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Sickle-Cell Trait as a Risk Factor for an Unprovoked Venous Thromboembolism: A Case Report

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Abstract

In this case report, we examine the increased risk of venous thromboembolism (VTE) in patients with sickle-cell trait (SCT), illustrated by a patient with SCT who developed pulmonary embolism (PE) despite low scores on conventional risk assessment tools. The case prompts both a discussion of risk assessment and management strategies in this population.

Categories: Internal Medicine, Pulmonology, Hematology
Keywords: sickle cell complications, deep vein thrombosis (dvt), risk assessment tools, sickle cell trait, venous thromboembolism (vte), pe

Introduction

Sickle-cell trait (SCT) is a state in which an individual possesses a single mutated allele for hemoglobin S (HbS) [1]. It is distinct from sickle-cell disease (SCD), in which both alleles are mutated. Although SCD is known for clinical complications such as pain crises and anemia, individuals with SCT remain predominantly asymptomatic [1-3].

In contrast to its reputation as a benign condition, recent studies have explored a potential association between SCT and an increased risk of venous thromboembolism (VTE), which encompasses conditions such as deep vein thrombosis (DVT) and pulmonary embolism (PE) [4-7]. The proposed mechanisms for this association include vessel occlusion, blood stasis, and continuous activation of the coagulation cascade, but the exact process has not been confirmed [8,9].

In support of this proposed connection, we present the case of a 44-year-old male with SCT and obesity with no other risk factors, who developed PE despite low pretest probability on several conventional risk stratification tools.

Case Presentation

A 44-year-old African American male presented to the clinic after experiencing three days of shortness of breath and chest pain on inspiration. Initially, the patient woke up with chest pressure and right-sided stabbing pain that worsened upon inspiration and radiated to his back. He reported difficulty in climbing stairs and breathlessness during basic activities. His symptoms improved over the next three days with only mild pain upon deep inspiration and minimal shortness of breath at the time of presentation.

The patient, an active real estate agent, reported no history of similar symptoms or periods of prolonged immobility. He had a medical history significant only for obesity (BMI 38.5), hyperlipidemia, and being a carrier of SCT.

Vitals were taken in the office (Table *1*). Of note, his in-office SpO_2 was 95%. Physical examination was unrevealing including negative Homan sign. Chest X-ray (Figure *1*) and electrocardiogram (Figure *2*) were non-contributory. Laboratory tests showed a normal complete blood count, comprehensive metabolic panel, and elevated D-dimer (Tables *2*-*3*).

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Measurement	Value
BP	131/82
Pulse	90
Temp	97.1 °F (36.2 °C) (Oral)
Resp	16
Ht	6' 8" (2.032 m)
Wt	350 lb (158.8 kg)
SpO_2	95%
BMI	38.45 kg/m²

TABLE 1: Vitals

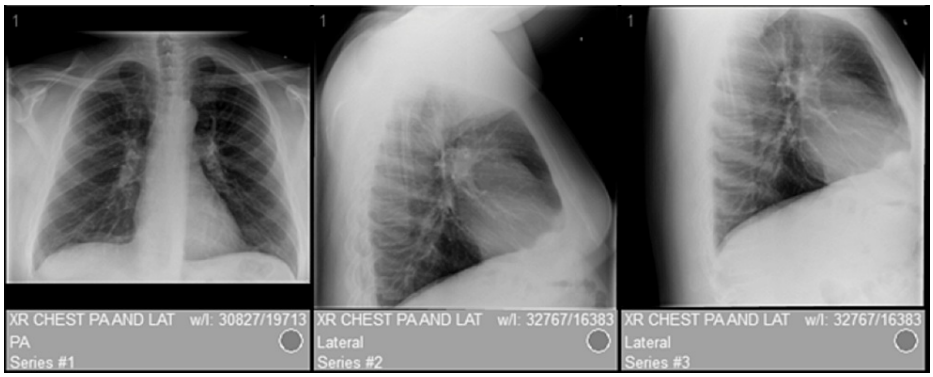

FIGURE 1: Chest X-rays showing no pathology.

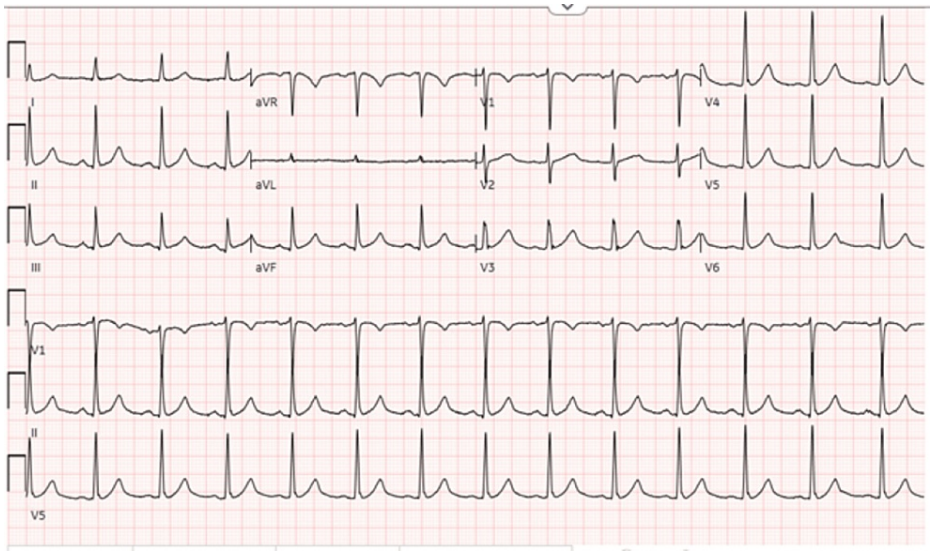

FIGURE 2: Electrocardiogram showing normal sinus rhythm.

Parameter	Patient Value	Reference Range
Hematocrit	42	41%-53%
Hgb	13.9	13.5-17.5 g/dL
MCH	27.5	25.4-34.6 pg/cell
MCHC	33.1	31%-36% Hb/cell
MCV	83	80-100 μm^3
Platelets	270	182-396 K/mm^3
RBC, Auto	5.06	4.70-6.10 M/uL
RDW, Blood	12.6	11.6%-14.8%
WBC's Auto	9.3	3.98-10.04K/mm^3
Neutrophils %	50.6	50.0%-70.0%
Lymphocytes	3.46	1.00-4.30 K/uL
Monos %	10.2	0.0%-15.0%
Monocytes	0.95	0.00-1.10 K/uL
Eosinophils %	1.3	0.0%-06.0%
Eosinophils	0.12	0.00-0.60 K/uL
Basophils %	0.5	0.0%-2.0%
Basophils	0.05	0.00-0.20 K/uL
Neutrophils	4.72	2.40-7.60 K/uL

TABLE 2: Complete blood count (CBC) with differential

Hgb: hemoglobin, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, MCV: mean corpuscular volume, RBC: red blood cell, RDW: red cell distribution width, WBC: white blood cells

Parameter	Patient Value	Reference Range
BUN	15	6-24 mg/dL
Creatinine	1	0.76-1.27 mg/dL
Sodium	142	134-144 mmol/L
Potassium	4.9	3.5-5.2 mmol/L
Chloride	104	96-106 mmol/L
CO_2	26	20-29 mmol/L
eGFR	>60	>59 mL/min/1.73
Calcium	9.7	8.7-10.2 mg/dL
Total Protein	7.1	6.0-8.5 g/dL
Alkaline Phosphatase	63	39-117 IU/L
Globulin	2.3	1.5-4.5 g/dL
ALT	7	0-44 IU/L
AST	10	0-40 IU/L
Bilirubin, Total	0.3	0.0-1.2 mg/dL
Albumin	4.8	3.5-5.5 g/dL
D-DIMER, EIA	**2.37 (H)**	**0-0.50 mg/L**

TABLE 3: CMP and D-dimer values

CMP: comprehensive metabolic panel, BUN: blood urea nitrogen, eGFR: estimated glomerular filtration rate, ALT: alanine aminotransferase, AST: aspartate aminotransferase, EIA: enzyme immunoassay

Given the low pretest probability based on the Wells and Geneva scores and having met pulmonary embolism rule-out criteria (PERC), initial assessments suggested a less than 1.5% risk for PE. Although this was the case his elevated D-dimer and shortness of breath prompted urgent computed tomography angiography (CTA) which identified extensive pulmonary emboli in the distal right pulmonary artery and the segmental and subsegmental pulmonary arteries supplying all five lobes, mild consolidative opacity in the right middle lobe (Figure *3*).

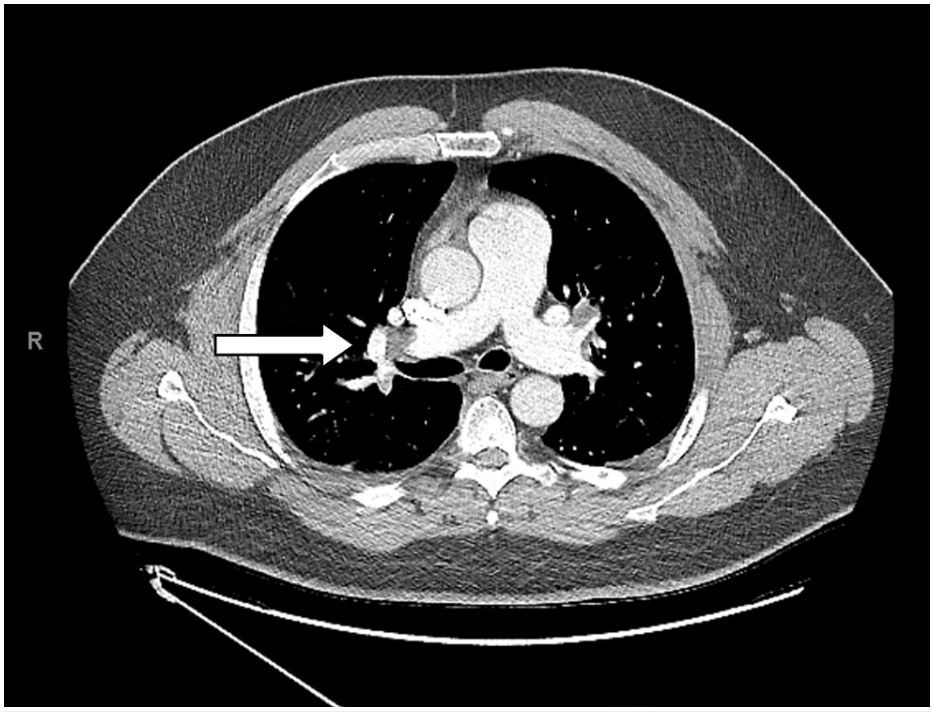

FIGURE 3: Computed tomography angiography (CTA) showing pulmonary embolism in the distal right pulmonary artery.

The patient was immediately started on rivaroxaban 15 mg two times a day and scheduled for an echocardiogram (ECHO) in three months to assess for pulmonary hypertension and low dose CT chest to follow up right middle lobe opacity. Given the patient's age, absence of clear provoking risk factors, and high risk of recurrent VTE, indefinite anticoagulation was recommended.

Discussion

In a population-based cohort study of 30,424 individuals, Little et al. demonstrated a higher incidence of VTE in 6,758 SCT carriers compared to non-carriers [4]. Notably, this association held even after accounting for variables like body mass index (BMI), which was the sole other risk factor of note in our case presentation. Given these findings and the contributions of Naik and Noubiap, which further emphasize an increased risk of PE in particular, we provide support for a possible inherent thrombotic risk associated with SCT in our case presentation [5,10].

As both our case presentation and recent research support a possible link, we favor a need for increased surveillance of these patients. In the event that genetic predisposition does contribute to PE, clinical scoring systems such as the Modified Wells, Revised Geneva, and PERC become of lesser use and potentially enable these patients to evade detection [11,12]. As seen in our case presentation, the patient exhibited <1.5% risk in these metrics and was not recommended to receive further workup based on PERC scores. This emphasizes the need for a more comprehensive approach to assessing PE risk in SCT carriers as the existing models, while robust, do not account for inherited risks.

In addition to risk assessment concerns, our case raises some questions about approaches to management. In patients with first-time unprovoked PE, indefinite anticoagulation is in line with current recommendations for those with persistent risk factors and low bleeding risk [13,14]. At this time, SCT is not considered a persistent risk factor but raises the question of whether or not it should be in the context of recent research. In which case, indefinite treatment should be discussed. Alternative options have been debated such as the use of Disabilities of the Arm, Shoulder and Hand (DASH) scores to further assess an annual risk of PE recurrence [13-16]. For example, a DASH score ⩽1, which indicates an annual PE risk of 3.1%, may lead some clinicians to consider discontinuing anticoagulation while continuing D-dimer monitoring [16]. This is an approach that could be relevant for SCT patients because it provides an assessment that remains uninfluenced by both inherent and modifiable risk factors.

Conclusions

This case report highlights the limitations of current risk assessment strategies for patients with SCT and provides comments on approaches to both VTE prevention and management. Given that recent research has

demonstrated an association with an increased risk of unprovoked VTE, there may now be a need to reason beyond current risk assessment tools and consider additional criteria that may enhance predictive capabilities in these patients.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: James D. Cross, Brendan P. Mackey

Acquisition, analysis, or interpretation of data: James D. Cross, Brendan P. Mackey, Umme Yasmin

Drafting of the manuscript: James D. Cross, Brendan P. Mackey

Critical review of the manuscript for important intellectual content: James D. Cross, Brendan P. Mackey, Umme Yasmin

Supervision: Umme Yasmin

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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