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Spontaneous coronary thrombosis following thrombolytic therapy for acute cardiovascular accident and stroke: a case study

Eric Wallace, DO¹ and Susan S. Smyth, MD, PhD¹

¹Division of Cardiovascular Medicine and the Gill Heart Institute, University of Kentucky, and the Lexington VA Medical Center, Lexington, Kentucky

Abstract

Cardiac complications following stroke or acute cerebrovascular accidents (CVA) are common; however, many of these complications are asymptomatic and do not cause adverse cardiac effects. Symptomatic events (such as acute myocardial infarction after CVA) rarely occur and are often the result of an underlying cardiac embolic source, such as a left ventricular thrombus. We report a case of spontaneous coronary thrombosis following thrombolytic therapy for acute CVA, and discuss the implication that an underlying systemic pro-thrombotic state may predispose individuals to thrombosis in disparate vascular beds.

Keywords

Stroke; Acute Cerebrovascular Accidents; Thrombosis; Thrombolytic Therapy

Introduction

Cardiac complications following stroke or acute cerebrovascular accidents (CVA) are common, occurring up to 12% of reported cases [1,2]. However, many of these complications are asymptomatic and are diagnosed as mild elevations in cardiac biomarkers, which do not cause adverse cardiac effects [3]. Symptomatic events such as acute myocardial infarction (MI) after CVA rarely occur and are often the result of an underlying cardiac embolic source for both events such as a left ventricular thrombus. Patients treated with systemic thrombolysis for an acute CVA may be at risk for subsequent MI, perhaps due to disruption of an existing LV thrombus [4–6]. In this report, we present a case of an individual, without prior MI or LV thrombus, who developed spontaneous coronary thrombosis following tissue plasminogen activator (tPA) administration and discuss the mechanisms of MI following acute CVA.

Case Report

A 70 year-old functional male presented to our institution for treatment of acute right-sided paralysis, suspicious for a CVA. Upon arrival a stroke alert was activated. The patient had been diagnosed with coronary artery disease (CAD), had prior coronary stenting, was not currently on medication, and was an active smoker. His initial blood pressure was 149/69, his heart rate was 56 beats per minute, and his weight was 86 kilograms. Examination

Address correspondence to: Eric Wallace, DO, The University of Kentucky, Division of Cardiovascular Medicine, The Gill Heart Institute, 900 S. Limestone Street, 326 CTW Building, Lexington, KY 40536-0200, Eric.Wallace@uky.edu, Tel: (859) 323-6195, Fax: (859) 323-6475.

demonstrated a dense right-sided hemiparesis with global aphasia. Laboratory results were unremarkable with normal renal function, hemoglobin, platelets, and cardiac biomarkers. Electrocardiogram (EKG) revealed normal sinus rhythm with no evidence of prior infarct or ischemic changes. A non-contrasted computed tomography (CT) of the head and CT angiography of the neck demonstrated complete occlusion of the left internal carotid artery, immediately distal to its origin within the carotid bifurcation. Within the left posterior parietal region, an age-indeterminate wedge-shaped infarction was present, consistent with an old posterior cerebral artery territory CVA (Figure 1). The NIH stroke scale was 12 [7]. The decision was made to administer thrombolytics and an 8 mg bolus of recombinant tissue plasminogen activator (rt-PA) was administered (treatment time was three hours, 56 minutes after symptom onset). The patient received the balance of the rt-PA infusion of 69 mg during the 60 minutes following the bolus administration.

Approximately three hours later, the patient developed bradycardia (heart rates in the 30 s), and hypotension-associated altered sensorium (blood pressure was 80/40). An EKG demonstrated complete heart block, new ST-segment elevations in the inferior leads, and ST-segment depressions in the posterior leads (Figure 2). The patient was emergently transferred to the cardiac catheterization laboratory for placement of a temporary pacemaker wire, and diagnostic coronary angiography. The patient was found to have significant coronary artery disease with occlusion of his right coronary artery (Figure 3). Thrombectomy via an aspiration catheter collected fresh thrombus and restored normal coronary blood flow. Percutaneous coronary intervention was performed with two, bare-metal stents to the right coronary artery and posterior descending artery bifurcation. Procedural anticoagulation included 4000 units of heparin, 325 mg aspirin, and 600 mg of clopidogrel. After revascularization, the patient's heart rhythm returned to normal sinus and hypotension was resolved. Repeat CT of the head excluded an intracerebral hemorrhage as the etiology of his mental status changes. An echocardiogram revealed a left-ventricular ejection fraction of $\approx 50\%$ with inferior hypokinesis, without evidence of intracardiac thrombus, prior infarction, or intracardiac shunt. The patient was ultimately discharged to a post-acute care facility for rehabilitation therapy.

Discussion

In this case, our patient suffered an MI within hours following administration of rt-PA. Although hemorrhage is the most common complication of IV-thrombolytic therapy for acute stroke, embolic complications have also been reported. Recombinant tissue plasminogen given for acute ischemic stroke may dislodge intracardiac thrombus, resulting in acute MI. Observational studies suggest that LV thrombus may be present in up to one quarter of patients who present with CVA or transient ischemic attack [8]. Change in LV thrombus size has also been reported following t-PA administration [9]. In this case, our patient was unlikely to have had a pre-existing LV thrombus, because his initial EKG lacked changes indicative of a previous infarct and his echocardiogram showed no evidence for wall motion defects or LV thrombus.

Individuals who have suffered a stroke are at increased long-term risk of MI to the point that CVA has emerged from large clinical studies as a coronary artery disease-equivalent [10,11]. A large, atherosclerotic disease burden may partially account for the association between MI and CVA. In addition to late-cardiac events, the MI rate is higher immediately following a stroke for reasons that are not well-understood. One possibility is that a systemic, pro-thrombotic state may predispose patients to acute thrombosis in different vascular beds. Wide variations in individual propensity for thrombosis exist [13], due in part to differences in intrinsic platelet function and response to environmental influences [14].

Thrombolytic therapy can also be associated with a pro-thrombotic state. Recombinant tissue plasminogen binds fibrin to enhance plasminogen activation and plasmin generation, which in turn degrades fibrin and results in clot lysis. An unwanted side effect of systemic thrombolytic therapy is an increase in thrombin activity with the potential for a heightened prothrombotic state [12]. Thrombin is one of the strongest activators of circulating platelets. A recent retrospective analysis of the National Institute of Neurological Disorders (NINDS) rt-PA stroke study evaluated systemic effects of thrombolytic therapy. In that analysis, mortality following rt-PA therapy was associated with elevated thrombin complex levels, within hours of lytic administration [15].

When systemic thrombolytic therapy is used for the treatment of ST- segment elevation MI (STEMI), unfractionated, or low-molecular weight heparin (or similar anti-coagulant) is used as adjunctive pharmacotherapy, in part to minimize the procoagulant effects of thrombolytics [12]. In the setting of STEMI, elevated systemic levels of procoagulation markers also predict recurrent thrombosis [16,17]. In addition to antiplatelet strategies, adjunctive therapy aimed at reducing thrombin activity in conjunction with thrombolytic therapy, reduces recurrent death or MI in the acute MI population [18], and is listed by the American Heart Association (AHA) as a Class I recommendation [12].

However, the use of adjunctive therapy in the acute CVA population receiving thrombolytics is not as well-defined. Despite molecular mechanisms supporting the same prothrombotic state as the coronary population, clinical data suggests only a mild cardiovascular improvement without mortality benefit [19,20]. Substantially higher bleeding rates (especially intracerebral hemorrhage, which can be nearly 15 times higher in individuals on warfarin [Coumadin]), make the risk of anticoagulation unacceptably high and limits clinical utility [21,22]. Thus, full anticoagulation remains an AHA Class III recommendation for at least 24 hours following t-PA administration [7].

Conclusions

Although there have been several postulated mechanisms of myocardial injury following acute CVA, perhaps a novel etiology still exists. Our case of coronary thrombosis in a patient with acute CVA following thrombolytic therapy supports the concept that a systemic, prothrombotic state predisposes individuals to thrombosis and may be an underappreciated mechanism of MI following acute CVA.

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Figure 1. Computed tomography (CT) of neck and head

Left: CT of the neck with sagittal view of left common carotid and bifurcation demonstrates an occlusion of the internal carotid artery just after the bifurcation (arrow). Right: CT of the head demonstrates a hypodensity posteriorly consistent with an old ischemic event (arrow)

Figure 2. EKG obtained for new-onset bradycardia

EKG demonstrates sinus bradycardia, AV dissociation (third-degree AV block), and ST-segment elevation in leads II, III, and aVF up to 2 mm and ST-depression in V1 and V2 consistent with an inferior MI with posterior extension

Figure 3. Angiography of the right coronary artery (RCA)

Left: Left anterior oblique projection of the RCA depicts inadequate contrast penetration to the distal vessel (arrow) Center: The contrast has “stained” the intravascular material (arrow), typical of coronary thrombus. In both pictures, a temporary pacing wire is present in the right ventricle. Right: images obtained after aspiration thrombectomy with guidewire in distal vessel. Coronary artery stenosis present at the posterior descending artery bifurcation is indicated by the arrow.