Open Journal of
Clinical & Medical
Case Reports

Volume 3 (2017)
Issue 17

ISSN 2379-1039

Superior vena cava thrombosis in sickle cell trait patient: Case report and literature review

Ahmed Q Hasan*; Ahmed Al-Khazraji; Zaid Al-Zubaidi; Huda Al-Jadiry

***Ahmed Q Hasan**

Department of emergency medicine, Louisiana state University, New Orleans, Louisiana
Email: ahmed.q.hasan@gmail.com

Abstract

Background: Sickle cell trait (HBAS; AS) is a condition that result from a point mutation of the beta chain of the hemoglobin Sickle cell trait was generally thought to be a benign carrier state where individuals have normal expectancy unless they were exposed to oxidative stress like sever tissue hypoxia, acidosis and dehydration to cause complications. Venous thromboembolism and exercise-related sudden death are the two most vitally concerning complications.

Case presentation: We are reporting a case of 19 years old sickle cell carrier male that presented to the emergency department with bilateral upper extremities swelling after exercising at the gym. Initial Blood work-up revealed positive D-dimer of 2.72 ng/ml and positive sickling test. Upper extremities Doppler ultrasound showed no evidence of deep venous thrombosis (DVT), Chest CT scans showed superior vena cava thrombosis involving the right subclavian vein and extending to the right basilic vein. Thrombosis was believed to be secondary to sickle cell trait.

Conclusion: This case demonstrates a rare complication of sickle cell trait. Exercise related sudden death and thrombosis are possible, lethal complications in SCT carriers.

Keywords

sickle cell trait; thrombosis; exercise; superior vena cava; basilica; subclavian

Introduction

Sickle cell trait (HBAS; AS) is a condition that result from a point mutation of the 6th codon of the beta chain of hemoglobin and around 200 million people are heterozygous carriers [20] with 30% to 40% in sub-Saharan Africa [1].

Sickle cell trait was generally thought to be benign carrier state where individuals have normal life expectancy unless they were exposed to oxidative stress like sever tissue hypoxia, acidosis and dehydration to cause complications [7]. Recent data have shown that sickle cell trait is a risk factor for adverse outcomes including; Increased risk of thromboembolism [7] hypercoagulability [8,21] and sudden death after extreme exertion [6,21]. Although the he exact mechanism of these events is unclear but the association between sickle cell trait and exercise-related adverse events can't be ignored, kark et al noted in his study a 30-fold increase in exercise related sudden death in black recruits with sickle cell trait [6]. Hypercoagulability could be the reason for this fatal outcome noted in sickle cell trait [8].

We are reporting an extremely rare and severe case of superior vena cava thrombosis with extension up to the basilic vein in SCT patient after exercise. We hope that this case can serve as an addition to the literature on relation between sickle cell trait and the risk of adverse and fatal events.

Case Presentation

A 19-year-old male presented to the emergency department with a chief complaint of bilateral upper extremities swelling for one day prior presentation. He reported initial swelling 1 week ago after weight lifting at the GYM for one hour. The swelling started on the right upper limb that progressed to the left upper limb over the last 2 days that became noticeable 1 day prior to his presentation. He denied any chest pain, shortness of breath, stridor, cough, fever or palpitation. No history of trauma, travel, insect bite and fever. He had a past medical history of intermittent bronchial asthma diagnosed 6 years ago. He had Positive family history of sick cell trait. Patient denied alcohol intake or eliciting drugs use. On examination patient was conscious, alert and oriented with stable vital signs, swelling of the neck with prominent congested vein, right and left upper extremities non tender swelling (right more than the left with circumference 36 centimeters (cm) and left arm 34 cm). No pitting or skin changes or lymphadenopathy. The rest of the physical exam is unremarkable. ECG showed normal sinus rhythm. Chest x-ray was normal. Initial Blood work-up was only significant with positive D-dimer of 2.72 ng/ml and positive sickling test. Upper extremities Doppler ultrasound showed no evidence of deep venous thrombosis (DVT), Chest CT scans showed a filling defect in the superior vena cava extending to the right subclavian vein and the right basilic vein. PT=11.2s (9-14), INR=0.96, APTT= 25.90s (20-30), Thrombin time=12s (12-16), Fibrinogen 3.61g/L (1.5-4.2). Haemoglobinopathy screening panel: Haemoglobin A (Adult) 60.4% Sickle cell trait-heterzygous HbS, Haemoglobin A2= 3.3% (1.5-3.5), Haemoglobin F= 1.1%, Haemoglobin S= 34.20%, HPLC Impression of blood= Sickle cell trait. Factor V Leiden mutation by PCR= Absence of Mutation, Prothrombin mutation= absence of mutation, Anti-Nuclear Antibody= Not reactive. Thrombophilia screening panel: 89.9% (60-124), Antithrombin assay= 98.7% (79-131), Protein C=111.9% (64-128), Activated protein Risis=1.0 ratio (069-2) and Fibrinogen= 2.66 g/L (1.5-4.2). HIV 1&2 screening (antigen & antibody) = Non-reactive, anti-Ds DNA Antibody (ELISA) = Non-reactive and Janus Kinase (JAK2) = Absence of mutation. Chest abdomen-pelvic CT scan showed no evidence of mass or malignancy. Systemic anti-coagulation therapy initiated (Low Molecular Weight Heparin and Warfarin) with good recovery without needing an endovascular treatment, a repeat CT scan showed only residual thrombus in the right basilic vein. Patient was discharged from hospital after 5 days was seen in the clinic after 9 days. After that, the patient lost follow-up. Superior vena cava thrombosis (SVCT) was believed to be secondary to sickle cell trait in the absence of malignancy.

Discussion

Sickle cell trait (SCT) is one of the most common benign hematological disorder that affects the hemoglobin (Hb) affecting approximately 300 million people all over the world higher in Mediterranean region, sub-Saharan Africa, parts of India and the Middle East [1,5]. Most of the SCT patients usually asymptomatic but serious potential complications can occur such as renal papillary necrosis leads to gross hematuria, renal medullary carcinoma, splenic sequestration, and infarction especially in high altitude, exertional rhabdomyolysis, exercise-related sudden death, fetal demise and venous thromboembolism [5,6,7].

The risk of thromboembolism from sickle cell disease (SCD) well described in the literature, sickle cell patients have an approximately 2-folds increased risk of venous thromboembolism in compare to normal individuals [9]. Complications starts with sickling is a process causing polymerization of the red blood cells which occurs due to dehydration, hypoxia, acidosis, hypothermia leads to hypercoagulability [3]. Primarily by having sickled red cells causing vascular endothelial damage which leads to activation of coagulation cascade (activating thrombin-anti-thrombin (TAT) complex, prothrombin fragments, and D-dimer) causing vaso-occlusive injury but this phenomena are even more complicated in SCD which involves alteration of normal cellular vascular physiology causing increment in an inflammatory cellular markers (Interleukins), Tumor necrotic factors (TNFs), Nitric oxide (NO) depletion and release of Microparticles (MP) which ultimately leads to cellular inflammation and vascular instability which ultimately causing hypercoagulability that leads to thromboembolism [6,10,13]. Cellular inflammation plays an important role in thromboembolic events in sickle cell patients especially with monocytes activation in SCT. Tantawy and his colleague's et al [11] have found higher-level of cellular receptor CD 163 expressed on the monocytes that was believed to be as a marker of coagulation cascade activation in SCT patients [11]. Another epidemiological study was done by Amin and his colleague's et al. [23] comparing 18 asymptomatic individuals with SCT (Hb AS) compared to 22 Sub-Saharan control individuals with normal (Hb AA) were compared to 22 patients with Hb SS SCD. The study showed that SCT patients have an equivalent risk factor for thromboembolic disease as compare to SCD patients. SCT have a high risk of developing a pulmonary embolism (PE) and deep venous thrombosis (DVT), there was a 30-fold increase exercise-related unexplained sudden death in African-Americans compared to normal population as observed by Kark JA [8]. Folsom AR and his colleagues in his prospective analysis for 249 participants looking for an incidence of DVT and PE among SCT individuals, he found that SCT patients have a two-fold increase risk of PE [12]. Venous thromboembolism and exercise-related sudden death are the two most vitally concerning complications. In 2011, Harmon et al reviewed all cases of sudden death associated with exercise between 2004 and 2008 in athletes from the NCAA (National Collegiate Athletic Association) in the United States. He found higher rates of exercise-related sudden death in SCT and higher rates in African-American SCT carriers [11]. Numerous studies have suggested the association of SCT and Exercise related sudden death, but it was very difficult to prove the etiology or reasoning behind this fact. One of the proposed theory, the increase in whole blood viscosity [12,13], oxidative stress [14], slight decrease in RBC deformability [13,15] and evidence of systemic inflammation [16,17] all are biological responses that happen during exercise.

While the association between SCT and thrombosis is reasonably well established in literature, but every study has its own limitation. In our case the patient lost follow-up because after his first appointment with the clinic that was a limiting factor to make a definitive conclusion. More importantly, we feel that this report will contribute to the growing literature on SCT adverse outcome and renew the interest in that topic.

Conclusion

In conclusion, SCT is not a benign disease phenotype, exercise-related sudden death and thrombosis are possible, lethal complications in SCT carriers. The association of the two is well-established fact in literature, but pathophysiology is not fully understood. Promoting physician's

awareness about the potentially life-threatening complications of sickle cell trait is paramount. Further research on the SCT adverse events and coagulation during exercise in SCT patients is warranted in order to have a better understanding of this disease process. Further future research should be made looking for the biochemical marker associated with thrombosis in SCT patients as well as the types of thromboembolic phenomena in SCT patients.

Figures

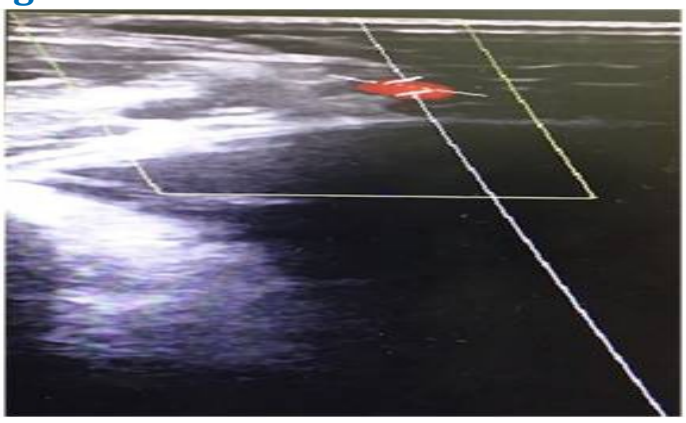

Figure 1: Axial color Doppler Ultrasound Image at the right axillary vein. The red color is the color signal from the patent right axillary vein. Dynamic images at the time of scan demonstrated compressible vein.

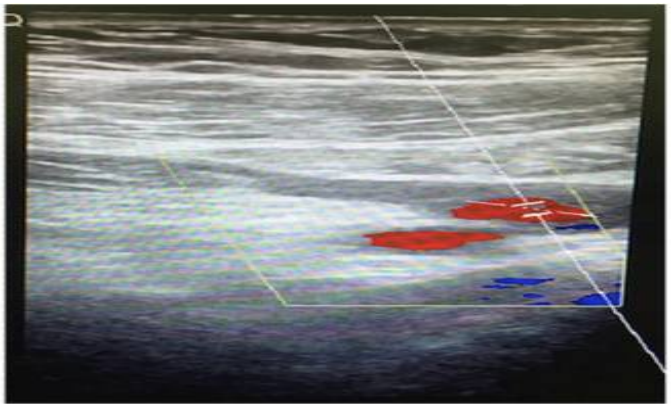

Figure 2: Longitudinal color Doppler Ultrasound of the right subclavian vein. The red color is the color signal from the patent subclavian vein. The Dynamic imaging demonstrated anechoic vein with no evidence of echogenic thrombus.

References

1. Bender MA, Hobbs W. Sickle cell disease. GeneReviews® [Internet].2003 Sep 15 [updated 2012 May 17].

2. Lange R. D., Minnich V., and Moore C. V., "In vitro differences in behavior of sickle cell anemia and trait erythrocytes produced by variations in O2 tension and pH," The Journal of Laboratory and Clinical Medicine, vol. 36, article 848, 1950.

3. Goldsmith JC, Bonham VL, Joiner CH, et al. Framing the research agenda for sickle cell trait: building on the current understanding of clinical events and their potential implications. Am. J. Hematol. 2012; 87: 340–6.

4. Tsaras G., Owusu-Ansah A., Boateng F. O., and Amoateng-Adjepong Y., "Complications associated with sickle cell trait: a brief narrative review," The American Journal of Medicine, vol. 122, no. 6, pp. 507–512, 2009.

5. Key N. S. And Derebail V. K., "Sickle-cell trait: novel clinical significance," American Society of Hematology, vol. 2010, no. 1, pp. 418–422, 2010.

6. Kark J.A., Posey D.M., Schumacher H.R., Ruehle C.J. Sickle-cell trait as a risk factor for sudden death in physical training. N Engl J Med, 317 (1987), pp. 781–787

7. Austin H, Key NS, Benson JM, Lally C, Dowling NF, Whitsett C, et al. Sickle cell trait and the risk of venous thromboembolism among blacks. Blood 2007; 110: 908–12.

8. Westerman MP, Green D, Gilman-Sachs A, Beaman K, Freels S, Boggio L, et al. Coagulation changes in individuals with sickle cell trait. Am J Hematol 2002; 69: 89–94.

9. Tantawy A.A., Adly A.A., Ismail E.A .Soluble CD163 in young sickle cell disease patients and their trait siblings: a biomarker for pulmonary hypertension and vaso-occlusive complications. Blood Coagulation Fibrinolysis, 23 (7) (2012), pp. 640–648

10. Folsom AR, Tang W, Roetker NS, Kshirsagar AV, Derebail VK, Lutsey PL et al. Prospective study of sickle cell trait and venous thromboembolism incidence.J Thromb Haemost. 2015 Jan;13(1): 2-9.

11. Harmon, K. G., Asif, I. M., Klossner, D., & Drezner, J. A. (2011). Incidence of Sudden Cardiac Death in National Collegiate Athletic Association Athletes Clinical Perspective. Circulation, 123(15), 1594-1600.

12. Diaw M, Connes P, Samb A, Sow AK, Sall ND, Sar FB, Ba A, Diop S, Niang MN, Tripette J. Intraday blood rheological changes induced by Ramadan fasting in sickle cell trait carriers. Chronobiol Int. 2013a; 30: 1116–1122.

13. Tripette J, Connes P, Beltan E, Chalabi T, Marlin L, Chout R, Baskurt OK, Hue O, Hardy-Dessources MD. Red blood cell deformability and aggregation, cell adhesion molecules, oxidative stress and nitric oxide markers after a short term, submaximal, exercise in sickle cell trait carriers. Clin Hemorheol Microcirc. 2010a; 45: 39–52.

14. Faes C, Balayssac-Siransy E, Connes P, Hivert L, Danho C, Bogui P, Martin C, Pialoux V. Moderate endurance exercise in patients with sickle cell anaemia: effects on oxidative stress and endothelial activation. Br J Haematol. 2014; 164: 124–130.

15. Martin TW, Weisman IM, Zeballos RJ, Stephenson SR. Exercise and hypoxia increase sickling in venous blood from an exercising limb in individuals with sickle cell trait. Am J Med. 1989; 87: 48–56.

16. Monchanin G, Serpero LD, Connes P, Tripette J, Wouassi D, Bezin L, Francina A, Ngongang J, de la Pena M, Massarelli R, Gozal D, Thiriet P, Martin C. Effects of progressive and maximal exercise on plasma levels of adhesion molecules in athletes with sickle cell trait with or without alpha-thalassemia. J Appl Physiol (1985). 2007; 102: 169–173.

17. Tripette J, Connes P, Hedreville M, Etienne-Julan M, Marlin L, Hue O, Hardy-Dessources MD. Patterns of exercise-related inflammatory response in sickle cell trait carriers. Br J Sports Med. 2010b; 44: 232–237.

18. Adam SS, Zaher G, Ibrahim M, Ataga KI, De Castro LM, Key NS. Markers of Coagulation Activation and Inflammation in Sickle Cell Disease and Sickle Cell Trait (Abstract). Blood 2008; 112: 4813.

19. Heller P, Best WR, Nelson RB, Becktel J. Clinical implications of sickle-cell trait and glucose-6-phosphate dehydrogenase deficiency in hospitalized black male patients. N Engl J Med 1979; 300: 1001–5.

20. Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Dewi M, Temperley WH, Williams TN, Weatherall DJ, Hay SI. Global epidemiology of sickle haemoglobin in neonates: a contemporary geostatistical model-based map and population estimates. Lancet. 2013; 381: 142–151.

21. Eichner ER. Sickle cell trait. J Sport Rehabil 2007; 16:197–203.

22. Sparkenbaugh E, Pawlinski R. et al. Interplay between coagulation and vascular inflammation in sickle cell disease. Br J Haematol. 2013 Jul;162(1):3-14 Sparkenbaugh E, Pawlinski R. et al. Interplay between coagulation and vascular inflammation in sickle cell disease. Br J Haematol. 2013 Jul; 162(1): 3-14.

23. Amin C and his colleauges et al. Coagulation activation in sickle cell trait: an exploratory study. Br J Haematol. 2015 Nov;171(4): 638-46.

Manuscript Information: Received: June 05, 2017; Accepted: August 14, 2017; Published: August 21, 2017

Authors Information: Ahmed Q. Hasan[1]*; Ahmed Al-Khazraji[2]; Zaid Al-Zubaidi[4]; Huda Al-Jadiry[3]

[1]Research fellow, Department of emergency medicine, Louisiana state University, New Orleans, Louisiana
[2]Department of Internal Medicine, Icahn School of Medicine at Mount Sinai, Elmhurst Hospital Center, New York
[3]Department of Neuro-Radiology, University of Texas Medical Branch, Galveston, Texas.
[4]Department of emergency medicine, Khoula Hospital, Muscat, Oman.

Citation: Hasan AQ, Al-Khazraji A, Al-Zubaidi Z, Al-Jadiry H. Superior vena cava thrombosis in sickle cell trait patient: Case report and literature review. Open J Clin Med Case Rep. 2017; 1303.

Journal: Open Journal of Clinical and Medical Case Reports is an international, open access, peer reviewed Journal focusing exclusively on case reports covering all areas of clinical & medical sciences.

Visit the journal website at **www.jclinmedcasereports.com**
For reprints and other information, contact editorial office at **info@jclinmedcasereports.com**