Factitious disorder presenting as sickle cell disease: a case report

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The Lancet Regional Health - Americas 2024;34: 100761

Published Online xxx https://doi.org/10.1016/j.lana.2024.100761

Introduction

Sickle cell disease (SCD) affects more than 7 million individuals worldwide.[1] Almost a quarter of individuals with SCD will suffer a stroke by the age of 45,[2] with a recurrence rate approaching 60% in the absence of therapy.[3] Rapid intervention is often necessary for stroke and other complications of SCD, typically before the results of hemoglobinopathy evaluation become available.[4] Unfortunately, this acuity of need may be exploited. Specifically, individuals may present with "factitious SCD", whereby individuals purport to have SCD and present with symptoms and signs suggestive of severe SCD complications necessitating urgent treatment/intervention, yet fail to show any objective evidence of the disease upon subsequent laboratory investigation.[5] First described in 1974,[6] and again in 1996,[5] these factitious cases risk immediate, unnecessary (and potentially harmful) interventions, including central venous access device (CVAD) placement and/or RBC exchange (RCE) transfusion. If patients present with acute stroke-like symptoms, thrombolytic therapy may also be administered.

Beyond the medical risks of unwarranted intervention for factitious SCD, individuals with true SCD are already stigmatized. They endure substandard clinical management, reflected by longer emergency department wait times, suboptimal pain control, and a lack of referral to behavioral and mental health services.[7–12] Patients with SCD are also more likely to be labeled as malingering or drug seeking.[13] While factitious SCD remains a rare—albeit serious—occurrence, it risks compounding discrimination against those with true SCD, while distracting healthcare practitioners from timely management of SCD complications that may be life-threatening (e.g., stroke). We describe a notable case of "factitious SCD" to promote awareness, outline approaches that may be used to recognize factitious presentations, minimize unnecessary medical procedures while still ensuring appropriate medical care, and prevent further stigmatization of an already vulnerable population.

Case description

In 2022, a Black male, purportedly 37-years-old, presented to a Connecticut hospital with acute onset facial drooping, left-sided visual field deficit, right-sided motor and sensory deficits, and right lower extremity pain. The patient reported a history of SCD and three prior strokes. He also endorsed protein C deficiency, and reported RBC transfusion in California one month prior

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to the index presentation. Physical examination was significant for left-sided facial droop and multiple healed scars from vascular access sites, which he reported had been used for prior RCE procedures. Lower extremity evaluation revealed an edematous and tender right calf, which was concerning for venous thrombosis. A head computed tomography (CT) scan did not demonstrate evidence of acute stroke; however, a chronic posterior left occipital infarct was noted, which may have explained his focal neurologic findings. Lower extremity ultrasonography findings were consistent with acute deep venous thrombosis (DVT). Given the patient's reported history and acute presentation, tissue plasminogen activator (tPA) was administered; the patient also received opioid analgesia and underwent a 13-unit RCE to rapidly lower HbS levels. The patient was well-informed about the RCE procedure, including technical aspects of vascular access, the number of RBC units required for RCE, and potential complications. Per protocol, hemoglobin electrophoresis was performed on blood samples that were collected before and after the RCE. These results, which were reported the day after the RCE had been performed, did not detect HbS, refuting a diagnosis of SCD. Opioid therapy was discontinued. Although treatment for DVT was recommended, the patient left the hospital against medical advice (AMA).

Unbeknownst to physicians at the time of the index presentation in Connecticut in 2022, a Black male had presented to hospitals in California in 2018, hospitals in New Mexico, Texas, and North Carolina in 2019, hospitals in Pennsylvania in 2020, and another hospital in Texas in 2021. At each presentation, his clinical history was almost indistinguishable from that of the index admission—he endorsed right-sided weakness and left-sided facial droop, stated a history of SCD and protein C deficiency, and typically reported recent RBC transfusion at an out-of-state hospital. In all instances, head CT demonstrated no evidence of acute ischemia or hemorrhage, but an old posterior left occipital infarct was consistently noted. Multiple institutions reported a reduced protein C activity level. ABO and RhD typing of the patient's blood bank sample was either group B RhD-positive or showed mixed field agglutination. The latter reflected recent RBC transfusion with compatible, but not identical, ABO units, thus corroborating aspects of the patient's story. He received tPA, emergent RCE, and opioid analgesia on numerous occasions; however, definitive testing for SCD via hemoglobin electrophoresis failed to detect the presence of HbS in all cases in which it was performed, and the patient ultimately left AMA from each hospital.

Three days after leaving the Connecticut hospital in 2022, the same individual presented to a hospital in Maryland under a different alias, where he endorsed a similar medical history. Hemoglobin solubility testing did not detect evidence of HbS. Discussions among an established network of transfusion medicine providers, including those at the Maryland, Connecticut, and Pennsylvania hospitals, resulted in comparisons of RBC antigen genotyping results performed on samples obtained during the respective admissions. The RBC genotypic analyses were identical, which when considered in the context of the clinical presentations, suggested that the same individual had presented to each of the three hospitals on at least one occasion over the course of two years. Communication with a broader group of transfusion medicine and hematology physicians prompted an expanded investigation: the index patient subsequently presented to hospitals in North Carolina, Georgia, Alabama, and Missouri in the weeks following his presentation to the Maryland hospital, and over a seven-year period, he had likely presented to at least 18 hospitals, spanning 13 states, in which he requested and received numerous doses of opioids and tPA, underwent multiple RCEs, and was transfused with hundreds of units of RBCs.

Discussion

Although the scope of factitious SCD remains unknown, inquiry of a national email listserv for transfusion medicine professionals suggests that similar encounters have transpired at hospitals across the United States (US), where individuals have sought care in multiple instances for SCD-related complications under false pretenses. Several of these encounters, including those of the index patient, transpired during the height of the COVID-19 pandemic, when hospitals were grappling with overwhelming patient volumes in emergency departments and intensive care units, as well as unprecedented staffing and blood shortages.[14] The ramifications of this behavior are not confined to wasted resources. Rather, there is risk of deleterious effect from the interventions (e.g., blood transfusion and tPA) that are commonly utilized for complications of "SCD". tPA, which may be employed in cases of suspected stroke, can result in hemorrhage, thus risking the very outcome (i.e., stroke) that was central to the index patient's spurious presentation. Blood transfusion confers risk of transfusion reactions, infectious, and immune (e.g., alloimmunization) sequelae,[15,16] while adverse effects of RCE extend to CVAD placement (e.g., thrombosis and infection) and the procedure itself (e.g., electrolyte disturbances secondary to citrate toxicity).[17,18] A diagnosis of factitious SCD does not preclude a legitimate, comorbid diagnosis that warrants urgent intervention; for example, our index patient had an acute DVT, predisposing him to a potentially fatal embolus. Indeed, most published cases of factitious SCD reported comorbid conditions that warranted medical management, such that the factitious aspect of their presentations impeded their optimal and timely therapy.

Recognition of factitious SCD and prevention of unnecessary medical treatment are challenging,

especially as pain is a subjective symptom. Acute neurologic events in SCD necessitate rapid intervention: the American Society of Hematology recommends simple transfusion or RCE within 2 h of presentation for medical care.[19] This urgency may cause practitioners, even those experienced in caring for patients with SCD, to overlook signs that suggest a factitious diagnosis. Moreover, recurrent SCD-related vaso-occlusive/pain crises may not be accompanied by physical signs, and the anecdotal reports of factitious SCD suggest that these individuals are well-informed, imparting a convincing presentation. When physical or radiological signs are present—as in the described case—this further complicates diagnosis, whereby the presenting features may be corroborated using findings from an unrelated, antecedent event. Central patient databases, which might facilitate identification of these individuals, are the exception in the US, and when available, are confined to discrete hospital networks. Nevertheless, even if linked databases become available, these patients may employ different aliases, further complicating recognition of factitious SCD. Our index patient presented to a single California hospital on seven separate occasions, all under different aliases, later determined using RBC antigen analysis.[20] At another California hospital, the same patient presented six times using four different aliases.[14] Only a centralized system that requires linkage to a unique national identifier might decrease the likelihood of this occurrence.

The acuity of presentation and need for urgent intervention render laboratory confirmation of a hemoglobinopathy via hemoglobin electrophoresis or genetic testing unfeasible at the time treatment decisions are required. To this end, the peripheral blood smear (PBS) is simple, rapid, and widely available; this may facilitate diagnosis, as the absence of sickle cells on PBS should evoke skepticism surrounding the diagnosis. The challenge is that of suboptimal sensitivity, particularly in recently transfused individuals.[21] Select tests may aid diagnosis in emergent situations, but these have not been approved for this specific purpose and have limitations. These include rapid, qualitative solubility testing for the presence of sickling hemoglobin variants (e.g., HbS). However, the test would be positive if the patient carried sickle cell trait or another sickling variant hemoglobin, even in the setting of factitious SCD. Another approach is hemoglobin A1c (HbA1c) assessment. Hemoglobin A1c testing is used to monitor diabetes as it reflects blood glucose levels over the life span of the RBC. In the setting of chronic hemolysis, as in true SCD, HbA1c should be abnormally low, given the reduced RBC lifespan. Therefore, a normal HbA1c should render the diagnosis of true SCD unlikely. Nonetheless, cut-offs have not been established for hemoglobinopathies and published findings regarding the ability of HbA1c testing to differentiate "true" from "spurious" SCD are conflicting.[22–24]

Given the lack of tests that can provide accurate, real-time diagnosis of SCD, careful clinical history collection and timely communication with physicians and centers endorsed for prior treatment may be the most effective methods to avoid unnecessary interventions. In several of this patient's presentations to California hospitals, the provided clinical history revealed discrepancies, including the provision of nonexistent primary healthcare providers or providers and medical centers possessing no record or knowledge of the patient. If encountered, these details should evoke suspicion of deceptive activity. Timely communication with medical centers where a patient endorses treatment also has the advantage of improving care for patients with true SCD, allowing for sharing of RBC alloantibody and/or RBC antigen phenotype/genotype to select appropriate blood products and minimize adverse outcomes.

The treatment of individuals with SCD is challenging and emblematic of health inequity. This multisystem, debilitating disease—almost exclusively—affects the Black and, to a lesser extent, Hispanic or Latino populations. Patients with SCD encounter myriad challenges, both from the disease itself, as well as those inherent to navigating a healthcare system that has often stigmatized and discriminated against them.[10,25] Encounters between healthcare providers and patients with factitious SCD may contribute to unconscious bias against patients with genuine SCD for the emergency department staff that are often the first point of contact for individuals with acute SCD-related complications. This bias may compound the risk of adverse outcomes in patients with SCD, wherein medical providers ignore pain that could be a sign of cardiac failure, splenic infarction, and other medical emergencies. Finally, while factitious SCD merits awareness, it must be placed in context as a rare disorder. The motives underlying the patient's reasoning for seeking care remain unknown. Importantly, it should not be used to undermine treatment of those with genuine SCD. Nonetheless, the medical community must remain vigilant to avoid unnecessary intervention and the associated complications in these rare occurrences.

Contributors

JWJ, JG, and EMB performed the literature review, drafted the manuscript, and approved the final version. JKK, BJG, AFZ, AMM, TCB, TJG, JDG, YAP, IP-A, JDB, ZWM, DCW, JSW, GSB, BDA, CBW, CY, GML, EA, MBM, ESA, RMF, EPC, AART, and CAT provided data, revised the manuscript, and approved the final version.

Declaration of interests

We declare no competing interests.

Acknowledgements

Funding: E.M.B effort is supported in part by the National Heart, Lung and Blood Institute (1K23HL15182).

Disclaimer: Drs. Bloch, Grossman, and Marques are members of the U.S. Food and Drug Administration (FDA) Blood Products Advisory Committee. Any views or opinions expressed in this manuscript are

those of the authors and are based on their own scientific expertise and professional judgment; they do not necessarily represent the views of the Blood Products Advisory Committee or the formal position of the FDA and also do not bind or otherwise obligate or commit either the Advisory Committee or the FDA to the views expressed.

References

1 Piel FB, Rees DC, DeBaun MR, et al. Defining global strategies to improve outcomes in sickle cell disease: a Lancet Haematology Commission. *Lancet Haematol*. 2023;10(8):e633–e686. https://doi.org/10.1016/S2352-3026(23)00096-0.

2 Verduzco LA, Nathan DG. Sickle cell disease and stroke. *Blood*. 2009;114(25):5117–5125.

3 Adams RJ. Stroke prevention and treatment in sickle cell disease. *Arch Neurol*. 2001;58(4):565–568.

4 Connelly-Smith L, Alquist CR, Aqui NA, et al. Guidelines on the use of therapeutic apheresis in clinical practice - evidence-based approach from the writing committee of the American society for apheresis: the ninth special issue. *J Clin Apher*. 2023;38(2):77–278.

5 Ballas SK. Factitious sickle cell acute painful episodes: a secondary type of Munchausen syndrome. *Am J Hematol*. 1996;53(4):254–258.

6 Lindenbaum J. Hemoglobin munchausen. *JAMA*. 1974;228(4):498.

7 Haywood C Jr, Tanabe P, Naik R, Beach MC, Lanzkron S. The impact of race and disease on sickle cell patient wait times in the emergency department. *Am J Emerg Med*. 2013;31(4):651–656.

8 Glassberg JA. Improving emergency department-based care of sickle cell pain. *Hematology Am Soc Hematol Educ Program*. 2017;2017(1):412–417. https://doi.org/10.1182/asheducation-2017.1.412.

9 Bergman EJ, Diamond NJ. Sickle cell disease and the "difficult patient" conundrum. *Am J Bioeth*. 2013;13(4):3–10.

10 Power-Hays A, McGann PT. When actions speak louder than words - racism and sickle cell disease. *N Engl J Med*. 2020;383(20):1902–1903.

11 Linton EA, Goodin DA, Hankins JS, et al. A survey-based needs assessment of barriers to optimal sickle cell disease care in the emergency department. *Ann Emerg Med*. 2020;76(3s):S64–s72.

12 Smeltzer MP, Howell KE, Treadwell M, et al. Identifying barriers to evidence-based care for sickle cell disease: results from the Sickle Cell Disease Implementation Consortium cross-sectional survey of healthcare providers in the USA. *BMJ Open*. 2021;11(11):e050880. https://doi.org/10.1136/bmjopen-2021-050880.

13 Jenerette CM, Brewer C. Health-related stigma in young adults with sickle cell disease. *J Natl Med Assoc*. 2010;102(11):1050–1055.

14 Perez-Alvarez I, Crews BO, Woo JS, Rezk S, Tran MH. A patient in need of a red cell exchange? *J Appl Lab Med*. 2021;6(4):1057–1061.

15 Goel R, Tobian AAR, Shaz BH. Noninfectious transfusion-associated adverse events and their mitigation strategies. *Blood*. 2019;133(17):1831–1839.

16 Tormey CA, Hendrickson JE. Transfusion-related red blood cell alloantibodies: induction and consequences. *Blood*. 2019;133(17):1821–1830.

17 Kim HC. Red cell exchange: special focus on sickle cell disease. *Hematol Am Soc Hematol Educ Program*. 2014;2014(1):450–456. https://doi.org/10.1182/asheducation-2014.1.450.

18 Biller E, Zhao Y, Berg M, et al. Red blood cell exchange in patients with sickle cell disease-indications and management: a review and consensus report by the therapeutic apheresis subsection of the AABB. *Transfusion*. 2018;58(8):1965–1972.

19 DeBaun MR, Jordan LC, King AA, et al. American Society of Hematology 2020 guidelines for sickle cell disease: prevention, diagnosis, and treatment of cerebrovascular disease in children and adults. *Blood Adv*. 2020;4(8):1554–1588. https://doi.org/10.1182/bloodadvances.2019001142.

20 Tyagi R, McGonigle A, Ziman A, Ward D, Mei Z. Recent institutional experience with a repeat patient feigning sickle cell. *Transfusion*. 2022;62(S2):9A–274A. https://doi.org/10.1111/trf.17058.

21 Kadima BT, Gini-Ehungu JL, Mbutiwi FIN, Bahati JT, Aloni MN. Validity of simple clinical and biological parameters as screening tool for sickle cell anemia for referral to tertiary center in highly resource constraints. *J Clin Lab Anal*. 2017;31(6):e22145. https://doi.org/10.1002/jcla.22145.

22 Lacy ME, Wellenius GA, Sumner AE, et al. Association of sickle cell trait with hemoglobin A1c in african Americans. *JAMA*. 2017;317(5):507–515.

23 Atabani GS, Hassan DA, Abdul Rahman AM, Saeed BO. Glycosylated hemoglobin levels in Sudanese sickle cell anemia patients. *Acta Haematol*. 1989;81(3):140–142. https://doi.org/10.1159/000205546.

24 Alzahrani BA, Salamatullah HK, Alsharm FS, et al. The effect of different types of anemia on HbA1c levels in non-diabetics. *BMC Endocr Disord*. 2023;23(1):24. https://doi.org/10.1186/s12902-023-01280-y.

25 Wailoo K. Sickle cell disease - a history of progress and peril. *N Engl J Med*. 2017;376(9):805–807.