A Young Patient with Emery-Dreifuss Muscular Dystrophy Treated with Endovascular Therapy for Cardioembolic Stroke: A Case Report

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We had a case of Emery-Dreifuss muscular dystrophy (EDMD) in an 18-year-old woman who underwent endovascular therapy for a cardioembolic stroke. At 5 years old, she showed a high creatine kinase level and atrial fibrillation on electrocardiography in our hospital. Finally, she was diagnosed as having EDMD by genetic screening that revealed mutations in the LMNA gene (c.810 + 1G > T). Before this event, she received no medications. At 18 years old, she was admitted to our hospital > 8 hours after the onset of sudden consciousness disturbance. Neurological examination on admission revealed consciousness disturbance and right hemiplegia. Magnetic resonance imaging revealed a cerebral infarction in the left insular cortex and putamen with left internal carotid artery occlusion. We performed endovascular therapy and completely recanalized her left internal carotid artery. Thereafter, her neurological symptoms improved. She was subsequently transferred to a rehabilitation hospital. EDMD is a rare genetic muscular disease that mainly presents with contractures, weakness, and cardiac conduction abnormalities. Although patients with EDMD are young with low $CHADS_2$ score, they have a disease-specific cardiovascular pathogenesis caused by a fatal risk factor. Therefore, we consider anticoagulant therapy necessary to prevent thrombotic events, even if the $CHADS_2$ score is low, in patients with EDMD.

Key words: Emery-Dreifuss muscular dystrophy, ischemic stroke, atrial fibrillation, heart failure, anticoagulant therapy

INTRODUCTION

Emery-Dreifuss muscular dystrophy (EDMD) is a rare genetic muscular disease [1]. It can be inherited as an X-linked recessive, autosomal dominant, or autosomal recessive disorder [2]. The characteristics of EDMD present mainly as contractures, muscle weakness, and cardiac conduction abnormalities [3]. Patients develop slowly progressive muscle weakness and atrophy during the first three decades of life [1]. Sudden systemic thrombosis will occur, caused by cardiac abnormalities [5]. Consequently, patients show limb paresis and gait disturbances. In general, patients with EDMD have no risk factors of lifestyle-related diseases such as hypertension, hyperlipidemia, and diabetes mellitus [1, 3]. Their $CHADS_2$ score is usually low. Therefore, the thrombotic prophylaxis in EDMD is made challenging by the limited knowledge about the disease-specific cardiovascular pathogenesis. Herein, we describe a rare case of EDMD in the setting of endovascular therapy for a cardioembolic stroke and discuss the necessity of anticoagulation therapy to prevent thrombotic events.

CASE REPORT

The patient was an 18-year-old woman with contracture of the elbows, knees, and heels with muscle wasting. Her birth history was uneventful. At age 3 years, she could not run fast and had mild weakness of both upper limbs. When she was 5 years old, she was brought to our hospital. Contractures of the elbows, knees, and heels were obvious in her physical examination. Her serum creatine kinase level was high (731 U/L, normal < 140 U/L), and electrocardiography revealed a conduction abnormality as an atrial fibrillation (AF). When she was 9 years old, she was diagnosed as having EDMD by genetic screening, which revealed mutations in the LMNA gene (c.810 + 1G > T), at another hospital. Although she had undergone catheter ablation several times, she was not treated with any medication, including anticoagulants.

At age 18 years, she was admitted to the emergency department of our hospital because of sudden consciousness disturbance > 8 hours after the onset. Neurological examination on admission revealed consciousness disturbance (Japan Coma Scale score of 20), disorientation, right conjugate deviation, slight dysarthria, and right hemiplegia. Her National Institutes of Health Stroke Scale (NIHSS) score was 19. Physical examination revealed a blood pressure of 110/70 mm Hg and an irregular heart rate of 70 beats/min. The laboratory data upon admission showed that her blood glucose, HbA1c, and LDL-cholesterol levels were within their normal ranges, but her B-type natriuretic peptide level was 465.6 pg/mL. Electromyography

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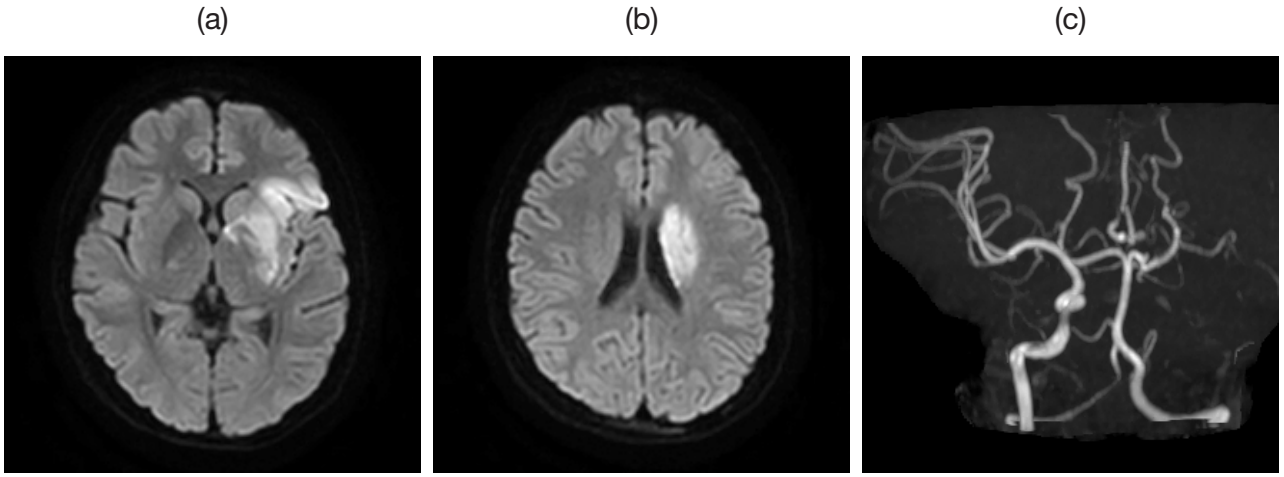

Fig. 1 The magnetic resonance image obtained at admission shows a cerebral infarction in the left insular cortex and putamen (a, b). The magnetic resonance angiogram shows a left internal carotid artery occlusion (c).

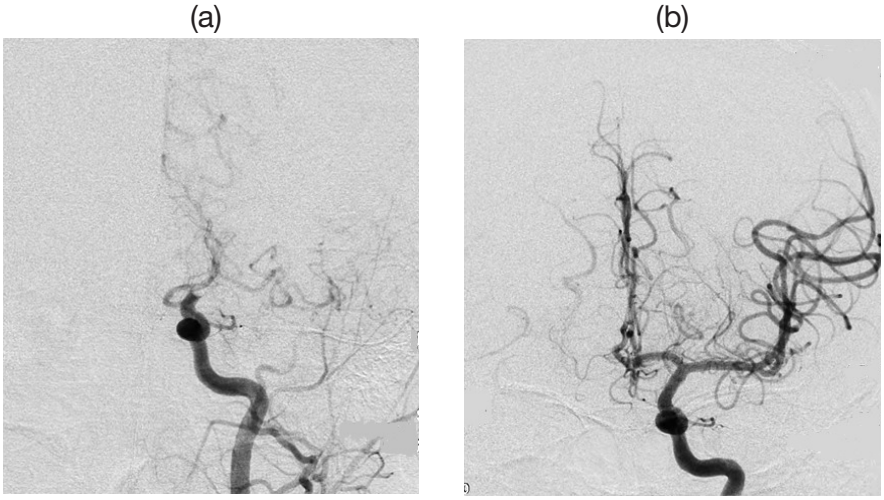

Fig. 2 (a) The left internal carotid artery angiogram shows an occlusion at its terminal. (b) After endovascular therapy, the left internal carotid artery was completely recanalized.

revealed atrial fibrillation with premature ventricular contraction. Her cardiac ultrasonogram showed mild atrial and severe ventricular dilatations on the left side and low ejection fraction (34%). These findings suggested severe hypocardiac function. Magnetic resonance imaging revealed a cerebral infarction in the left insular cortex and putamen, with left internal carotid artery occlusion, which was suspected as an embolic infarction (Fig. 1a–c). However, we could not first perform recombinant tissue plasminogen activator therapy because of insufficient adaptation time. Thus, we performed endovascular therapy. Consequently, her left internal carotid artery was completely recanalized (Fig. 2a, b). Her neurological symptoms, including the consciousness disturbance, were improved. We considered the stroke etiology to be a cardiac embolism caused by arterial fibrillation and initiated a direct oral anticoagulation therapy on the next day. Her NIHSS score was 2 at 14 days after admission. She was subsequently transferred to a rehabilitation hospital.

DISCUSSION

EDMD has been reported as an abnormality of six genes. It is characteristically an X-linked recessive disease (MIM 310300) and is linked to mutation in the EMD or emerin gene on Xq 28. The EMD gene, which encodes emerin, causes the X-linked form of EDMD, while the LMNA gene, which encodes lamins A and C, is responsible for autosomal formations, usually with a dominant transmission [6]. In this case, the patient had mutations in the LMNA gene (c.810 + 1G > T). No other family member was reported to have the same abnormalities. On the basis of the clinical features, the sporadic autosomal dominant form of EDMD was suspected.

LMNA encodes the intermediate filament protein lamins A and C, which constitute the major scaffolding protein of the inner nuclear membrane. The lamin A/C protein is expressed in the nuclear envelope of many tissues, primarily in the skeletal and cardiac muscle. A replacement of normal atrial muscle with non-functional fibrous tissue was caused by an LMNA function disorder. This condition results in conduction block

and re-entrant arrhythmias [7]. Atrial paralysis and other forms of bradyarrhythmia carry a significant risk of systemic embolism in EDMD with cardiac involvement. Autosomal dominant and X-linked EDMD are associated with bradyarrhythmia, AF/atrial flutter, heart block, and ventricular dilation with or without systolic dysfunction [8], whereas autosomal recessive EDMD is associated with conduction defects and premature atrial and ventricular contractions [9].

The benefit of anticoagulation therapy for adults with AF/atrial flutter is well established. However, data in children and those with neuromuscular diseases are lacking. The hypercoagulable state found in heart failure is attributable to a combination of stasis, platelet activation, increased blood viscosity, and increased fibrinolytic activity. Patients with low left ventricular ejection fraction (LVEF) measured using transthoracic echocardiography are known to be at increased risk of embolism events. A previous study reported that AF/atrial flutter and thromboembolic complications occurred in 11 (61%) and 4 (22%) of 18 patients with EDMD, respectively [10]. Another study described stroke or embolism in 6.5% of patients with neuromuscular disease with AF/atrial flutter, none of whom were undergoing oral anticoagulation therapy before stroke [11]. The American Heart Association statement recommends that thrombosis prophylaxis may be considered for children with neuromuscular disease, normal systolic ventricular function, and AF/atrial flutter, with the type of therapy determined on the basis of the individual patient's thrombosis risk [9]. In our case, because AF and low LVEF were observed, the patient should have received anticoagulation therapy. Her attending physician recommended anticoagulation therapy to her parents. However, her parents worried about the adverse events of anticoagulation, such as major bleeding, because she was too young at that time.

Finally, heart failure is a clue risk factor of embolism in patients with EDMD. When heart failure occurs in these patients, administration of anticoagulation therapy should be initiated. Anticoagulation therapy should be considered in EDMD even if cardiac symptoms are mild.

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