



## Case Report

# AngioJet™ rheolytic thrombectomy induced intravascular haemolysis leading to Acute Kidney Injury requiring Dialysis

Hultin Sebastian<sup>1\*</sup>, Nguyen Tam<sup>2</sup> and Murali Karumathil<sup>1</sup><sup>1</sup>The Wollongong Hospital, Department of Renal Medicine, Australia<sup>2</sup>The Wollongong Hospital, Department of Vascular Surgery, Australia

**\*Address for Correspondence:** Sebastian Hultin, The Wollongong Hospital, Department of Renal Medicine, Australia, Email: sebastian.hultin@doctors.org.uk

**Submitted:** 11 July 2018

**Approved:** 02 August 2018

**Published:** 03 August 2018

**Copyright:** © 2018 Sebastian H. et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

## Abstract

**Background:** AngioJet™ rheolytic thrombectomy has been used in the treatment of deep vein thrombosis (DVT) to prevent post-thrombotic syndrome. Though not widely appreciated, it has the potential to cause intravascular haemolysis.

**Report:** A 37 year old man with no previous medical history presented to his GP with a three week history of progressive right upper limb swelling. Doppler imaging confirmed right upper limb DVT and CT scan demonstrated thoracic outlet syndrome. The patient underwent AngioJet™ thrombectomy followed by IV heparin infusion. Successful revascularisation of the occluded vein was achieved. Overnight he developed haematuria, which was initially attributed to IV heparin. Urinalysis however revealed no red cells or casts. Apart from an Hb drop from 134 to 117 his blood profile and blood film showed no abnormality. He subsequently developed progressive oliguria with marked oedema and acute kidney injury (AKI). His creatinine peaked at 1070µmol/l at 96 hours post procedure and he was started on intermittent dialysis. He remained dialysis dependent for 6 days. Ultrasound imaging excluded urinary obstruction. Autoimmune and vasculitic serology were negative. Intravascular haemolysis and haemoglobinuria was confirmed by raised LDH (1714u/L) and low haptoglobin (<0.1units). Direct Coomb's test, Cold agglutinin test and paroxysmal nocturnal haemoglobinuria screen were negative. The patient's renal function normalised over 3 months.

**Conclusions:** The likely cause of this man's AKI is heme pigment nephropathy from intra-vascular haemolysis. Increased awareness of this condition may allow early identification and intervention to reduce the risk of renal injury from AngioJet™ associated haemolysis.

## Introduction

We report a case of dialysis-requiring acute kidney injury AKI following AngioJet™ rheolytic thrombectomy in a 37 year old mine worker, likely secondary to mechanical haemolysis induced by the procedure. The increasing availability of percutaneous mechanical thrombectomy (PMT) has offered a novel avenue for management of both venous and arterial thromboses. Benefit has been demonstrated in lower limb DVTs particularly in the prevention of post thrombotic syndrome [1]. Although its benefit in upper limb DVT is less clear [2], the presence of a large symptomatic thrombus prompted decision to proceed with thrombolysis and PMT in addition to anticoagulation. Targeted therapy for thrombus dissolution also remains an attractive strategy in patients with significant bleeding risk or where systemic thrombolysis is not an option [3]. AngioJet™, available at our facility, creates a hydrodynamic vortex through retrogradely oriented high speed fluid jets allowing selective trapping and dissolving of thrombi [4].

While AngioJet™ thrombectomy is recognised as an effective treatment for DVT, adverse effect data has focused on mortality (0%), thromboembolic events



(<1%) and requirements for blood transfusion (4.2-14%) despite an insignificant incidence of major bleeding [5]. A systematic case series review in 2011 concluded that PMT was a feasible treatment for DVT and possibly safe, although the authors concluded that the level of evidence was for adverse events was lacking [5]. A more recent systematic review of percutaneous thrombectomy in pulmonary embolism in 2013 highlighted significant cardiovascular risk associated with AngioJet™ with cardiovascular complications reported in 21.1% of all cases with massive embolism and 17.4% of cases with submassive embolism [6]. There was also a significant risk of risk of bradyarrhythmia (11.6%) and asystole (1%) in addition to a higher rate of bleeding (14.5%). The same review found an incidence of 11.7% of renal impairment, which may have been significantly under reported due to post intervention routine biochemical testing not always taking place.

Although PMT induced haemolysis is well described in the literature, there has been historical under-appreciation of the potential for severe AKI largely due to lack of in-vivo trials evaluating renal function as an outcome and lack of reporting on renal function change as a complication [7]. Early studies have demonstrated intravascular haemolysis following procedure with clinically insignificant drops in Hb concentrations, elevated LDH and low haptoglobin consistent with haemolysis, and less frequently an increase in creatinine [8]. In 2009 [3] reported a presumed first case of severe AKI requiring dialysis following AngioJet™ PMT in a patient with pulmonary embolus [3]. Prior to this in 2007, however, a prior paediatric case of AKI involving PMT had already been reported in a 16 year old patient with severe clot burden DVT and multiple administration of contrast resulting in severe AKI requiring peritoneal dialysis [9]. More recently in 2016 a further case of AKI requiring dialysis following PMT treatment of an extensive lower limb and IVC DVT [10] was reported. Our case adds to a growing case series of severe AKI requiring short to medium term RRT.

## Case Report

Mr. CM, a 37 year old caucasian male, first presented to his general practitioner complaining of progressive right upper limb swelling. His past medical history was unremarkable except for a 20 pack year history of smoking. He was not taking regular medications and had no allergies. Outpatient ultrasound of the upper limb revealed extensive thrombus within the right subclavian vein and he was referred to the emergency department for further management. Clinical examination at presentation revealed distended proximal axillary veins with swelling of the distal limb. He was haemodynamically stable with a normal cardiopulmonary examination, a blood pressure of 110/74mmHg, heart rate of 72 beats per minute, respiratory rate of 14 breaths per minute and oxygen saturation of 98% on room air. His haematological and biochemical profiles at presentation were unremarkable. Computed tomography excluded pulmonary embolism, but confirmed a proximal subclavian thrombus with attenuation of the subclavian vein between the medial aspect of the right clavicle and the first rib with arms elevated, suggestive of thoracic outlet syndrome. He was started on intravenous heparin but due to the size of the thrombus and perceived benefits of thrombolysis in deep venous thrombosis (DVT) with regards to post thrombotic syndrome [5], decision to proceed to rheolytic thrombolysis was made. AngioJet™ thrombolysis was undertaken, during which he received 3000u of Heparin followed by 500'000u Urokinase, preceding suction thrombectomy and venoplasty of the proximal subclavian stenosis using an 8x20mm balloon. Standard non-iodinated contrast was administered as per protocol during procedure and to confirm vessel patency post procedure. There were no intraoperative complications. Post operatively intravenous heparin was continued for the next 72hours and he also received intravenous fluids at 80mL/h. There were no documented episodes of hypotension.

24 hours post procedure, the patient developed sudden onset painless haematuria, suspected initially to be secondary to the urinary catheter in the presence of heparin anticoagulation. He remained haemodynamically stable. Blood profile at 48 hours,



however, indicated an AKI with a rise in creatinine to 436  $\mu\text{mol/L}$  (baseline creatinine 90  $\mu\text{mol/L}$ ), associated with drop in haemoglobin from 134g/L to 117 g/L. His biochemistry also revealed mild liver function test derangement with ALP 113U/L, ALT 90U/L, AST 348U/L, but normal bilirubin. He became progressively oliguric, despite a positive fluid balance (5000mL over 72 hours) and progressively worsening signs of fluid overload. His creatinine peaked at 1020  $\mu\text{mol/L}$  at 72 hours post procedure, necessitating commencement of haemodialysis for symptomatic fluid overload, uraemia and metabolic acidosis, despite optimal medical therapy. Investigation to evaluate his AKI revealed proteinuria with urine albumin:creatinine ratio of 202.6mg/mmol and protein:creatinine ratio of 471mg/mmol - nonspecific in the setting of oliguric renal failure. Urinalysis showed 3+ blood, but urine microscopy was repeatedly negative for microhaematuria or casts. Serum creatine kinase (CK) and serum myoglobin were raised at 348U/L and 254ng/L respectively. Renal imaging revealed bilateral peri-nephric stranding without evidence of infarction or ureteric obstruction. Renal vasculature was without abnormality on duplex ultrasound. Autoimmune and vasculitic serology were negative. Further biochemical investigations confirmed intravascular haemolysis with LDH markedly raised at 1714u/L and very low haptoglobin (<0.1u/L). Direct Agglutinin Test (DAT / Coombs test) and cold agglutinin tests were negative. Peripheral blood flow cytometry showed normal GPI-linked protein profile. Renal biopsy was not undertaken due to risk of bleeding from anticoagulation therapy. His urine output improved over the ensuing week and renal replacement therapy (RRT) was discontinued. The patient's creatinine continued to improve and normalised over the next 3 months. He was maintained on warfarin whilst awaiting first rib resection.

## Discussion

We present a case of a heme pigment AKI following rheolytic thrombectomy induced haemolysis. This case adds to a growing cohort of cases of AngioJet™ related renal impairment with significant morbidity. In the setting of lack of appreciation for potentially severe intravascular haemolysis from the PMT device, AKI was initially attributed to dehydration and contrast nephropathy. Haemoglobinuria was suspected following a positive urinalysis for haematuria but negative urine microscopy and a positive haemolysis screen. Elevated serum myoglobin raised the possibility of myoglobinuria from rhabdomyolysis, but made unlikely by the relatively modest elevation of CK. The relative low titres and low specificity of serum myoglobin titres was non-specific. Paroxysmal nocturnal haemoglobinuria screen was negative and negative Direct Agglutinin and Cold Agglutinin tests supported PMT mechanical haemolysis as the primary aetiology, and a diagnosis of haeme pigment nephropathy was made. The lack of cardiovascular and renal comorbidities in our case and previously reported cases of AngioJet™ related AKI requiring RRT, makes the severity of kidney injury unexpected. There are, however, some similarities which may offer avenues for future research and risk stratification for AKI in patients undergoing PMT. The concomitant contrast administration from both CT angiography prior to PMT may have contributed to the severity of the AKI [8,9]. The prolonged use of PMT, particularly in a patent vessel, has been further identified as potentially increasing risk of haemolytic and heme pigment nephropathy with a haematocrit drop >10% independently increasing odds for AKI [7]. Using short bursts of thrombolysis rather than prolonged activation may further limit haemolysis burden [11].

Consideration surrounding the uncertainty of risk stratification should be taken into account when referring a patient for PMT of both venous and arterial thromboses. Appropriate intravenous fluid administration pre- and post- AngioJet™ thrombectomy as well as avoidance of other nephrotoxic insult followed by close biochemical monitoring to identify clues to haemolysis and AKI would be prudent steps, because once AKI sets in, the treatment options are limited to largely supportive and symptomatic measures.



## References

1. Tadavarthi SM, Murray PD, Inampudi S, Nazarian GK, Amplatz K. Mechanical thrombectomy with Amplatz device: human experience. *J Vasc Interv Radiol.* 1997; 5: 715-724. [Ref.: https://tinyurl.com/yavvgkpe](https://tinyurl.com/yavvgkpe)
2. Nazarian GK, Qian Z, Coleman CC, Rengel G, Castaneda-Zuniga WR, Hunter DW, et al. Hemolytic effect of the Amplatz thrombectomy device. *J Vasc Interv Radiol.* 1994; 5: 155-160. [Ref.: https://tinyurl.com/y7b7gvqh](https://tinyurl.com/y7b7gvqh)
3. Dukkipati R, Yang EH, Adler S, Vintch J. Acute kidney injury caused by intravascular haemolysis after mechanical thrombectomy. *Nephrology.* 2009; 5: 112-116. [Ref.: https://tinyurl.com/ybkr1tpe](https://tinyurl.com/ybkr1tpe)
4. Wagner HJ, Müller-Hülsbeck S, Pitton MB, Weiss W, Wess M. Rapid thrombectomy with hydrodynamic catheter: results from a prospective multicentre trial. *Radiol.* 1997; 205: 675-681. [Ref.: https://tinyurl.com/ybefcvvy](https://tinyurl.com/ybefcvvy)
5. Karthikesalingam A, Young EL, Hinchliffe RJ, Loftus IM, Thompson MM, et al. A systematic review of percutaneous mechanical thrombectomy in the treatment of DVT. *Eur J Vasc Endovasc Surg.* 2011; 41: 554-565. [Ref.: https://tinyurl.com/y6uutp9z](https://tinyurl.com/y6uutp9z)
6. Bunwaree S, Marco Roffi, John M Bonvini, Stéphane Noble, Marc Righini, et al. AngioJet® rheolytic thrombectomy: a new treatment option in cases of massive pulmonary embolism. *Interv Cardiol.* 2013; 5: 71-87. [Ref.: https://tinyurl.com/ydhthtwa](https://tinyurl.com/ydhthtwa)
7. Escobar GA, Dillon B, Matthew RA, Mohammed FF, Ahsan TA, Lewis CL, et al. Risk of Acute Kidney Injury after Percutaneous Pharmacomechanical Thrombectomy Using AngioJet in Venous and Arterial Thrombosis. *Ann Vasc Surg.* 2017; 42: 238-245. [Ref.: https://tinyurl.com/y8mqdmcc](https://tinyurl.com/y8mqdmcc)
8. Mair D, T Eastlund, G Rosen, R Covin, JV Harmon, et al. Haemolysis during percutaneous mechanical thrombectomy can mimic a haemolytic transfusion reaction. *Transfusion.* 2005; 45: 1291-1294. [Ref.: https://tinyurl.com/y8txwjtu](https://tinyurl.com/y8txwjtu)
9. Arslan B, Ulku Cenk Turba, Alan H Matsumoto. Acute Renal Failure Associated with Percutaneous Mechanical Thrombectomy for Iliacaval Venous Thrombosis. *Semin Intervent Radiol.* 2007; 24: 288-295. [Ref.: https://tinyurl.com/y9n4zker](https://tinyurl.com/y9n4zker)
10. Bedi P, Daniel Addanki, Aaron Reichman, Shyan-Yih Chou, Ira Reiser. Acute kidney injury requiring renal replacement therapy due to severe hemolysis after mechanical thrombectomy. *Case Rep Int Med.* 2016; 3: 87-90. [Ref.: https://tinyurl.com/yayrvft2](https://tinyurl.com/yayrvft2)
11. Whisenant BK, Baim DS, Kuntz RE, Garcia LA, Ramee SR, et al. Rheolytic thrombectomy with the Possis AngioJet: technical considerations and initial clinical experience. *J Invasive Cardiol.* 1999; 11: 421-426. [Ref.: https://tinyurl.com/y8ze2b8m](https://tinyurl.com/y8ze2b8m)
12. Kasirajan K, Gray B, Ouriel K. Percutaneous AngioJet thrombectomy in the management of extensive deep venous thrombosis. *J Vasc Int Radiol.* 2001; 12: 179-185. [Ref.: https://tinyurl.com/y7jqqrfr](https://tinyurl.com/y7jqqrfr)
13. Plate G, Eklöf B, Norgren L, Ohlin P, Dahlström JA. Venous thrombectomy for iliofemoral vein thrombosis—10 year results of a prospective randomised study. *Eur J Vasc Endovasc Surg.* 1997; 14: 367-374. [Ref.: https://tinyurl.com/yd2z36ho](https://tinyurl.com/yd2z36ho)
14. Han X, Baolei Z, Xuemin W, Wenming W, Chao M, et al. Mechanical thrombectomy device AngioJet™ is effective for the treatment of acute deep venous thrombosis. *Biomedical Research.* 2017; 28: 5084-5088. [Ref.: https://tinyurl.com/ya29rvco](https://tinyurl.com/ya29rvco)