SUCCESSFUL TREATMENT OF RENAL ARTERY EMBOLISM EVEN FORTY-EIGHT HOURS AFTER EVENT

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SUMMARY – Renal artery embolism is a disease that is easily missed due to its infrequent and nonspecific presentations. Although early diagnosis and optimal thrombolytic treatment can sometimes restore renal function, therapeutic guidelines have not yet been established. However, early anticoagulant therapy is beneficial and selective infusion of lytic agents into renal artery has been reported with increasing frequency and efficacy if used in the early stage. We report that intra-arterial thrombolytic therapy with low dose of 35 mg recombinant tissue plasminogen activator (t-PA) may be an effective and safe strategy for the treatment of renal artery embolism, despite the period of ischemia being longer than 48 hours.

Key words: *Atrial fibrillation; Flank pain; Renal artery obstruction; Thrombolytic therapy; Thromboembolism – therapy; Case report*

Introduction

Renal artery embolism (RAE) is a disease that is easily missed due to its infrequent and nonspecific presentations[1]. Hazanov *et al.* in their meta-analysis report that the diagnosis of RAE was made on admission in only up to 40% of patients[2]. Several coexisting conditions have been associated with RAE including ischemic and valvular heart disease, aneurysmal disease and advanced malignancy, but is typically seen in patients with atrial fibrillation[3]. Clinical manifestations of RAE are variable; severe flank pain, abdominal pain or both, accompanied by vomiting or nausea are typical signs and symptoms[4]. Early diagnosis and optimal thrombolytic treatment can sometimes restore renal function[5]. Regarding treatment, therapeutic guidelines have not yet been accepted. However, early anticoagulant therapy is beneficial and selective infusion of lytic agents into renal artery has been reported with increasing frequency and efficacy if used in the early stage[5-8].

In this case report, we describe a patient with abdominal and right flank pain who was diagnosed as having RAE and treated by catheter directed intra-arterial thrombolysis more than 48 h after symptom onset.

Case Report

A 61-year-old woman was admitted to the hospital with a 1-day history of diffuse abdominal pain with right flank pain. She graded the pain as 'severe' and described it as sharp and constant. It had not changed in quality or intensity since its onset. She had no other systemic symptoms. She had a medical history of hypertrophic cardiomyopathy and persistent atrial fibrillation without any prior history of thromboembolic disease. Her medications included acetylsalicylic acid and bisoprolol.

Physical examination showed body temperature of 36.7 °C, arterial blood pressure 135/80 mm Hg, heart rate of 80 beats *per* minute and respiratory rate

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of 16 breaths *per* minute. Her abdominal examination revealed soft abdomen with some tenderness in the right upper quadrant, with no rebound, distention or organomegaly. The remainder of the examination was normal.

The initial emergency department evaluation included an electrocardiogram that showed atrial fibrillation with a ventricular rate of 80. Hematologic data and biochemistry on admission showed the following results: white blood cell (WBC) count 12.3x109/L; serum creatinine 122 μmol/L; glutamic pyruvate transaminase (GPT) 41 U/L, glutamic oxalacetate transaminase (GOT) 23 U/L; lactate dehydrogenase (LDH) 1322 U/L; amylase 264 U/L. Urine output was maintained and urine analysis was positive for microscopic hematuria.

Contrast-enhanced computed tomography (CT) of the abdomen was performed, which revealed a normal sized right kidney with global absence of the nephrogram except for some spared areas on the periphery, consistent with a cortical rim sign (spared peripheral circulation via capsular collateral arterioles). Spiral computed tomography-angiography (spiral CT-A) confirmed suspicion of acute renal ischemia and revealed disappearance of the main stem of the right renal artery with no visualization of the interparenchymal arterial branches.

A diagnosis of acute renal artery embolism was made and interventional radiologist was consulted for possible intra-arterial thrombolysis because the duration of symptoms suggested prolonged arterial occlusion. Interventional radiologist accepted intervention and aortography with selective catheterization of the renal artery was performed, which demonstrated a right renal artery embolus at 3 cm to its origin. The radiologist started thrombolysis more than 48 h after the symptom onset, *via* direct transcatheter injection as a single bolus of 35 mg tissue plasminogen activator (tPA, Actilyse, Boehringer Ingelheim, Germany) along with 4000 units of intra-arterial heparin (Fig. 1). Postprocedure, the symptoms settled completely and the patient was restarted on warfarin therapy (target INR 2.5-3) with a covering heparin infusion until her INR became therapeutic.

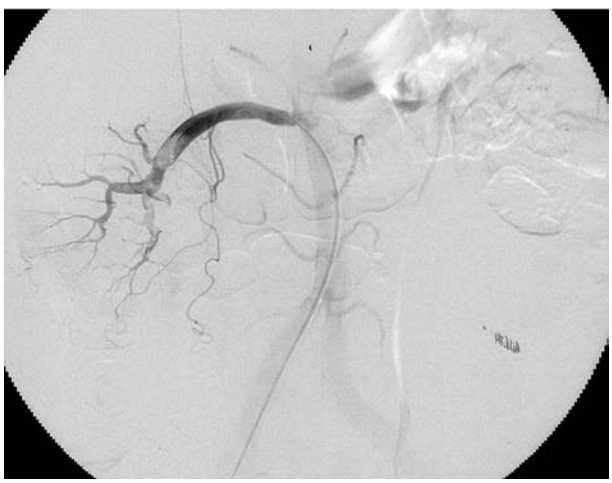

Fig. 1. Check angiogram performed nearly 15 minutes after the start of the procedure, showing almost restored main stem of the right renal artery as well as restored intraparenchymal vessel patency.

Two days later, follow up angiography demonstrated complete lysis of the thrombus in the renal artery, but there was no visible nephrogram. On the same day, scintigraphic detection of kidney function was performed and it showed that the right kidney did not contribute to total tubular excretion rate.

Once stabilized on warfarin therapy (INR 2.52), the patient was discharged home. Her renal function on discharge was deteriorated slightly compared to that on admission, with serum creatinine 130 μmol/L. On the day of discharge, serum LDH was 343 U/L. Three weeks after discharge, follow up control renal scintigraphy showed that the right kidney contributed to total tubular excretion rate with 25% and serum creatinine was 114 μmol/L.

Discussion

We present a rare case of RAE. Since the period from the onset of symptoms to the intervention was longer than 48 h, it is remarkable that kidney function recovered substantially. Acute RAE requires prompt diagnosis and precise definition of the lesion. Angiography is still considered the gold standard to confirm the diagnosis of acute RAE[9]. Optimal therapy for RAE still remains controversial even though various methods of management have been applied in the last decades including surgical intervention, anticoagulant therapy, systemic and selective thrombolytic therapy[10]. With respect to the higher mortality rate and no evidence for improved renal function recovery following embolectomy or vascular reconstruction, drug treatments are generally preferred[10]. The drug treatment

strategy for RAE includes anticoagulation with or without thrombolysis. Patients are typically anticoagulated with intravenous heparin and oral warfarin. This helps prevent further embolic events[11]. Both systemic and selective intra-arterial thrombolysis has been successful in producing clot lysis. Selective infusion minimizes systemic bleeding and is the preferred approach[12,13].

Since fibrinolytic therapy was successfully introduced by Halpern[14], many reports have been published on intra-arterial fibrinolysis as the therapy of choice, especially when the embolism takes place at intra-renal arteries. Both intra-arterial perfusion of streptokinase[15] and urokinase[16], and later on tPA[17] have been successfully used. After thrombolysis, it is important to keep the patient anticoagulated for a 24-h period with sodium heparin infusion, aiming to keep the activated partial thromboplastin ratio within the range of 1.5-2[18].

There are data that suggest thrombolysis only when ischemic renal tissue is still viable, which is within 60-90 min at normothermia[19,20]. Conflicting data suggest that renal recovery can be accomplished after prolonged occlusion[21,22]. In 2007, Cheng *et al*. reported a case of a 33-year-old man with atrial fibrillation; the condition was successfully managed 28 h after the onset of symptoms by administering t-PA[10].

In reality, there is evidence that ischemia can be reversed after longer periods of renal artery occlusion, and this almost certainly reflects the extent of collateral renal circulation[18]. Many patients do develop some degree of renal insufficiency during the acute episode, but the majority return to their baseline renal function[19]. In the report by Salam *et al*., 70% of the patients had their renal perfusion restored by lytic therapy, but only 30% recovered normal function of the affected kidney[21].

In the case presented, scintigraphy performed 2 days after thrombolysis showed no function of the right kidney, probably because our patient had acute tubular necrosis due to prolonged ischemia. Follow up scintigraphy 3 weeks after discharge showed that the right kidney function improved substantially according to the healed tubular lesions. This case demonstrates that intra-arterial thrombolytic therapy with a low dosage of 35 mg tPA may be an effective and safe strategy for the treatment of RAE, despite the period of ischemia being longer than 48 h. The presented results suggest that re-establishing of the blood flow to occluded kidneys should be attempted with no regard to strict time frames.

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Sažetak

USPJEŠNO LIJEČENJE EMBOLIJE BUBREŽNE ARTERIJE ČAK 48 SATI NAKON ISPADA

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Embolija bubrežne arterije je bolest koja se lako previdi zbog rijetke pojavnosti i nespecifične prezentacije. Iako rana dijagnoza i optimalno trombolitičko liječenje ponekad može vratiti bubrežnu funkciju, terapijske smjernice još nisu uspostavljene. Međutim, rana primjena antikoagulantne terapije je korisna, a o selektivnoj infuziji litičkih sredstava u bubrežne arterije, ako se primijeni u ranom stadiju, sve se češće izvješćuje u smislu povećanja njene učinkovitosti. Mi smo opisali kako intraarterijska trombolitička terapija s niskim dozama od 35 mg rekombinantnog tkivnog aktivatora plazminogena (t-PA) može biti učinkovita i sigurna strategija za liječenje embolije bubrežne arterije unatoč tomu što je razdoblje ishemije bilo duže od 48 sati.

Ključne riječi: *Atrijska fibrilacija; Bol u slabinama; Bubrežna arterija, opstrukcija; Trombolitička terapija; Tromboembolizam – terapija; Prikaz slučaja*