



Renal Failure Secondary to Intravascular Hemolysis From AngioJet® Necessitating Hemodialysis

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Introduction

Percutaneous mechanical thrombectomy (PMT) consists of a group of devices and techniques designed to clear intravascular thrombus. Although not approved by the Food and Drug Administration (FDA) for use in pulmonary embolism (PE), a handful of case reports have shown some effectiveness of AngioJet in treating this disease. Adverse effects that have occurred with this procedure including intravascular hemolysis, leading to hemoglobinuria which can damage the renal tubules. To our knowledge, we report the first known case of a patient undergoing AngioJet for pulmonary embolism which resulted in massive intravascular hemolysis leading to acute renal failure, necessitating dialysis.

Case Summary

•A 43 year old African-American female, G5P0, with an 8 week intrauterine pregnancy presented to the ED with crampy abdominal pain, shortness of breath, and shoulder pain. The patient's past medical history was significant for hypertension, uterine fibroids, and a history of 1 spontaneous abortion in the first trimester, and 3 elective therapeutic abortions. She was not taking any medications. Her social history was notable for smoking one pack of cigarettes per week for 25 years, and denied alcohol or illicit drug use.

•On physical exam, her vital signs were notable for HR of 118, BP of 142/87, and RR of 30. Oxygen saturation was 100% on a nonrebreather mask. The patient was alert and oriented, diaphoretic, and in visible distress. She was unable to speak full sentences. Her jugular venous pressure was elevated to the jawline. The heart exam revealed no murmurs, rubs or gallops. Her lungs were clear. Her abdominal was notable for a palpable fibroid uterus. Her extremities were cool.

•An acute pulmonary embolism was diagnosed on spiral CT. The patient developed hemodynamic instability. Given concurrent vaginal bleeding and a threatened abortion, she was deemed not to be a surgical candidate and thrombolytics were relatively contraindicated. She underwent AngioJet thrombectomy of the right pulmonary artery and inferior vena cava (IVC) filter placement. The procedure was terminated because of bradycardia.

•The patient had red colored urine and hyperkalemia after the procedure.

•A urine sample was centrifuged which showed a red supernatant which was consistent with hemoglobinuria or myoglobinuria. The blood was then centrifuged, showing red plasma which was consistent with hemoglobinuria. Alkalinization of the urine and hydration were started. Hemodialysis (HD) was initiated for the management of persistent hyperkalemia.

•She remained on HD for the next 20 days. Gradually, her urine output improved, and on hospital day 21 HD was discontinued. She exhibited signs of recovery of her renal function with improving daily urine output, Her creatinine returned to normal on hospital day 25.

Results

Chemistry on admission:

137	106	8	140
3.6	18	1.1	

The patient's creatinine peaked at 10.7 mg/dL on Hospital Day #15.

Following the AngioJet procedure, a repeat chemistry showed:

135	109	14	177
7.8	10	2.1	

Urinalysis:
Red Color
+1 leukocyte esterase
4.0 urobilinogen
+2 blood
+1 bilirubin
17 White blood cells
64 Red Blood Cells

Potassium was labeled as "grossly hemolyzed"

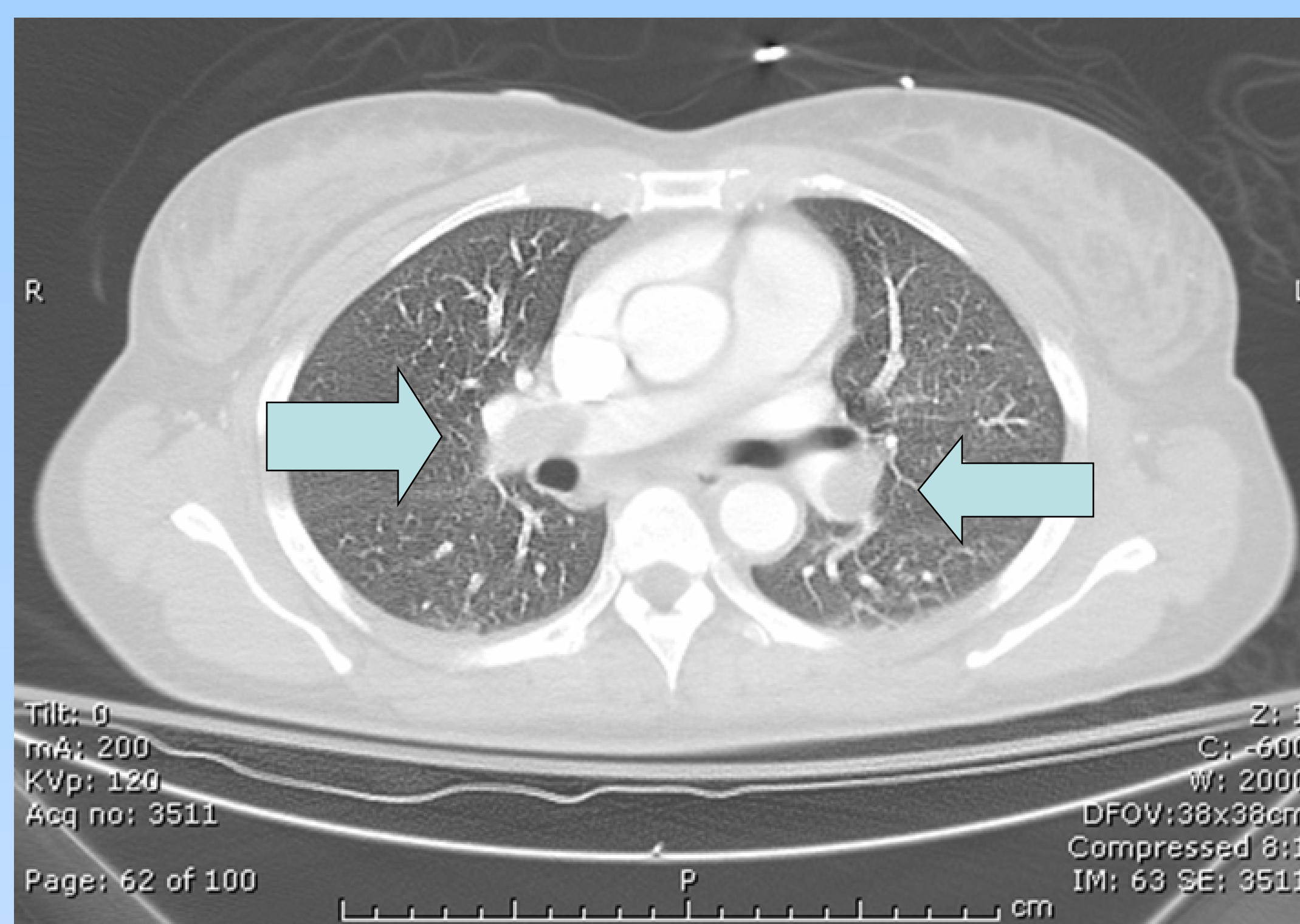
•A CT of the chest with intravenous contrast revealed large acute pulmonary emboli in the bilateral mainstem arteries extending to the subsegmental levels, with evidence of right heart strain.

•A transthoracic echocardiogram showed an ejection fraction of 65-70%, a severely dilated hypokinetic right ventricle with systolic function moderate-to-severely reduced. A flattened septum was seen consistent with right ventricular pressure/volume overload, with mild pulmonary hypertension with a systolic pressure of 42 mm Hg.



Pulmonary angiogram showing pulmonary embolus with filling defects from injected contrast in the right pulmonary artery.

Results



Computed Tomography of the chest with IV contrast showing pulmonary emboli at the main and subsegmental level of the right and left pulmonary arteries. (Arrows)

Discussion

•Intravascular hemolysis can result in acute tubular necrosis due to hemoglobinuria. The evidence that this patient had intravascular hemolysis were the presence of red urine, low haptoglobin, elevated LDH, and elevated bilirubin.

•Diagnostic clues can be obtained when urine and blood are centrifuged.

- Urine supernatant appears red and is dipstick positive for heme. This strongly suggests that the red urine is due to either hemoglobinuria or myoglobinuria.

- If the supernatant appears red but is dipstick negative for heme, then presence of porphyria, ingestion of beets, food dyes, the bladder analgesic phenazopyridine, or other medications should be explored

- Centrifugation of the patient's blood will help differentiate if the red urine is due to hemoglobinuria or myoglobinuria. When blood is centrifuged in patients with hemoglobinuria, the plasma is red or pink in color, whereas the plasma remains clear if red urine is due to myoglobinuria.

•Myoglobin is a non-protein bound small molecule with a molecular weight of 17,000 kDa which is filtered and excreted rapidly in the presence of normal renal function so is generally not found in plasma.

• Hemoglobin is a larger molecule with a molecular weight of 69,000 kDa in its tetramer form and 34,000 kDa in dimer form. The tetramer form is bound to haptoglobin restricting its filtration and excretion. The dimeric form is filtered and reabsorbed and can only be excreted once the proximal tubule reabsorptive capacity is overwhelmed by a high free dimer concentration in the plasma .

•Hemoglobin in the bloodstream is normally cleared by several self-regulatory mechanisms, including the binding of haptoglobin, reactions with nitric oxide, and the oxidation of ferric heme, which is degraded by the liver.

Discussion

•This patient developed intravascular hemolysis after PMT with Rheolytic AngioJet thrombectomy. Rheolytic AngioJet thrombectomy has been shown to be one of the most efficacious techniques in removing clot in cases such as peripheral arterial thrombosis and graft occlusions; a few case reports have shown effectiveness of AngioJet in treating pulmonary embolism.

•Rheolytic AngioJet works by selective trapping and destruction of thrombus by hydraulic recirculation, in which a hydrodynamic vortex is created by high-speed fluid jets from the tip of the catheter. This results in a stagnation pressure gradient known as the Venturi effect, which traps, solubilizes, and passively evacuates the thrombus. This also results in non-immune mechanical lysis of red blood cells in a non-immune fashion.

•This patient underwent AngioJet because of hemodynamic instability and her contraindications to anticoagulation. There are case reports of its use when there is massive clot burden in the absence of the contraindications to anticoagulation.

•While the exact mechanism of hemoglobinuria causing renal failure is unclear, it is thought to be a nephrotoxic effect of heme proteins causing cast formation and obstruction, resulting in acute tubular necrosis in the proximal tubular cells (PTC) of the kidney. Experimental animal studies conducted in rats showed that multifactorial insult predisposed them to renal failure, including induction of renal ischemia along with infusion of hemoglobin. In addition, the presence of methemoglobin (produced from oxidation of hemoglobin through nitric oxide scavenging), produced severe azotemia and tubular necrosis. Infusion of hemoglobin under acidic conditions also caused moderate azotemia, but not as severe as methemoglobin. Tubular obstruction was induced by various mechanisms (methemoglobin casts, uterine ligation, ischemic acute renal failure), which increased proximal tubular hemoglobin uptake, causing lysosomal overload and PTC necrosis. Hyperkalemia can represent a true in-vivo hemolysis of red blood cells in the circulation of the affected patients and urgent initiation of dialysis can be indicated in this setting.

•The prognosis of acute renal failure in this setting appears to be good in the absence of any other contributing factors. To our knowledge, this is the first case report of acute renal failure requiring renal replacement therapy due to hemoglobinuria induced by AngioJet.

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