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Case report

Vacuum-Assisted Thrombo-Aspiration for Paradoxical Embolism in Left Renal Artery: A Case Report and Literature Review

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Paradoxical embolism through the foramen ovale is a rare and devastating event requiring urgent treatment. Herein, we present the case of a 23-year-old male who presented with a pulmonary embolism complicated by a left renal artery paradoxical embolism. Urgent vacuum-assisted thrombo-aspiration restored normal perfusion of the left kidney within 5 hours. The patient had a patent foramen ovale and heterozygous thrombophilia. However, a radioisotopic scan performed 2 years later revealed an unexpected decrease in left renal perfusion. Therefore, despite the angiographic success, functional evaluation using a renal scan should be performed to assess renal function.

Key Words: Embolism, Paradoxical, Foramen ovale, Thrombectomy, Renal

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INTRODUCTION

Paradoxical embolism (PDE) is an infrequent yet severe complication of venous thromboembolic disease (VTE) in patients with intracardiac defects, and cases of renal artery occlusion are rarely described in the literature [1]. We present the case of a young male admitted with a pulmonary embolism (PE) complicated by left renal artery PDE due to a patent foramen ovale (PFO). Successful renal artery recanalization was achieved with urgent thrombo-aspiration. Thrombo-aspiration was initially developed for acute ischemic stroke and is currently used to treat acute limb and splanchnic ischemia [2]. Its role in the treatment of renal thromboembolism is increasing, with the available literature supporting its safety and efficacy.

CASE

A 23-year-old male presented to the emergency department with chest pain, fatigue, and tachycardia. He was an athlete, a current smoker, and had a history of cruciate ligament injury in his left knee 21 days prior to presentation. He was advised to limit mobilization, use an orthopedic brace, and receive prophylactic antithrombotic treatment with subcutaneous tinzaparin (4,500 IU once daily). Unfortunately, 3 days before his presentation, he discontinued heparin because of a mild decrease in platelet levels to approximately 100,000/mm^3. Clinical examination results were unremarkable except for arterial blood oxygen saturation levels, which were low (92%). Computed tomography pulmonary angiography (CTPA) revealed the presence of pulmonary emboli in the distal parts of both main pulmonary arteries, extending into their segmental branches. Upon completion of the examination, the patient experienced intense abdominal pain and vomiting. Physical examination revealed moderate tenderness at the left costovertebral angle. Subsequent contrast-enhanced CT showed an occluded left renal artery and lack of contrast enhancement of the ipsilateral renal parenchyma, which was attributed to left renal artery thromboembolism (Fig. 1). The delayed phase of the CT scan was identical to the arterial phase in terms of renal parenchyma enhancement. The patient was transferred urgently to the Interventional Radiology (IR) suite, where a left renal artery mechanical thrombectomy using Penumbra's Indigo vacuum-assisted thrombo-aspiration device (Penumbra Inc.) was performed. After percutaneous catheterization of the right common femoral artery, a 6F sheath was introduced up to the orifice of the renal artery. Subsequently, a 6F Penumbra Indigo aspiration catheter was advanced over a 0.014 guidewire which aspirated thrombi and recanalized the renal artery and its branches. Notably, 5 mg of recombinant tissue-type plasminogen activator (r-tPA) was administered locally.

After the thrombectomy, 80% of the renal parenchyma showed normal perfusion (Fig. 2). On completion angiography, right common femoral artery obstruction was observed at the site of the vascular access sheath (Fig. 3). This was attributed to common femoral artery thromboembolism resulting from the thrombus removal manipulations with the aspiration catheter at the renal level. The protrusion of the renal thrombus into the aortic lumen may have played a role (Fig. 1). Open thrombectomy and sheath removal were performed after the patient was transferred to the operating room. It would be helpful if this could be managed with thrombo-aspiration at the same time as renal thrombectomy in the IR suite, obviating the need for patient transfer to the operating

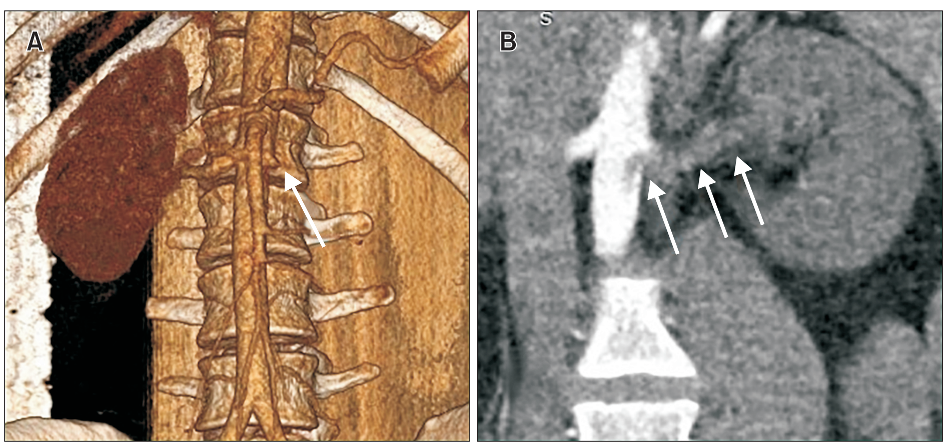

Fig. 1. Abdominal CTA. (A) Three-dimensional volume-rendering CTA depicted non-opacification of the left renal artery and kidney (arrow). (B) Multi-planar reconstruction image showed the culprit embolus in the left renal artery, protruding into the aortic lumen as a free-floating thrombus (arrows). This feature may have contributed to the common femoral artery embolism during thrombo-aspiration manipulations. CTA, computed tomography angiography.

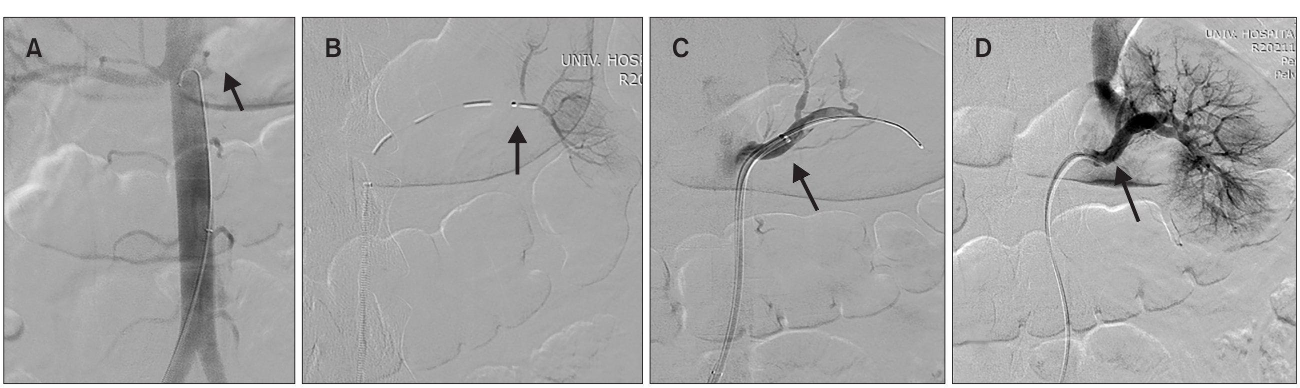

Fig. 2. Digital subtraction angiography. (A) A "cup" sign indicated renal artery embolism (arrow). (B) The guiding catheter transversed the thrombo-emboli, revealing patent distal renal vasculature (arrow). (C) Thrombo-aspiration with a 6F Penumbra Indigo aspiration catheter (arrow). (D) Completion angiography revealed normal patency (arrow).

theater, where general anesthesia was necessary. Unfortunately, this was technically unfeasible owing to the presence of the sheath. Any manipulation at the right common femoral level after gaining access from the contralateral common femoral artery carried the risk of further distal embolism.

Transthoracic echocardiography performed the next morning revealed a newly diagnosed PFO, which was later confirmed by transesophageal echocardiography (Fig. 4). Subsequent thrombophilia testing revealed inherited moderate to severe thrombophilia attributed to the heterozygous prothrombin G20210A mutations, heterozygous MTHFR C677T mutation, heterozygous MTHFR A1298C mutation, and PAI-1 4G/5G polymorphism. The patient was discharged on postoperative day 10 and was advised to take rivaroxaban 20 mg and clopidogrel 75 mg once daily on a long-term basis. Fourteen months later, the patient underwent percutaneous PFO repair with a 25/30 Amplatzer occluder (Abbott) at the cardiothoracic center (Fig. 4). The rivaroxaban dose was reduced to 10 mg once daily 6 months after the PE episode. Follow-up CTPA performed 6 and 12 months post-PE was normal.

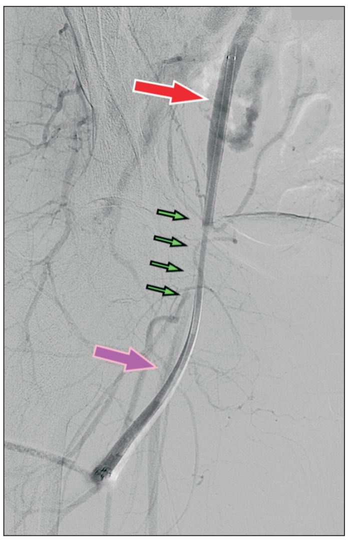

Fig. 3. Digital subtraction angiography. An obstruction in the right common femoral artery was detected from dislodging thrombus (green arrows). External iliac artery (red arrow) and superficial femoral artery (purple arrow) showed normal patency.

Two years after renal thrombectomy, the patient underwent a Tc-99m dimercaptosuccinic acid (DMSA) renal scan, which depicted widespread nonfunctional parenchyma of the left kidney with only a few functional islets on the upper pole (Fig. 5). Eventually, the left kidney contributed only 12% of the total renal function, although the creatinine level remained normal. The estimated glomerular filtration rate according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, based on a serum creatinine level of 1 mg/dL, was calculated to be 106 mL/min/1.73 m^2. Magnetic resonance angiography (MRA) confirmed patent renal arteries and some segmental branches; however, extended renal infarcts, parenchymal scarring, and shrinkage of the entire left kidney were observed (Fig. 6). Longitudinal dimensions were 10.6 cm for the right and 8.2 cm for the left kidney. The patient was in excellent physical condition

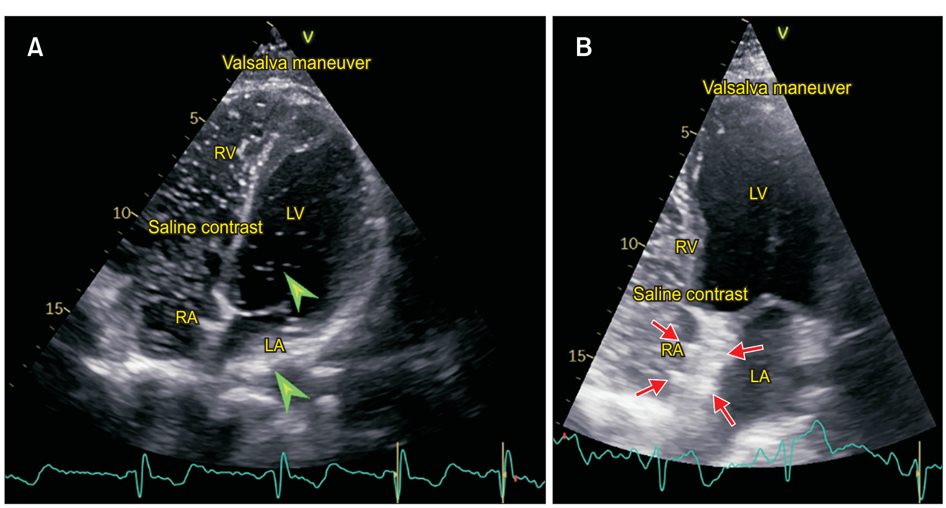

Fig. 4. Transthoracic cardiac ultrasound with intravenous contrast (shaken saline) injection, during the Valsalva maneuver, in the acute phase of pulmonary embolism. (A) Bubbles were clearly seen in the left atrium and left ventricle (green arrowheads) as they passed through the PFO. The PFO opened due to increased right atrial pressure caused by the right heart pressure overload from the pulmonary embolism. (B) After closure of the PFO by an Amplatzer device (red arrows), no bubbles were observed in the left heart. RV, right ventricle; LV, left ventricle; RA, right atrium; LA, left atrium; PFO, patent foramen ovale.

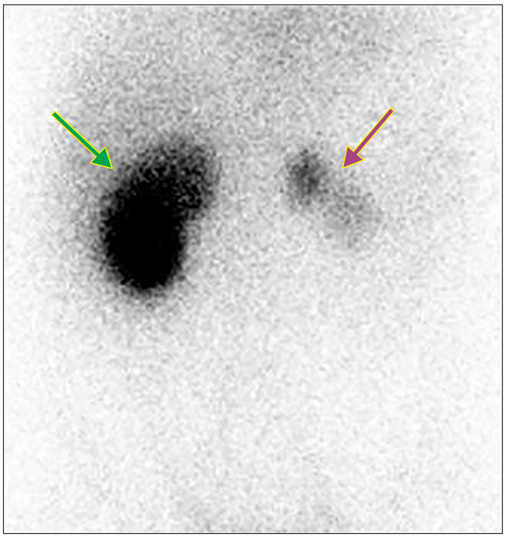

Fig. 5. Tc-99m dimercaptosuccinic acid renal scan, performed 2 years later. Extensive non-functioning parenchyma, with only a few functional areas in the upper pole (red arrow), was observed. Perfusion of the right kidney was normal (green arrow).

Fig. 6. Magnetic resonance angiography performed 2 years later. (A) The upper part of the left kidney was viable, but the middle and inferior parts were scarred. (B) Segmental branches were obstructed in the scarred area.

and had returned to his daily activities long ago. Regarding medical treatment, the plan was to further decrease the rivaroxaban dose to 2.5 mg twice daily in the next trimester after his scheduled consultation with a hematologist. The long-term plan was to stop rivaroxaban 2.5 twice daily after 1 year and take anticoagulants only in special circumstances (e.g., a scheduled operation). Additionally, a combination of clopidogrel 75 mg is always mandatory on a lifelong basis following both the renal intevention and PFO closure. This case report was approved by the Institutional Review Board of the University Hospital of Patras (IRB No. 29/11-07-2018). Informed consent was obtained.

DISCUSSION

PDE is an embolic event that occurs due to a right-to-left circulatory shunt when a venous thrombus is present. The most common type of shunt is a PFO, which is present in approximately 20% (9%-35%) of the general population [1,3]. PE increases the prevalence of PDE in cases of VTE and PFO due to right heart pressure overload [1]. The Valsalva maneuver is necessary during transthoracic echocardiography to unmask the PFO [4]. Therefore, a microbubble test is often required. Additionally, transesophageal echocardiography has a high sensitivity and specificity for PFO detection, reaching 95% [4]. In our patient, deep venous thrombosis was not confirmed by color Doppler ultrasound, suggesting that the entire thrombus had detached, leading to PE and PDE.

PDE may affect almost every part of the arterial vasculature, with clinical symptoms depending on the specific territory affected. Renal artery embolism, which has an incidence of 0.004%-0.007% in the general population, manifests as nonspecific symptoms such as abdominal pain, vomiting, fever, and hypertension [5-7]. Laboratory findings are variable and can include leukocytosis, elevated C-reactive protein levels, and hematuria [6]. High serum lactate dehydrogenase appears to be the most sensitive marker, but associated with poor specificity [8,9]. Diagnosis is usually established using nuclear isotope scanning and excretion urography. However, the best diagnostic method is computed tomography angiography (CTA), which has a sensitivity nearly similar to the digital subtraction angiography (DSA), traditionally considered the gold standard for diagnosis [8,9].

The triggering cause of the PDE in our patient was PE due to limited mobilization, discontinuation of tinzaprin for the previous 3 days (due to a mild decrease in platelet count), and moderate-to-severe thrombophilia. Heparin-induced thrombocytopenia type II was not included in the differential diagnosis. The patient had already stopped low molecular weight heparin, and after reinitiating low molecular weight heparin at his admission, no decrease in platelet count was observed; therefore, further testing for antibodies against complexes of heparin and platelet factor 4 was not followed.

Various therapeutic modalities have been used for the management of renal artery embolism including anticoagulation therapy for prevention of new embolic events, surgical embolectomy, thrombolysis, thrombo-aspiration with the use of syringe, as well as mechanical and pharmacomechanical thrombectomy [6,9]. Surgical revascularization techniques are less effective and have higher morbidity rates compared to thrombolysis [8,9]. Selective thrombolysis is preferred over systemic thrombolysis due to its lower risk of hemorrhage [8]. The most commonly reported devices for mechanical and pharmacomechanical thrombectomy are the AngioJet Rheolytic Thrombectomy (Boston Scientific) and Penumbra's Indigo Thrombo-aspiration. These devices offer rapid procedures and reduce the need for thrombolysis, minimizing bleeding risk and improving perfusion results [8,9]. Medical therapy and thrombolysis are appropriate treatments for renal infarcts involving the patent renal artery. However, in acute total renal artery embolic occlusion with impending renal parenchymal necrosis, the ideal time interval to restore patency is only 30-40 minutes. Thrombo-aspiration offers rapid reperfusion compared to thrombolysis, which is critical for this condition. The AngioJet Rheolytic Thrombectomy uses high-velocity saline jets to create a vacuum effect that breaks up and removes the thrombus. Penumbra's Indigo Thrombo-aspiration system consists of a catheter, separator, and aspiration pump. The catheter is inserted into the vessel and connected to the aspiration pump, which provides strong suction to remove the thrombus. The choice depends on the availability of a specific device and familiarity of the expert team.

We reviewed English literature on mechanical and pharmacomechanical thrombectomy in patients with renal artery embolisms. We identified nine similar cases (Table 1) [6,9-16]. Patients with thrombosed renal arteries due to atherosclerosis or hypercoagulable states, thrombosed renal side branches of aortic endografts, occlusion of renal transplant arteries, or aortorenal bypasses were excluded.

Although there is no consensus regarding the optimal treatment for renal artery embolism, these cases delineate the reliability of thrombo-aspiration techniques for urgent renal recanalization without significant complications. All but one of the authors reported postprocedural renal function improvement based mainly on laboratory markers. Tan et al. [13] observed an increase in creatinine levels in patients with a solitary kidney. Evaluation of renal function with nuclear scintigraphy was used in only one case. Despite a satisfactory angiographic result, a technetium-

Table 1. Cases of renal artery embolism treated with mechanical and pharmacomechanical thrombectomy techniques

Author	Year	No. of Pts	Related history	Procedure	Thrombolytic agent	Outcome
Li et al. [6]	2022	1	AFib	Thrombo-aspiration with the use of syringe	Urokinase	Normal perfusion, normal Cr
Wang et al. [9]	2013	1	Sick sinus syndrome, AFib	Thrombo-aspiration (Thrombuster II)	Urokinase	Normal Cr, improved perfusion
Greenberg et al. [10]	2002	1	AFib	Balloon angioplasty, rheolytic thrombectomy (AngioJet)	rtPA	Improved Cr (abnormal Cr before treatment)
Siablis et al. [11]	2005	1	None	Rheolytic thrombectomy (AngioJet)	Urokinase	Normal Cr
Syed et al. [12]	2010	1	None	Power-pulse Spray thrombectomy (AngioJet)	rtPA	Normal Cr, normal perfusion, good function
Tan et al. [13]	2011	1	Aortic thrombus, solitary kidney	Rheolytic thrombectomy (AngioJet), balloon angioplasty	rtPA	Increased Cr, normal perfusion
Komolafe et al. [14]	2012	1	AFib, cardioverter	Aspiration and rheolytic thrombectomy, drug-eluting stent	None	Normal Cr
Yousif et al. [15]	2018	1	AFib	Thrombo-aspiration (Penumbra's Indigo)	None	Normal Cr
Lim et al. [16]	2022	1	PFO	Mechanical and suction thrombectomy	Urokinase	Improved perfusion, improved Cr
Present case	2023	1	VTE-PFO	Thrombo-aspiration (Penumbra's Indigo)	None	Normal perfusion, Normal Cr, good function

'Perfusion' refers to the angiographic result, while 'function' refers to radio-isotopic scan evaluation.
PFO, patent foramen ovale; VTE, venous thromboembolic disease; Pts, patients; AFib, atrial fibrillation; rtPA, recombinant tissue plasminogen activator; Cr, creatinine.

99m MAG-3 (mercaptoacetyltriglycine) renal scan showed minimal function 3 days postoperatively, but improved significantly 2 years later [12].

Based on the experience accumulated over the last 2 decades in donation after organ circulatory death, the safe warm ischemic time for kidneys should not exceed 30 minutes [17]. Predictors of renal function recovery in renal artery occlusion include CTA with distal reconstitution of the occluded renal artery or visible distal segmental arteries on delayed- or venous-phase imaging. When the entire kidney is underperfused, it is often difficult to determine the presence of salvageable renal parenchyma. Studies in experimental animals with acute renal artery occlusion have shown that collateral circulation can maintain renal viability for up to 3 hours after occlusion [18].

Nuclear scintigraphy can accurately evaluate kidney function as well as the anatomy observed with other diagnostic imaging modalities and remains superior to other imaging modalities in the evaluation of renal flow. Renal scintigraphy with tubular retention agents such as DMSA provides excellent cortical imaging and is used in cases of infarction or established renal scarring. In our case, DMSA was used 2 years after the procedure and revealed an almost totally scarred left kidney. Although primary thrombo-aspiration was successful and the left renal artery remained patent, function in the left kidney did not recover completely. This highlights that technical success does not always translate to functional recovery; thus, consecutive renal function assessments with renal scintigraphy are recommended.

Comparing the initial DSA (selective renal angiography after wire passage and catheter insertion) before the thrombectomy with the DMSA and MRA, we observe that the upper part of the renal parenchyma, which remained functional, corresponds to the area opacified in the initial DSA beyond the renal artery obstruction. This suggest that the size of the distal arterial reconstitution may predict the final functional parenchyma volume.

Complete obstruction of the arterial inflow is a major risk factor for developing microthrombi in the renal parenchymal vasculature, with consequent cortical necrosis. The risk is heightened in patients with a moderate-to-severe thrombophilic profile. Extended loss of blood supply in the segmental branches beyond a critical time interval results in irreversible ischemia in the corresponding cortex because they are terminal arteries with no collaterals. There is a lack of evidence in the literature for the widely accepted interval of 4-6 hours to intervene for recanalization, and many patients are treated beyond this time limit with reported satisfactory results [19]. There is a large lack of confirmatory renal scintigraphy findings after "successful" recanalization in the literature; therefore, the success of urgent thrombectomy must be reconsidered. The creatinine levels and urine output are usually unaffected because the contralateral kidney is normal. Notably, renal function, as depicted by serum creatinine measurement and estimated by validated equations (preferably the CKD-EPI equation), is normal in patients without pre-existing chronic kidney disease, who may lose all or part of the renal parenchyma of one kidney. In our opinion, renal scintigraphy must be incorporated into standard clinical practice after successful renal thrombectomy. Although there are no specific guidelines on the timing of radioisotopic imaging, it is sensible to delay imaging until recovery from acute tubular necrosis to obtain reliable results.

In our review of the literature, all but one case of renal artery embolism had an arterial origin, and only one patient was treated with the Penumbra Indigo Thrombo-aspiration device. Our case is the first in the literature in which a renal artery embolism was originated from VTE and managed with Penumbra Indigo device. In a recent report, venous thrombi were successfully removed from the left renal vein using the Penumbra Indigo device [20].

In conclusion, we emphasize that Penumbra Indigo Thrombo-aspiration technique is valuable for prompt restoration of renal artery flow. However, the time required to restore the flow usually exceeds the safe time interval of 30-40 minutes, potentially leading to varying degrees of parenchyma necrosis. Therefore, we strongly suggest long-term functional renal studies, such as renal scintigraphy, to assess the amount of functional renal parenchyma.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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