A Case of Paradoxical Cerebral Embolism and Ischemic Stroke after Local Thrombolysis for Deep Vein Thrombosis

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Abstract

Case: A 68-year-old woman presented to our emergency room with subjective fevers, non-productive cough and severe pain in the right lower extremity. Of note, she had sustained a right patellar fracture 6 weeks earlier, treated with a brace. Physical examination showed right lower extremity swelling. Subsequently, she was diagnosed with extensive right deep venous thrombosis (DVT). Local thrombolysis of the DVT was achieved by injecting tissue plasminogen activator (tpa) followed by mechanical aspiration. Immediately post procedure, the patient experienced an acute deterioration in her mental status with left hemiparesis. CT angiography of the head confirmed a right middle cerebral artery (MCA) ischemic stroke. Successful reperfusion was achieved by performing an emergent embolectomy in the M1 branch of the MCA. A bubble contrast transthoracic echocardiogram showed a patent foramen ovale (PFO). The patient’s neurological symptoms gradually improved and at 6 month follow up she had no focal neurological deficits.

Discussion: We describe the first case of an embolic stroke complicating catheter directed thrombolysis (CDT) for DVT in patient with elevated pulmonary arterial pressure as a result of acute pulmonary emboli. Currently there are no guidelines mandating routine checks for PFOs prior to performing CDT. This case illustrates the need for high clinical vigilance for PFO in patients being evaluated for CDT and provides a unique insight into a rare complication.

ABBREVIATIONS

VTE: Venous Thrombo Embolism; DVT: Deep Venous Thrombosis; CDT: Catheter Directed Thrombolysis; tpa: tissue plasminogen activator; PTS: Post Thrombotic Syndrome; PFO: Patent Foramen Ovale; TOAST: Trial of Org 10172 in Acute Stroke Treatment; CT: Computed Tomographic; MCA: Middle Cerebral Artery; PE: Pulmonary Embolism; IVC: Inferior Vena Cava; TIA: Transient Ischemic Attack

INTRODUCTION

Venous thromboembolism (VTE) is the third leading cause of cardiovascular mortality, after coronary artery disease and stroke [1]. The mainstay of treatment is anticoagulation, as it helps prevent formation of new clot, while allowing clot lysis by the body’s own endogenous mechanisms. Even after adequate treatment with anticoagulation, around 40-50% of patients develop post thrombotic syndrome (PTS), especially following a proximal deep venous thrombosis (DVT) [2]. PTS usually happens due to damage to the venous valves, which in turn leads to impedance in cephalad venous drainage. This can cause leg swelling, edema, heaviness, skin discoloration and in its most severe form, can cause chronic skin ulceration [3]. It has been shown that by wearing elastic stockings, the incidence of PTS can be reduced by 50% [2], but even with this recommended treatment, one in five patients will still develop PTS. To reduce the incidence of PTS even further, studies have been performed to evaluate the role of catheter directed thrombolysis (CDT). Several trials and small case series [4,5] have shown that CDT can reduce the incidence of PTS even further, but may result in increased bleeding events, length of stay and blood transfusions.
A paradoxical embolism occurs when venous clot passes through an intracardiac defect with a right-to-left shunt and is propagated into the arterial circulation. In general, paradoxical embolism is relatively rare, consisting of less than 2% of all arterial emboli [6,7]. Paradoxical embolism is most commonly due to an identified patent foramen ovale (PFO), atrial septal defect, pulmonary arteriovenous malformations, and ventricular septal defect [8]. Most frequently, paradoxical emboli travel to the extremities, the brain, and less likely the coronary, renal, or splenic arteries [8].

Here, we present the first reported case of a patient developing a paradoxical embolism resulting in ‘ischemic’ cerebro-vascular accident post CDT.

CASE PRESENTATION

A 68-year-old woman presented to our emergency room with subjective fevers, dyspnea, and right leg swelling and non-productive cough of several days’ duration. Of note, she had sustained a right patellar fracture 6 weeks earlier that was treated with a brace. She had no other significant past medical history and was not taking any prescription medications. There was a non-family history of thromboembolic disease. Vital signs on admission were unremarkable. Physical examination showed right lower extremity swelling extending up to the groin. Venous Doppler ultrasound revealed deep venous thrombosis extending from the right common femoral vein to the proximal popliteal vein. Subsequently, a computed tomographic (CT) angiogram of the chest showed bilateral pulmonary emboli in segmental branches supplying right upper lobe, lingula and both lower lobes. Heparin drip was started and due to the extensive DVT, it was decided by the treating team to administer localized treatment to help reduce the clot burden. CDT with 9mg of t-PA was performed in the right common femoral vein, followed by mechanical aspiration using the AngioJet system. Follow up venography showed a small amount of residual thrombus in the central portion of the right femoral vein with establishment of flow distally.

About 2 minutes after administering t-PA, the patient experienced an acute deterioration in her mental status with left hemiparesis. Rapid sequence intubation was performed and the patient underwent immediate CT angiogram of her brain, which revealed a right middle cerebral artery (MCA) embolic stroke. This was followed by magnetic resonance imaging of the brain (Figure 1) which confirmed the stroke in right cerebral territory. Successful reperfusion was achieved by performing an emergent embolectomy in the M1 branch of the MCA along with administration of intra-arterial t-PA. Intravenous thrombolysis was contraindicated as the patient had received t-PA moments earlier. A 2-D echocardiogram showed elevated right ventricular systolic pressure to 38 mmHg. This was followed by a bubble study which revealed a patent foramen ovale (PFO), later confirmed by a trans-esophageal echocardiogram, that was otherwise not consistent with any cardio embolic source. An inferior vena cava filter was inserted as anticoagulation was not deemed safe in the setting of an acute ischemic stroke. She was subsequently started on heparin and warfarin and was discharged home after two weeks. Over the course of six months, she made good neurological recovery with no residual weakness.

DISCUSSION

Catheter directed thrombolysis is a novel technique which permits delivery of thrombolytic locally with minimal systemic side effects. The catheter is introduced into the affected vein and advanced into the area of thrombosis. Thrombolytic scan can be injected or mechanical techniques may be used to cause clot lysis and aspiration, thereby requiring a much lower dose than needed for systemic thrombolysis. CDT can be used in patients with contraindication to anti-coagulation and can reduce the incidence of PTS. The main complications of CDT for DVT are local and distant bleeding complications, infection and local failure with occlusion or stenosis of the vessel [5,9]. Large trials evaluating the role of CDT [5,9] have not reported cerebrovascular accidents, although we do not know if these patients had an associated pulmonary embolism. Three intra-cerebral bleeds were observed in a Cochrane review evaluating utility of thrombolysis in DVT [10]. In 2 cases, streptokinase was administered, while in the third case - t-PA was the culprit and in all these cases thrombolysis was administered systemically via a peripheral vein.

We found three other cases that are somewhat related to our presented case but secondary to systemic anticoagulation for PE. One case report described a patient who underwent thrombolysis with 40 mg alteplase for massive PE and subsequently developed an absent left femoral pulse from paradoxical embolism to the left femoral artery [11]. Second case report described a patient who underwent thrombolysis with urokinase for PE and subsequently developed ischemic stroke from paradoxical embolism to the right internal carotid artery [12]. Third case underwent thrombolysis of a PE and subsequently developed a fatal stroke [13].

A patent foramen ovale may occur in up to 27.3% of the general population [14] and it increases the risk of recurrent stroke [15]. Independent risk factors for development of paradoxical embolism in patients who develop cryptogenic stroke include: a history of DVT or PE, migraine, recent prolonged
travel, sleep apnea, waking up with a transient ischemic attack (TIA) or stroke, and Valsalva maneuver prior to the event [16]. Paradoxical embolism is extremely rare after thrombolysis.

Box 1 The criteria for diagnosis of paradoxical embolism are the following [7]

1. Embolism in arterial system that is not originated from the left heart or from the arterial system itself.
2. Abnormal communication between the arterial and venous systems as evidenced by imaging tests.
3. Presence of venous thrombosis or embolism in the form of DVT or pulmonary embolism (PE).
4. Increased right-sided pressure which contributes right to left shunting be it transient or longstanding.
5. Demonstration of a thrombus trapped in a PFO (straddling thrombus) is extremely rare but highly specific for diagnosing paradoxical embolism.

As far as we know, this is the first reported case of an ischemic stroke as a result of CDT for a pelvic DVT. We postulate that upon localized CDT, smaller thrombi that were broken off migrated through the PFO into the left atrium aided by the increased right-sided pressures, as a result of the coexisting pulmonary emboli. This brings up the question of whether or not, clinicians should routinely check for the presence of a PFO prior to thrombolysis of either a DVT or PE, or whether CDT for DVT should be pursued in the presence of a PFO. We believe that, despite the rarity of developing a paradoxical embolism, it is worthwhile to do screening echocardiography prior to pursuing CDT in hemodynamically stable patient given the multitude of complications associated with an ischemic stroke.

CONCLUSION

As experience and use of CDT increases, there is likely to be an increased incidence of similar cases of paradoxical embolism. This case illustrates the need for high clinical vigilance for a PFO and provides unique insight into an exceedingly rare complication resulting from a fairly common procedure.

REFERENCES