BILATERAL PULMONARY EMBOLISM IN AN ADOLESCENT WITH SICKLE CELL DISEASE AND A RECENT TOTAL HIP ARTHROPLASTY: A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Pulmonary embolism is a life-threatening but treatable condition. Factors such as hypercoagulability and recent lower extremity surgery are associated with a higher incidence of thrombus formation and pulmonary embolism. Patients with sickle cell disease have a baseline hypercoaguable state and are at a greater risk forming deep vein thrombosis and pulmonary embolism than the general population. This increased risk is rarely cited in the literature. We describe a sickle cell patient two-weeks status-post total hip arthroplasty who presented with bilateral pulmonary embolism complaining of chest and shoulder pain. We highlight the need to include pulmonary embolism in the differential diagnosis of all sickle cell patients complaining of chest pain.

INTRODUCTION

Pulmonary embolism (PE) is a potentially fatal disease that requires prompt diagnosis and early treatment. The incidence of PE in the general population is between 0.023% and 0.205%[1] and is even lower in children[2]. However, the mortality rate can approach 8.65-15.1% in treated patients[1,3] and 25-35.5% in untreated patients[4,5]. Factors associated with an increased risk for PE and its usual precursor, deep vein thrombosis (DVT), include recent total knee or hip arthroplasty[6-8], clotting disorders such as sickle cell disease[2,9,10], cancer, obesity, decreased mobility, family history of venous thromboembolism[11], and African American race[1,10]. As this case demonstrates, pulmonary embolism should be considered in the differential diagnosis for any sickle cell patient presenting with an insidious onset of chest or thorax pain, especially in those with other predisposing factors for venous thrombosis.

Case Report

An eighteen-year-old African American male with type SS sickle cell disease was admitted to the pediatric ward of the hospital 14 days status-post total hip arthroplasty (THA). He complained of left-sided chest and shoulder pain that began three days prior to admission. The pain initially started in the region of his left ribs and began radiating to the superior aspect of his left shoulder one day prior to admission. The patient had been discharged from the hospital after his surgery 12 days prior to this admission. Although our institution encourages early mobilization, the patient was not fully ambulatory until about five days prior to the onset of symptoms. The reasons for this delayed mobilization are unclear, although it was likely due to a combination of social factors and general fatigue postoperatively. He described his pain on readmission as sharp, severe, and worse with inspiration. He denied any trauma or recent respiratory infection.

His past medical history was significant for sickle cell disease, bilateral avascular necrosis of his hips, and multiple hospitalizations for vaso-occlusive crises, acute chest syndrome, and priapism. He had been treated prophylactically after surgery (starting 12 hours postoperatively) with low molecular weight heparin (LMWH) for two days until discharge, although he was not compliant with his outpatient LMWH. His current medications consisted of 1200 mg of hydroxyurea and 1 mg of folic acid daily.

On exam, the patient was afebrile and did not appear to be in respiratory distress, although he exhibited shallow respirations due to pain. He had no tenderness to palpation, ecchymosis, swelling, or erythema in the regions of his pain. His lungs were clear to auscultation bilaterally with diminished breath sounds in his left lower lobe. He had no swelling of his extremities and had a negative Homans sign. His pulse oximeter showed oxygen saturations of 96-98% on room air. All other vital signs and physical exam findings were normal. Chemistry studies were within normal limits except for a C-

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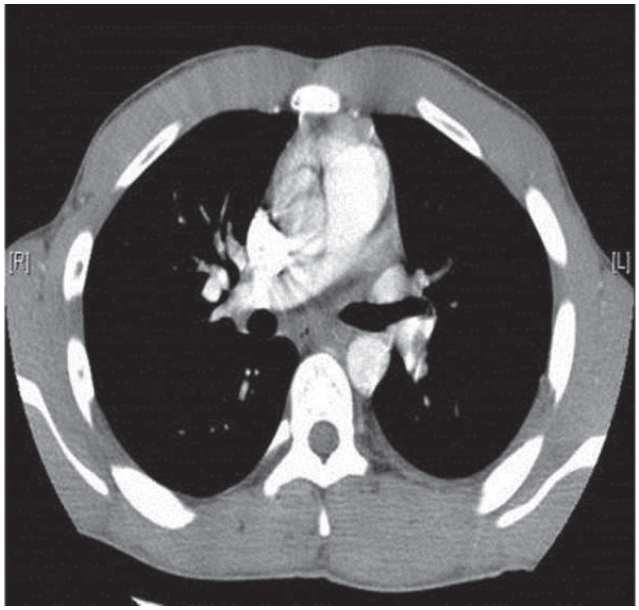

Figure 1 Spiral CT showed bilateral PEs.

reactive protein of 7.52 mg/L. His hemoglobin was 11.3 g/dL, hematocrit was 34.0%, and his reticulocyte count was 5.1%, all of which were improved from his lab values at discharge two weeks prior to admission. Prothrombin time (PT), partial thromboplastin time (PTT), and international normalized ratio (INR) were within normal limits. An AP and lateral chest X-ray did not show any pleural effusions, consolidation, vascular congestion, or other acute abnormalities or interval changes from prior chest X-rays. A PE protocol spiral CT scan (Figure 1) showed bilateral PE, worse on the left side, with a left lower lobe wedge infarct and subsegmental infarcts on the right side. The patient was started on 12,500 units of Fragmin.

On hospital day two, the patient had an ultrasound of the bilateral lower extremities, which was negative for deep vein thrombosis. The patient was clinically stable, denied shortness of breath, and complained of continued pain with respirations. His Fragmin was continued and he was started on 4 mg of Coumadin with a goal INR of 2-3. The patient's clinical condition gradually improved, and on hospital day eight he reported no pain with inspiration. His INR was near therapeutic at 1.92. As the patient did not have a strong social support system and had a history of medication noncompliance, we planned to keep him admitted until his INR was therapeutic. However, the patient checked out against medical advice that evening.

DISCUSSION

Venous stasis, turbulent blood flow, and a hypercoaguable state often lead to DVT and PE[8]. Patients with sickle cell disease exhibit an elevated baseline level of coagulation[9,10]. Although this multifactorial hypercoagulability is a risk factor for thrombosis formation, DVT and PE are rarely cited as potential complications of sickle cell disease[9]. Recent studies have demonstrated that patients with sickle cell disease, and even sickle cell trait, are at a higher risk for developing venous thrombosis and subsequent PEs[9,10]. Since the treatment of a PE can greatly reduce mortality[4,5], a high index of suspicion should be maintained in sickle cell patients presenting with chest pain.

When venous stasis occurs, platelets aggregate, often in the valve cusps of lower extremity veins. A clot forms and is neutralized by fibrin. This process is repeated, forming multiple layers of fibrin and clots, ultimately resulting in a venous thrombosis[12]. Anything that increases coagulability or causes venous stasis will increase the rate of DVT and PE. Factors associated with thrombosis and embolism in children include cancer, trauma, congestive heart disease, infection, lupus, liver failure, and sickle cell disease[2]. Additional risk factors are prolonged bed rest[3,12], Factor V Leiden[1], smoking, increased blood viscosity[12], hip fracture, pelvis fracture, and recent lower extremity orthopaedic surgery[8].

Total hip arthroplasty (THA) is one of the most common surgeries associated with venous thrombosis[8,12], with DVT forming in up to 70% of patients with no prophylaxis[7]. The pathophysiology of thrombus formation after a THA is partially due to endothelial injury. This can occur via kinking of the femoral vein during manipulation of the leg or through direct vascular injury, releasing clotting factors from the endothelium[8]. In addition, venous stasis may occur as a result of immobilization after surgery or swelling in the affected leg, and coagulability may be increased by thromboplastin release from the femoral canal[8]. Sickle cell patients often undergo THA due to osteonecrosis of the hip[13,14], and they are at an increased risk of thrombotic complications due to their hypercoaguable state[9,10].

A thrombus that breaks off and enters the pulmonary vasculature becomes a PE, and is a potentially fatal condition[3,7,8,12]. Historically, up to 35.5% of untreated patients with PE died[4], and two thirds did so within the first thirty minutes[6] . However, early diagnosis and proper treatment can reduce the mortality rate substantially[4-6,12,15]. Recent studies have shown that the current all cause fatality rate for hospitalized patients with PE is as low as 7.4%[21] and death from PE to be less than 1%[17,18]. Over 50% of fatal PE's after THA occur in the second postoperative week and over 20% occur in the third postoperative week.

The median time to symptomatic DVT occurs at 17 days postoperatively[6]. Dyspnea, tachypnea, tachycardia, and pleuritic pain are often seen at presentation[8,12]. Common modalities used in diagnosis include pulmonary angiography[8,12,15,21], nuclear medicine ventilation-perfusion scan[8,12,15], spiral CT scan[8,12,15,21], and D-dimer levels[15,21]. Doppler venous ultrasound and testing for the presence of Homans sign can be useful in detecting DVT[12], and high pretest probability and positive physical examination findings increase the sensitivity of these tests[12,15,21].

The prevalence of PE is higher for hospitalized sickle cell patients compared to similar non-sickle cell patients[9], and is likely under-diagnosed[19]. The symptoms associated with PE are often mistaken for another pulmonary condition common in sickle cell disease, acute chest syndrome (ACS). ACS is a leading cause of death in sickle cell disease and manifests as a variety of respiratory symptoms including pulmonary infiltrates, chest pain, tachypnea, hypoxia, fever, and pulmonary hypertension[20]. As Stein et al. describe, ACS often leads to vascular occlusion and pulmonary infarction, likely due to thrombosis *in situ*[16]. While PE affects elastic vessels >1mm in diameter, thrombosis *in situ* affects the smaller muscular arterioles. This difference can be detected with standard or CT pulmonary angiography[9]. PE is not thought to be a cause of ACS, although some studies show that 17% of patients with ACS go on to develop PE[19]. Treatment for ACS and PE differ, and anticoagulation is not used therapeutically in ACS. Any patient with sickle cell disease who does not improve with standard ACS treatment modalities should be evaluated for PE.

Although the literature is sparse regarding prophylaxis and treatment of PE in sickle cell patients after THA, the traditional management of symptomatic DVT or PE consists of anticoagulants and supportive therapy[4,5,8,12]. Intravenous heparin was formerly the mainstay of treatment[4,5,8], but low-molecular-weight heparins are increasingly being used[8]. Both have been shown to substantially reduce the incidence of thrombosis[7,12]. Either of these therapies should be transitioned to long-term warfarin treatment, usually for three to six months[8]. Intravenous or low-molecular weight heparin should be discontinued after the INR level is 2.0-2.5 for two days[6,8].

CONCLUSION

Patients with sickle cell disease exhibit a baseline hypercoaguable state and are at an increased risk for venous thrombosis and pulmonary embolism[9,10]. This association is rarely listed in the literature. Orthopaedic surgeries commonly performed on sickle cell patients[13,12] can significantly increase the risk of thrombus formation[8,12,14]. Our case report demonstrates the need for a high index of suspicion in sickle cell patients presenting with pleuritic chest pain.

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