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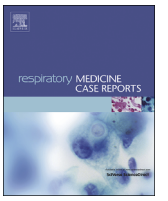

Case Report

Point of care ultrasound detection of thrombus straddling a patent foramen ovale in a patient with acute chest syndrome

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ABSTRACT

Patients with sickle cell disease can develop acute chest syndrome and are at high risk of developing pulmonary thrombosis. We report a case of a young woman with sickle cell disease who was hospitalized for vaso-occlusive crisis and subsequently developed worsening acute chest syndrome and stroke, discovered on point of care ultrasound to have right heart failure and a thrombus straddling a patent foramen oval. POCUS is highly specific for the detection of right heart dilation/dysfunction and should be a routine component of the assessment of acutely decompensating patients.

1. Introduction

Sickle cell disease (SCD) is characterized by a mutated beta chain of hemoglobin, resulting in decreased red blood cell (RBC) deformability, hemolysis, and a hypercoagulable state [1]. Patients with SCD can develop acute chest syndrome (ACS) and pulmonary thrombosis, both causing significant morbidity and mortality. These conditions coexist and have overlapping symptoms, making them challenging to differentiate. Point of Care Ultrasound (POCUS) has improved our ability to detect cardiopulmonary pathology. We present a case in which POCUS identified right heart failure and a thrombus straddling a patent foramen ovale (PFO) in a patient with SCD, stroke, and ACS. Our case highlights the importance of POCUS in acutely decompensating patients.

2. Case description

A 37-year-old woman with a past medical history of SCD complicated by multiple episodes of ACS presented to the emergency department with acute onset, diffuse pain. She was febrile, tachycardic, and tachypneic with an oxygen saturation of 97% on room air. Examination revealed bilateral lower lobe crackles. Laboratory workup revealed a white blood cell (WBC) count of 19.3 WBC/mL, hemoglobin of 10 gm/dL, platelets of 353,000 cells/mL, creatinine of 0.7 mg/dL, lactate dehydrogenase (LDH) of 565 IU/L, and an undetectable troponin I. Her chest x-ray was clear, and computed tomography (CT) of the chest showed bibasilar consolidation without evident pulmonary embolism (PE) or aortic dissection. She was diagnosed with vaso-occlusive crisis (VOC) and ACS and treated with intravenous (IV) analgesia, antibiotics, and IV fluids.

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On hospital day two, her hemoglobin decreased to 7.4 mg/dL for which she was transfused with 1 unit of packed red blood cells (PRBC). Over the course of the day, she became lethargic and hypoxic requiring supplemental oxygen, and ultimately developed a left sided facial droop with decreased muscle tone in her left upper/lower extremities. CT angiogram of the head and neck showed hypoattenuation in the right parietal region likely representing early infarct, and increasing upper lobe airspace opacities compared to the initial CT chest. She was transferred to the intensive care unit (ICU) where her hypoxia worsened, requiring heated, humidified high flow nasal cannula. Repeat laboratory investigations revealed an increasing creatinine, bicarbonate of 14 mMol/L, total bilirubin of 4.2 mg/dL, lactate of 12 mMol/L, alanine aminotransferase 93 IU/L, Aspartate transaminase 195 IU/L, troponin I of 1.43 ng/mL, WBC count of 33.8 WBC/mL, hemoglobin of 9.5 mg/dL, platelets of 266,000 cells/mL, and LDH of 2563 IU/L. Her clinical presentation, imaging and laboratory profile was compatible with worsening VOC and progressive ACS.

POCUS was performed on arrival to the ICU and revealed a severely dilated right ventricle (RV) (Image 1) with decreased function, septal flattening (Video 1), a mobile echogenic structure between the right and left atrium, consistent with a thrombus trapped in a patent foramen ovale (PFO; Videos 1 and 2 and Fig. 1), and an inferior vena cava (IVC) greater than 2.1cm with less than 50% collapsibility (Fig. 2).

Video 1: Parasternal Short axis and Right Ventricular Focused Apical 4 Chamber.

Video 2: Parasternal Long Axis and Right Ventricular Inflow.

There was no evidence of deep vein thrombosis (DVT) using 2-point examination (compression of femoral vein above/below/at the saphenous vein junction and the popliteal vein through trifurcation). It was determined she was not a candidate for surgical thrombectomy given the severity of her ACS and received 100 mg of alteplase in addition to unfractionated heparin IV for presumed PE and thrombus trapped in a PFO. Arrangements were made for emergent erythrocytopheresis with transfusion (automated exchange transfusion), but the patient required endotracheal intubation after an aspiration event, and then progressed rapidly to multiorgan system failure complicated by refractory acidosis. She developed cardiac arrest within 18 hours of ICU admission and attempts to resuscitate her were unsuccessful. Autopsy revealed death from multisystem organ failure from SCD and right middle cerebral artery stroke. Diffuse bone marrow necrosis was seen on histologic section of vertebrae. Histologic sections of the lungs revealed mul-

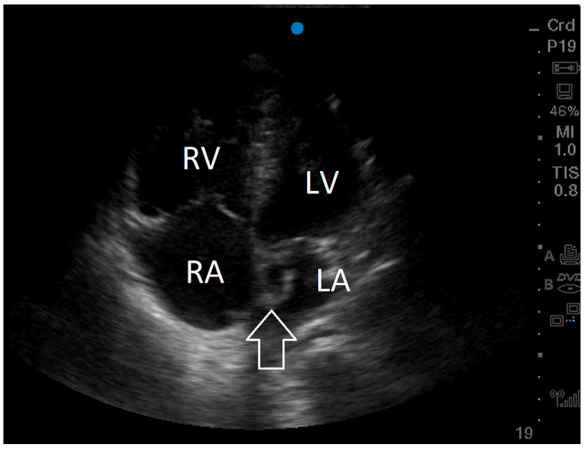

Fig. 1. Still image of the apical 4 chamber view shows a severely dilated right ventricle which is larger than the left ventricle with an arrow highlighting a hyperechoic structure extending from the interatrial septum into the left atrium. RV = Right ventricle. RA = Right Atrium. LV = Left Ventricle. LA = Left Atrium.

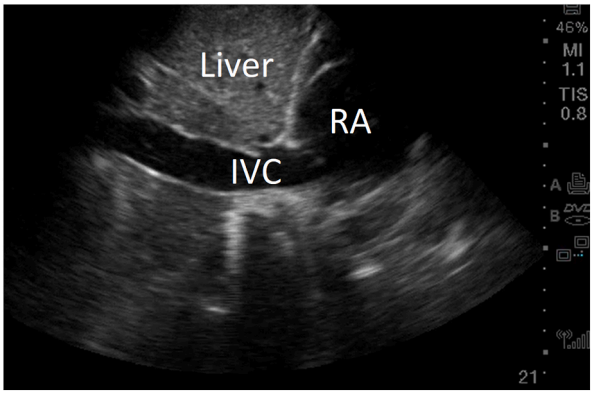

Fig. 2. Still image of the patient's plethoric IVC. The IVC was >2.1cm in diameter just distal to the entrance of the hepatic vein and collapsed <50% despite vigorous inspiratory effort by the patient while receiving supplemental oxygen via nasal canula, suggesting elevated right atrial pressures. IVC = Inferior Vena Cava.

tiple emboli of necrotic tissue and adipocytes consistent with necrotic fat/bone marrow emboli (Fig. 3). Notably, there were no identifiable thrombi in the pulmonary vasculature.

3. Discussion

3.1. Clinical discussion

ACS is characterized by chest pain, fever, dyspnea, and hypoxemia and develops in patients with SCD, typically 2–3 days after admission for VOC [2]. A common trigger for ACS in adults with severe VOC is embolization of fat from necrotic bone marrow [3]. Patients with SCD are also at a high risk for venous thromboembolism (VTE) compared to the general population, and the incidence of PE in ACS has been reported to be as high as 17% [4,5].

Our patient had progressive hypoxic respiratory failure from ACS and an ischemic stroke. Both are indications for exchange transfusion, the most aggressive treatment for any severe, acute complication of SCD [6]. Arguably, an earlier and more aggressive transfusion strategy might have benefited this patient, but her relatively high initial hemoglobin prevented the administration of simple transfusions, and exchange transfusion was not yet indicated according to guidelines [7]. An acute elevation of pulmonary pressures is common in ACS, increasing the risk of right to left intracardiac shunt [8,9]. Initial evaluation with POCUS lead to discovery of thrombus trapped in the patient's PFO, providing an explanation for her neurologic symptoms and right heart failure. We were unable to determine if the right heart failure was attributable to PE or ACS, but progression of respiratory failure and shock influenced the decision to pursue thrombolytics.

4. Imaging discussion

Our patient's initial CT chest showed ACS limited to the lower lobes and no evidence of PE, but she subsequently developed upper lobe infiltrates visualized on CT angiogram of her head and neck. POCUS revealed evidence of right heart failure, including a severely dilated RV, decreased RV function, evidence of RV volume (diastolic septal bowing into the left ventricular cavity on parasternal short axis) and pressure (systolic septal bowing into the left ventricular cavity on parasternal short axis) overload, and plethoric IVC. These findings are not specific to PE, particularly in the setting of coexisting respiratory failure, however the identification of a mobile thrombus trapped in the patient's PFO established a diagnosis and provides an explanation for the neurologic changes. The diagnosis of paradoxical embolism should be considered in any patient with hypoxia and neurologic symptoms, but particularly in patients with SCD and ACS where VTE is common.

5. Pathologic discussion

Histopathologic findings on autopsy showed a right middle cerebral artery stroke and confirmed death from multisystem organ failure from SCD with histology showing emboli of necrotic tissue and adipocytes in the lungs and bone marrow necrosis in the vertebrae (Fig. 3). Due to the lack of identifiable thrombi within the pulmonary vasculature, we entertained the possibility of the presumed thrombus within the PFO being related to fat emboli in transit, but we were unable to find evidence of fat emboli in the brain. This may have been due to the difficulty in identifying acute cerebral micro-emboli on autopsy, as they require Oil-Red-O staining on frozen sections, which we were unable to obtain because of lack of access to non-embedded fixed tissue. Additionally, the patient had thrombolytics administered hours prior to autopsy, potentially leading to dissolution of the thrombi. On autopsy studies, filling defects on CT angiogram can be derived from (1) propagation from distal thrombus, (2) in situ thrombosis, and/or (3) embolism of bone marrow/fat [10,11]. Clinically distinguishing fat/marrow embolism from in situ thrombosis or distal propagation is not possible, thus treatment with anticoagulation and possibly thrombolytics is recommended [1,12].

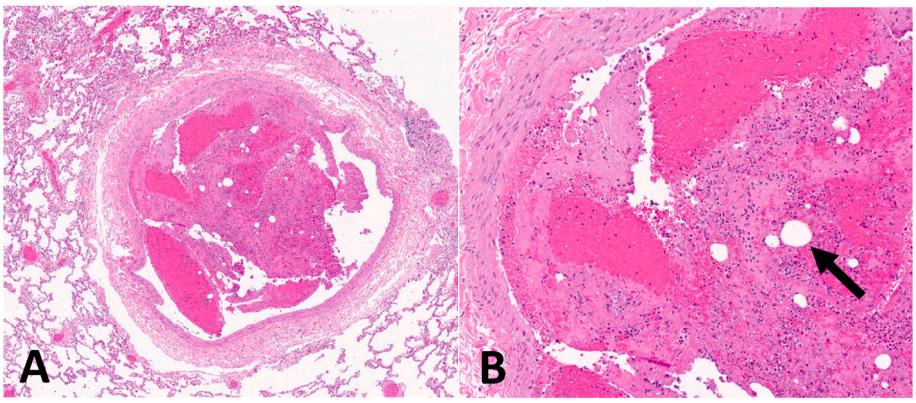

Fig. 3. Histopathological features, stained with hematoxylin and eosin. (a) Low power-pulmonary vessel emboli with hemorrhage, necrotic material, and adipocytes (consistent with a necrotic fat/bone marrow emboli) with adjacent lung parenchyma. (b) High power-necrotic and hemorrhagic material with inflammatory cells and adipocytes (arrow) in a pulmonary vessel.

6. Brief review of the literature

6.1. Role of POCUS in the evaluation of ACS and PE

Right heart failure and PE have been described in severe ACS, and both can be detected with POCUS [9,13,14]. When performed by trained emergency department physicians, POCUS has a high specificity for detection of right heart dilation/dysfunction [15–17]. Echocardiographic RV dilation/dysfunction are not specific to PE, but detection of a clot in transit (mobile thrombus detected in the right ventricle or atrium), including detection of a thrombus straddling a PFO as in our patient, can confirm the diagnosis [18]. POCUS can aid in the differential diagnosis of shock, including tamponade or severe systolic dysfunction, and exclude massive PE as the cause of shock if the RV is normal in size/function [18]. Thrombus in transit has been identified by POCUS, but detected thrombus within a PFO has not been reported [19,20].

7. Conclusion

Our patient experienced rapid decline resulting in multi-organ system failure, with persistent lactic acidosis, acute kidney injury, increasing oxygen requirements, and a stroke. Despite an initial negative CT angiogram, she was found to have right heart failure and a clot straddling a PFO detected with POCUS. The decision to administer thrombolytics was motivated by the rapid patient's decompensation and her being deemed not to be a surgical candidate [19]. This highlights the importance of prompt evaluation with POCUS for patients admitted to the ICU.

- Patients with SCD are at high risk for VTE and clinicians should have a high index of suspicion for coexistence of VTE in the setting of ACS.
- The diagnosis of paradoxical embolism should be considered in any patient with hypoxia and neurologic symptoms
- POCUS is highly specific for the detection of right heart dilation/dysfunction and should be a routine component of the assessment of acutely decompensating patients.

Video 1: The first half of the video shows the parasternal short axis view with an enlarged right ventricle which is greater than the left ventricle, consistent with severe right ventricular dilation. The red arrow points to the interventricular septum with flattening, consistent with “D-sign”. The flattening is most obvious during diastole, consistent with right ventricular volume overload, but persists during systole, consistent with right ventricular pressure overload. The second half of the video shows a right ventricular focused apical 4 chamber with a mobile hypoechoic structure traversing the interatrial septum in the region of the foramen ovale. The right ventricle is greater in diameter than the left ventricle, consistent with severe enlargement. Although not measured, it can be appreciated that the tricuspid annular plane systolic excursion (TAPSE) is reduced, consistent with reduced right ventricular systolic function.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.rmcr.2022.101724

Video 2: The first half of the video shows parasternal long axis view with an enlarged right ventricular outflow tract. The red arrow points to the left atrium where a mobile, hyperechoic structure is seen moving in and out of plane. The second half of the video shows the right ventricular inflow view with a dilated right ventricle. Red arrow points out a hyperechoic mobile structure in the right atrium.

Supplementary video related to this article can be found at https://doi.org/10.1016/j.rmcr.2022.101724

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Author contributions

Matthew Gorgone: Conceptualization; Data curation; Investigation; Methodology; Resources; Software; Roles/Writing - original draft; Writing - review & editing. Stephanie I. Maximous: Conceptualization; Supervision; Roles/Writing - review & editing. Phillip E. Lamberty: Conceptualization; Supervision; Roles/Writing - review & editing. Enrico M. Novelli: Conceptualization; Supervision; Writing - review & editing. Laura M De Castro: Conceptualization; Supervision; Writing - review & editing. Simmi Patel: Data curation; Formal analysis; Writing - review & editing. Mark T. Gladwin: Conceptualization; Data curation; Formal analysis; Funding acquisition; Supervision; Roles/Writing - original draft; Writing - review & editing.

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Declaration of competing interest

Dr. Gladwin is a co-inventor of patents and patent applications directed to the use of recombinant neuroglobin and heme-based molecules as antidotes for CO poisoning, which have been licensed by Globin Solutions, Inc. Dr. Gladwin is a shareholder, advisor,

and director in Globin Solutions, Inc. Dr. Gladwin is also co-inventor on patents directed to the use of nitrite salts in cardiovascular diseases, which were previously licensed to United Therapeutics, and is now licensed to Globin Solutions and Hope Pharmaceuticals. Dr. Gladwin is a principal investigator in a research collaboration with Bayer Pharmaceuticals to evaluate riociguat as a treatment for patients with SCD. Dr. Gladwin receives research support from NIH grants 5R01HL098032, 2R01HL125886, 5P01HL103455, 5T32HL110849, UH3HL143192, the Burroughs Wellcome Foundation, Globin Solutions, Inc., the Institute for Transfusion Medicine and the Hemophilia Center of Western Pennsylvania.

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