Mechanical thrombectomy in a young stroke patient with Duchenne muscular dystrophy

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Abstract

Background: Duchenne muscular dystrophy (DMD) is an X-linked recessive skeletal muscle myopathy which is caused by mutations in the dystrophin gene. Lack of dystrophin also results to cardiomyopathy, which raises significantly the stroke risk in DMD-patients. However, data about therapeutic opportunities in the acute setting are scarce in literature. So far, only two cases receiving IV thrombolysis are described, one of them with fatal outcome.

Method: Case report of a case of successful mechanical thrombectomy (MTE) in an acute ischemic stroke (AIS) patient with DMD and associated dilatative cardiomyopathy.

Results: A 20-year old DMD-patient was transferred at 08:56 h to our department due to wake up stroke with severe right-sided hemiparesis and aphasia (NIHSS=20). Last-seen-normal was at 03:00 h. Cerebral CT-scan revealed only slight early ischemic changes (ASPECT-Score=8). CT-angiography detected occlusion of left middle cerebral artery (LMCA). MTE started rapidly at 9:23 h and using direct thrombus aspiration (Penumbra System®) complete recanalization was achieved 20 min later (TICI-grade 3). Considering the specific risks of general anesthesia in DMD, the procedure was performed with propofol, remifentanil and rocuronium. The patient recovered quickly from the acute symptoms, due to preexisting hypotonic tetraparesis his NIHSS-score at discharge was 12 points.

Conclusions: To the best of our knowledge, this is the first report on MTE in a patient with DMD related cardioembolic stroke. In contrast to the few reports with IV thrombolysis, MTE seems to represent an optimal treatment option. Specific characteristics of DMD-patients like anesthetic regimen should be taken into account.

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Introduction

Duchenne muscular dystrophy (DMD) is a skeletal muscle myopathy caused by mutations in the dystrophin gene, identified in 1986 by Louis Kunkel and coworkers.[1,2] This X-linked recessive disorder is the most frequent muscular dystrophy, with an incidence of 1 in 3300–3600 male births.[3] In DMD, progressive muscle weakness due to dystrophic muscle changes presenting as delayed motor milestones or classic Gower's maneuver is usually encountered within the first 3–5 years of life.[3] After progressive loss of skeletal muscle, most boys are restricted to a wheelchair at the age of 13–16.[3] Furthermore, a lack of dystrophin is responsible for dilated cardiomyopathy as it is located on the inner side of skeletal and cardiac myocytes.[4] Thus, DMD is often associated with cardiomyopathy and clinically detectable cardiomyopathy has already onset by the age of 10.[5] Since advances in clinical care have led to an improved survival of respiratory and musculoskeletal complications, the incidence of cardiomyopathy in these patients increases.[5] Approximately 20% of patients with DMD suffer a cardiac-related death.[5] Dystrophin is also expressed in the brain and in retinal cells, and the mild cognitive impairment in DMD patients is attributed to mutated dystrophin in the brain.[3]

Concerning arterial ischemic stroke, recently an incidence rate of 1 per 100 patients-years has been identified in patients with DMD between 3.8 and 35.0 years,[6] which is much higher than the overall arterial ischemic stroke incidence in childhood (1.6 per 100,000 per year).[7] Arterial ischemic stroke in DMD is thought to be largely due to cardiomyopathy and the associated risk of

thromboembolism. So far, only two cases have been described in the literature relating to recanalization therapy (particularly intravenous thrombolysis solely, without an intravascular procedure), one of which had a fatal outcome.[6] We report here on a 20-year-old patient with DMD and acute ischemic stroke due to embolic occlusion of the left middle cerebral artery (LMCA), who was successfully treated by mechanical thrombectomy (MT). To the best of our knowledge, this is the first report on endovascular recanalization by MT in a patient with a DMD-related cardioembolic stroke. Written informed consent for publication of this case study (patient information and images) has been obtained from the legally authorized representative of this patient (his mother).

Case report

A 20-year old male patient with genetically confirmed DMD with known associated dilated cardiomyopathy was transferred to our supraregional stroke unit due to a wake-up stroke with severe right-sided sensomotoric hemiparesis and aphasia as he was right-hand dominant. Due to status post detection of a thrombus in the left ventricle in August 2015, the patient was on an anticoagulation regime with low molecular weight heparin (LMWH), which was interrupted in error because of a misapprehension the day before. In addition to LMWH, the patient was treated with bisoprolol, magnesium and vitamin D. A moderate- to high-grade hypotonic tetraparesis due to the DMD-related muscle weakness was already known. The acute presentation of the patient was due to a substantial worsening of the preexisting weakness on the right side, including a new facial weakness and aphasia, resulting in a formal NIHSS score of 20 points. The time at which the new symptoms were recognized was 08:15; last-seen-normal (LSN) was about 03:00. Initially the patient was brought by paramedics to the pediatric hospital at which he is best known. An immediate transfer to our department was performed, and the patient arrived at 08:56 in our emergency room.

Vital parameters were stable, the international normalized ratio was 0.9 measured by CoaguChek® (Roche Diagnostics) in the emergency room. Cerebral CT scan revealed only slight early ischemic changes in the LMCA territory (ASPECT-Score = 8 points) but with hyperdense media sign on the left (Figure 1(a)). Subsequent CT angiography confirmed a proximal occlusion of the LMCA (Figure 1(b)).

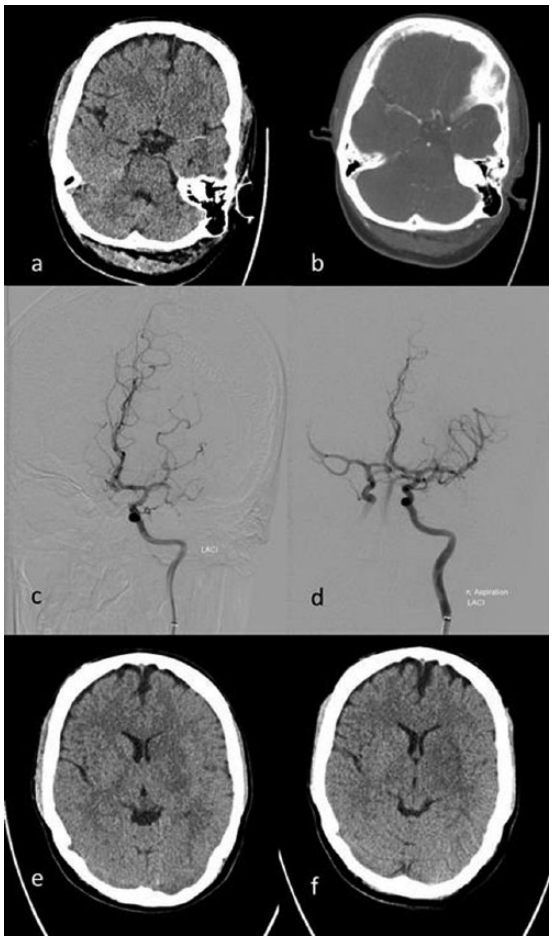

Figure 1. Initial CT scan showing the hyperdense media sign (a), proximal occlusion of LMCA (b), MT before aspiration of the thrombus (c) and after aspiration (d). Follow-up CT scans showed a hypodensity in the left area of the basal ganglia with a mild edema (e and f).

Patient education took place, including the patient's mother as his legally authorized representative, so MT started quickly at 09:23 (door-to-groin time = 27 min). Considering the specific risks of general anesthesia in DMD, the procedure was performed with propofol, remifentanil and rocuronium. At 24 min after groin puncture, the recanalization was successfully completed (TICI grade 3) by direct thrombus aspiration using the Penumbra System® (Penumbra Inc. Alameda, CA, USA). Since the patient formally exceeded even the extended time window of 6 h after LSN, no additional IV thrombolysis was performed.

Shortly after successful recanalization (Figure 1(c–d)) and directly after recovering from anesthesia, the half-sided motoric worsening of the preexisting hypotonic tetraparesis improved, but

the aphasia persisted to a reduced extent (NIHSS score of 14 points). With logopedic speech therapy, the aphasia resolved almost completely in the further course of his hospitalization. The daily NIHSS score showed an improvement up to 12 points within 9 days.

Transthoracic and transesophageal echocardiography revealed no evidence of an intracardial thrombus, but a relevant reduced ejection fraction. No atrial fibrillation was detectable *via* prolonged ECG monitoring. Laboratory investigations found high creatine kinase at 1883 U/L (38–174), high lactate dehydrogenase at 321 U/L (135–225) and a high creatine kinase-muscle/brain at 144.5 U/L (<24). Due to the low muscle mass, creatinine serum level was extremely low at 0.25 mg/dl (0.70–0.12), so it could not serve as a reliable kidney retention parameter in this case. Consequently, we determined the kidney function via cystatin C, where a concentration of 1.10 mg/L (0.61–0.95) with a resulting glomerular filtration rate of 83 ml/min (⩾90 ml/min) was shown. Further hemostaseological investigations revealed no thrombophilia.

Follow-up CT scans revealed a demarcation of the ischemia in the left area of the basal ganglia with a mild edema (Figure 1(e–f)). After discussing the specific considerations of indicated anticoagulation with the patient and his mother, oral anticoagulation with dabigatran (150 mg bid) was initiated for secondary prophylaxis.

At discharge from our stroke unit and transfer to a rehabilitation center after 9 days of hospitalization, the patient showed a complete recovery from the ischemia-induced central hemiparesis. Only a slight aphasic component was present, resulting to an NIHSS score of 12 points at discharge, which was mainly due to his preexisting DMD symptoms.

Discussion

Ventricular dysfunction, dilatation and failure are typical results of cardiac involvement in patients with DMD.[8] Dilated cardiomyopathy represents a well-known risk factor for cardial thrombus formation[9] due to blood flow disturbances in the left ventricle.[10] This risk can effectively be reduced by anticoagulation.[11] In the SAVE trial, the cumulative stroke risk in patients with myocardial ischemia negatively correlated with the left ventricular ejection fraction (4.1% in patients with LVEF > 35% and 8.9% in patients with LVEF < 38%).[12] However, the risk of systemic thromboembolism in patients with heart failure with sinus rhythm seems to be low in general.[13] Thus, chronic heart failure represents no clear indication for prophylactic anticoagulation.

There are only limited epidemiological data on ischemic strokes in patients with primary myopathy.[14] Winterholler and colleagues recently described an increased risk for ischemic strokes in DMD patients and reported four cases of ischemic strokes in young DMD patients.[6] One patient showed an incomplete recovery of his acute motoric symptoms with full recovery of his language skills after systemic thrombolysis. However, two of these four patients died and one patient did not recover from his severe symptoms (aphasia and paresis of his left arm).[6] Two of these four patients with DMD had a dilated cardiomyopathy; the other two had reduced left ventricular systolic function.[6] In none of these patients was atrial fibrillation detectable, so it seems very likely that the embolic stroke was related to cardiomyopathy.[6] Interestingly, atrial fibrillation as a typical risk factor for cardioembolic stroke seems not to be frequently present in patients with DMD with dilated cardiomyopathy.[15] Two of these four reported patients with DMD received systemic thrombolysis, while one of them showed a fatal outcome due to cardiac failure and septic pneumonia.[6] As these two patients are still the only reported DMD patients treated with systemic thrombolysis, further data are needed to assess the risk factors of thrombolysis in this special patient group.

Recently, seven randomized controlled clinical trials evaluating the safety and efficacy of endovascular therapy in patients with acute ischemic stroke due to emergent large vessel occlusion have changed the treatment paradigm by establishing MT as the most effective acute stroke therapy.[16] Thus, MT might represent an optimal reperfusion therapy also in patients with DMD suffering acute ischemic stroke due to embolic occlusion of a large intracranial vessel. As modern therapy and care increases the life expectancy of patients with DMD, cardiomyopathy is becoming a more relevant topic.[11] However, there are no guidelines regarding primary or secondary prevention of cerebral ischemia in this patient group.[6] Two small randomized studies (HELAS 2006 and WASH 2004) do not support the routine use of oral anticoagulation.[17,18] On the other hand, in patients with high risk for embolism (e.g. intracardiac thrombi), an individual decision

regarding initiation of oral anticoagulation is recommended.[19]

In addition to the protective effect of anticoagulation, the risk of bleeding has to be considered. Especially in patients with congestive heart failure, optimal control of anticoagulation is known to be difficult.[20] Thus, novel oral anticoagulants (NOACs) might be advantageous with regard to this specific point. On the other hand, it should be considered that formally, NOACs are indicated for stroke prevention only in patients with non-valvular atrial fibrillation.

Moreover, treatment with NOACs depends on renal function. In patients with DMD, low creatinine levels are caused by reduced muscle mass, so creatinine levels cannot serve as a reliable kidney retention parameter in this patient group. Thus, glomerular filtration rate should be calculated using serum cystatin C levels, as these do not correlate to muscle quantity.[21]

In the literature, there are recommendations for secondary stroke prevention in pediatric patients, using 3–5 mg/kg/day acetylsalicylic acid.[22] However, there is evidence that oral anticoagulation therapy is associated with fewer nonfatal strokes than therapy with aspirin or clopidogrel in patients with chronic heart failure.[23]

Management of general anesthesia represents a further important point that should be considered in patients with DMD who are receiving endovascular therapy. Succinylcholine is known to cause perioperative rhabdomyolysis, hyperthermia, hyperkalemia and cardiac arrest, but complication during and after anesthesia seems to be unpredictable regardless of anesthetic use.[24] However, in our case we alternatively used rocuronium, an aminosteroid non-depolarizing neuromuscular blocker, which was tolerated without complications.

Summary

To the best of our knowledge, this case report is the first described case of MT in an acute ischemic stroke patient with DMD and associated dilatative cardiomyopathy and resulting embolic cerebral vessel occlusion.

Although ischemic stroke risk is increased in patients with DMD, data about therapeutic opportunities are scarce in the literature. In our case, MT represented an optimal treatment option with the best possible outcome and without complications. Specific characteristics of patients with primary myopathy, like anesthetic regimen and calculation of glomerular filtration rate on the basis of cystatin C, should be considered as discussed in the present case report.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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