an intracorporeal type left VAD in a pediatric patient and obtained favorable outcome. Acute revascularization by neurointervention may be effective for cerebral embolism in VAD-implanted children, and prompt diagnosis and treatment may be necessary.

Disclosure Statement

The first author and co-authors have no conflicts of interest.

References


