

Myocardial Infarction and Transient Ventricular Dysfunction in an Adolescent With Sickle Cell Disease

Andreas J. Deymann, MD, and Kenneth K. Goertz, MD

ABSTRACT. We report a case of an adolescent who had sickle cell disease and previous evidence of myocardial damage and presented with abdominal pain and rapid progression to cardiogenic shock and subsequent development of myocardial infarction. To our knowledge, this represents only the second report of a case of acute myocardial ischemia and subsequent infarction resulting in transient ventricular dysfunction reported in a child with sickle cell disease successfully treated with exchange transfusion. The pathophysiology of this complication remains unclear, and cardiac complications may remain undetected as lung, bone, and brain infarcts are more common and the pain associated with sickle cell crisis may mask the ischemic symptoms. Multiple factors may contribute to ischemia in addition to the presence of a vaso-occlusive crisis or infection. Acute or chronic myocardial ischemia are probably more prevalent than currently known. *Pediatrics* 2003;111:e183–e187. URL: <http://www.pediatrics.org/cgi/content/full/111/2/e183>; sickle cell disease, myocardial infarction, ischemia, exchange transfusion.

ABBREVIATIONS. ECG, electrocardiogram; EF, ejection fraction.

Vascular injury that leads to thrombosis and hyperplastic remodeling of large arterial vessels¹ is believed to be the cause of ischemic or embolic stroke in sickle cell disease. Pathologic examination of the affected cerebral vasculature reveals intimal proliferation with a break-up of the elastic lamina. Endothelial cells repopulate denuded areas only in monolayers, and the hyperplastic intima consists of fibroblasts, fibrous tissue, and scattered smooth muscle cells leading to a narrowed vascular lumen and increased fragility of the affected cerebral vessels. In comparison with stroke, myocardial infarction is rare in young adults with sickle cell disease^{2–10} and may be attributable in large part to acute microvascular occlusion of small vessels. Epicardial coronary artery disease is notably uncommon in sickle cell disease. Several mechanisms may lead to impairment of microvascular circulation. In addition to impairment of circulation by sickled cells, thrombosis of small vessels is thought to be the result of endothelial damage attributable to shear injury and

resulting procoagulant state and embolization of endothelial cells into the microvasculature.^{3,11,12} Fibromuscular dysplasia of small cardiac vessels has been demonstrated in patients with sickle cell disease and may explain chronic ischemic changes and apoptosis in myocytes.^{3,12} Echocardiographic and electrocardiogram (ECG) changes may be more prevalent in sickle cell disease than currently known. Myocardial necrosis has been observed by autopsy in 1 child with hemoglobin sickle cell disease¹³ and has been reported in adults.^{3,12} Chronic myocardial dysfunction can occur and may be complicated by volume overload of anemia and coexisting renal and lung disease.² Myocardial ischemia may be a cause of chest pain during crisis in adults^{8,14} and is a possible cause for chest pain in children with sickle cell disease. Only 1 previous report of myocardial dysfunction with signs of myocardial infarction suggests reversibility of ischemia after exchange transfusion.^{1,15} We report an adolescent who had previous evidence of myocardial dysfunction with findings suggesting acute myocardial infarction and rapid development of severe cardiac dysfunction and who responded to exchange transfusion.

CASE REPORT

A 16-year-old, 53-kg black male with homozygous hemoglobin S disease and previous admissions for pain crisis and priapism was evaluated for chest pain at age 13. At that time, he was found to have ECG abnormalities consistent with left ventricular hypertrophy and an abnormal stress test with angina 7 minutes into the test as well as 2-mm ST depression in the inferior lateral leads. A resting echocardiogram showed a moderately decreased ejection fraction (EF) of 42% with no focal wall abnormality. After exercise, multiple segmental wall motion abnormalities could be seen (hypokinetic apical, midanterior, midanterolateral and midanteroseptal areas) and a Cardiolite single photon emission computed tomography study subsequently revealed a reversible perfusion defect of the inferior portion of the cardiac apex (Fig 1). Thereafter, he was lost to follow-up until the day of admission, when he presented with nausea, abdominal pain, and diaphoresis. He was afebrile and had no detectable focus of infection. His initial vital signs revealed a pulse of 102, respiratory rate of 32, a blood pressure of 88/48 mmHg, and 96% oxygen saturation on room air. His initial chest radiograph revealed a minimal prominence of pulmonary vascular markings. Prochlorperazine (Compazine) was given for nausea, and his oxygen requirement increased rapidly after arriving on the ward. After receiving a 1 L of normal saline fluid bolus over 1 hour, he developed respiratory failure and was intubated as he rapidly developed cardiogenic shock and ventricular dysrhythmia. Aggressive inotropic support with dopamine, milrinone, and norepinephrine was required to maintain his blood pressure in the low normal range. Ventricular tachycardia was treated with lidocaine during the initial phase of myocardial ischemia.

His first ECG revealed 4-mm ST depression in V₄ to V₆ and loss of R waves in V₁ and V₂. His cardiac enzymes (Fig 2) were highly

From the Department of Pediatrics, Division of Pediatric Critical Care and Cardiology, University of Kansas Medical Center, Kansas City, Kansas. Received for publication Apr 22, 2002; accepted Sep 23, 2002. Reprint requests to (A.J.D.) Department of Pediatrics University of Kansas, Kansas City, KS 66160. E-mail: adeymann@kumc.edu PEDIATRICS (ISSN 0031 4005). Copyright © 2003 by the American Academy of Pediatrics.

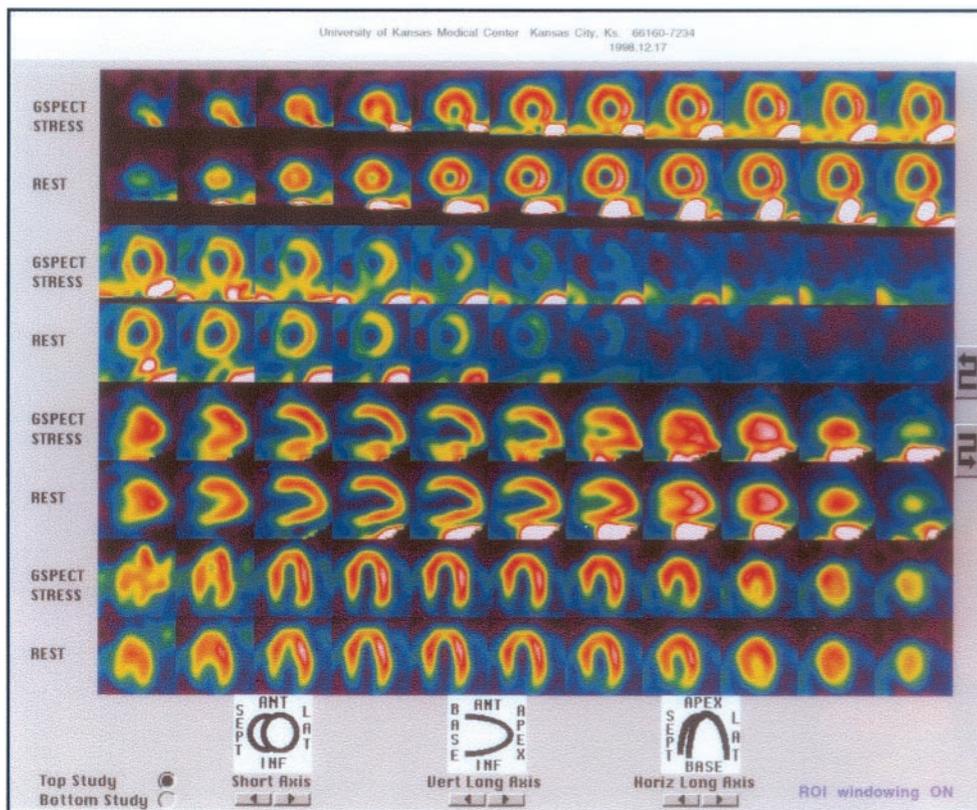


Fig 1. Cardiac perfusion stress test at age 13.

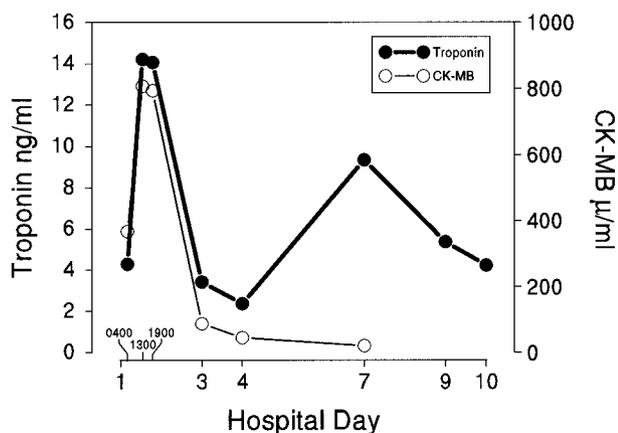


Fig 2. Cardiac enzyme profile during hospitalization (age 16).

abnormal, suggesting myocardial tissue damage. Electrolytes were normal with an HCO_3^- of 20 mmol/L and glucose of 9.88 mmol/L (178 mg/dL). A moderate degree of hemolysis was present with a hemoglobin of 7.2g/L and absolute reticulocyte count of $156 \times 10^3/\mu\text{L}$, uncorrected of 6% and corrected of 2.6% combined with a total bilirubin of 65 $\mu\text{mol/L}$ (3.8 mg/dL), direct bilirubin 5.13 $\mu\text{mol/L}$ (0.3 mg/dL). His white blood cell count was $23.7 \times 10^9/\text{L}$, and his temperature was 35.2°C orally. He was started on Ceftriaxone (Rocephin) and low molecular weight heparin.

At this time, the decision was made to perform an exchange transfusion to improve microvascular circulation in light of myocardial ischemia and dysfunction. The resulting hemoglobin S after exchange transfusion was 30% with a total hemoglobin of 10.5 mg/dL. Before exchange transfusion, his echocardiogram showed paradoxical septal motion, severe global akinesis of the myocardium, and an unmeasurable EF on transthoracic echocardiogram. Three hours after exchange transfusion, his myocardial contractility was dramatically improved and his EF was estimated

to be 46%. During the next 24 hours, his cardiogenic shock improved and he was weaned off inotropes on hospital day 4. He was extubated on hospital day 5. His ECG changes resolved within the first 24 hours, and his ECG pattern returned to his baseline abnormalities with absent R waves in V_1 and V_2 . His ST segment changes had resolved (Figs 3–5). On hospital day 10 a stress perfusion scan revealed no fixed or reversible perfusion deficits and an EF of 40% (Figs 2 and 6). He was started on β -blockers and angiotensin-converting enzyme inhibition. Incidentally, the patient disclosed after extubation that he had experienced chest pain on the day of admission during physical exercise.

DISCUSSION

We conclude that our patient experienced myocardial injury in the past and had transient myocardial ischemia with necrosis of myocardium during this admission, resulting in severe myocardial dysfunction. Infection could not be documented, and myocarditis was deemed unlikely. His impaired myocardial function and significant area under the curve for creatine kinase-MB release from myocytes suggest infarction. Focal myocardial scarring is likely to have occurred in the past as preexisting ECG changes and a cardiac perfusion scan suggest (Figs 3–6). Although thallium scintigraphy may not detect non-transmural or microinfarcts, it is a highly sensitive test of malperfusion and excludes the likelihood of epicardial vessel disease. His EF, measured before discharge, may have been artificially increased as inotropic support with dobutamine and milrinone are known to exert inotropy for some time after discontinuation. The interesting resolution of previous perfusion deficits on Cardiolite perfusion scanning after exchange transfusion before discharge

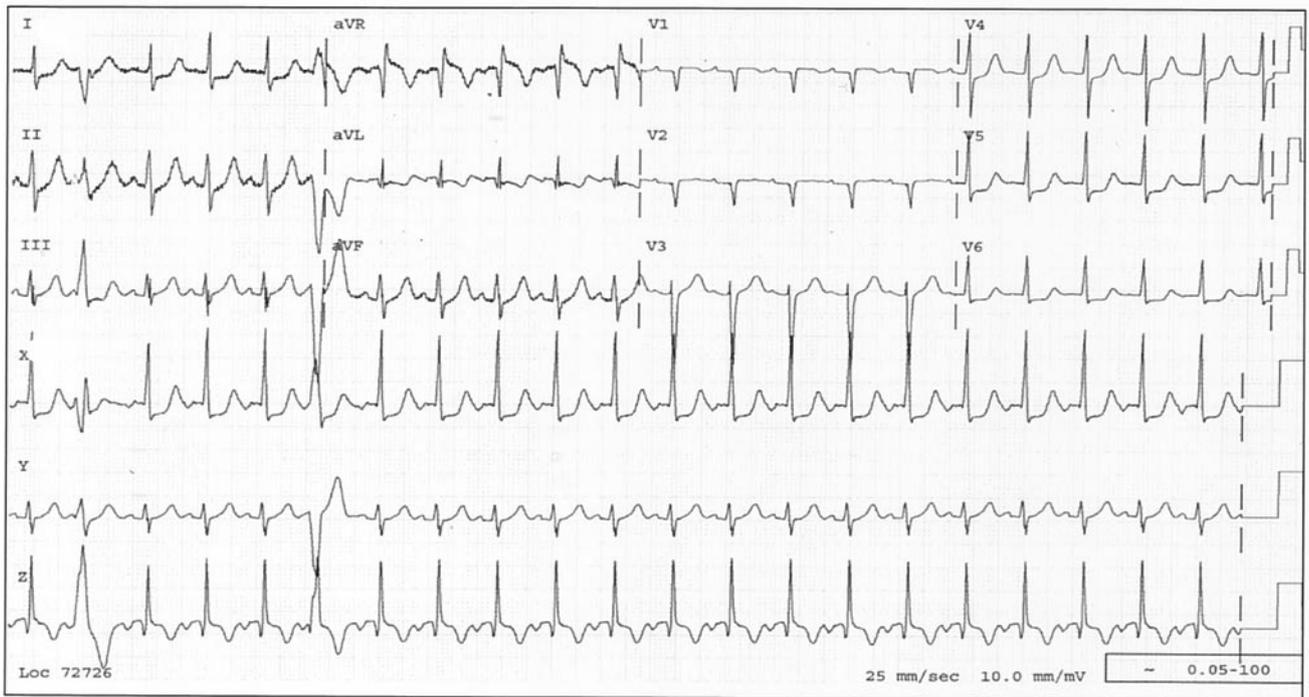


Fig 3. EKG at admission with ischemic changes (age 16).

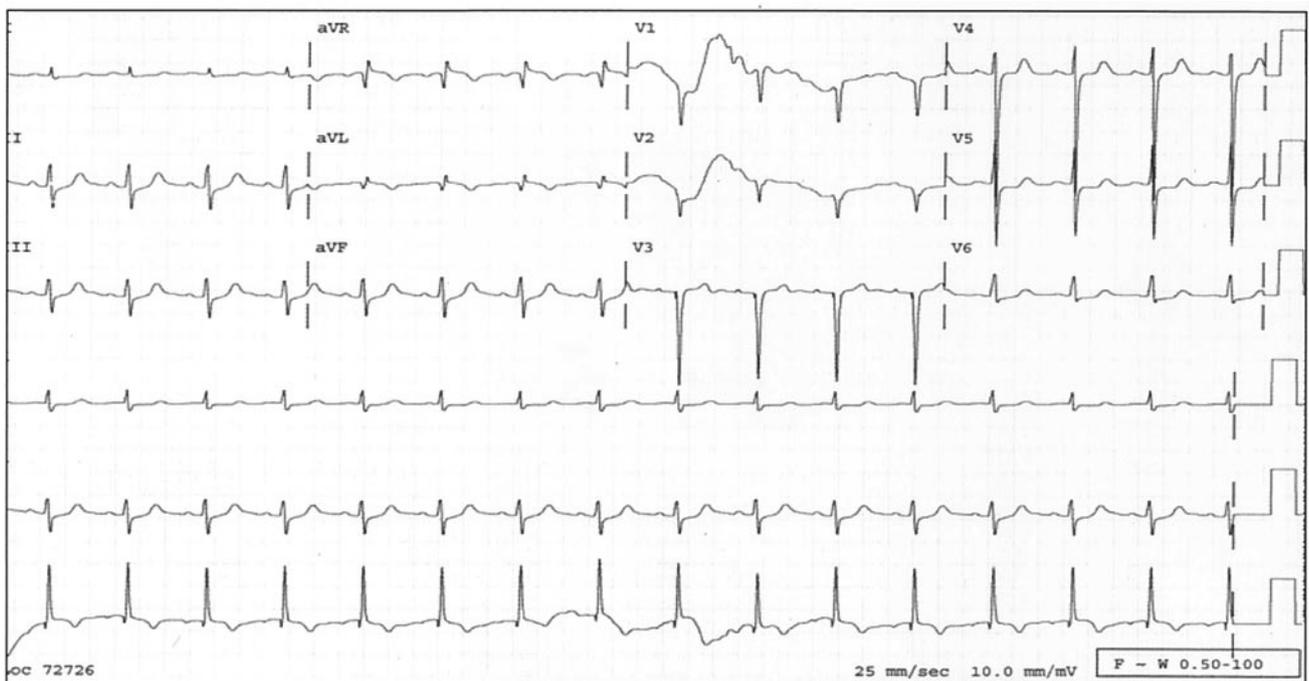


Fig 4. EKG after exchange transfusion (age 16).

suggests improved microvascular flow as a result of the absence of significant amounts of sickled red blood cells (Figs 1 and 6).

The true incidence of myocardial ischemia in sickle cell disease remains unknown. The pathophysiologic mechanism of acute and chronic microvascular occlusion, complicated by endothelial dysfunction as a result of endothelial cell damage by sickled red blood cells, can occur in any vascular bed. The heart seems to be protected by an unknown mechanism, especially when taking into consideration the high car-

diac oxygen extraction as hypoxemia promotes sickling of red blood cells.

Acute exchange transfusion seems to have improved myocardial dysfunction promptly in our case. Thrombolytic agents have not been adequately tested in sickle cell disease, although there is evidence of altered homeostasis and presence of a procoagulant state.¹¹ Anticoagulation was initiated with low molecular weight heparin as anticoagulation therapy for myocardial infarction, but its value has not been established in ischemia associated with

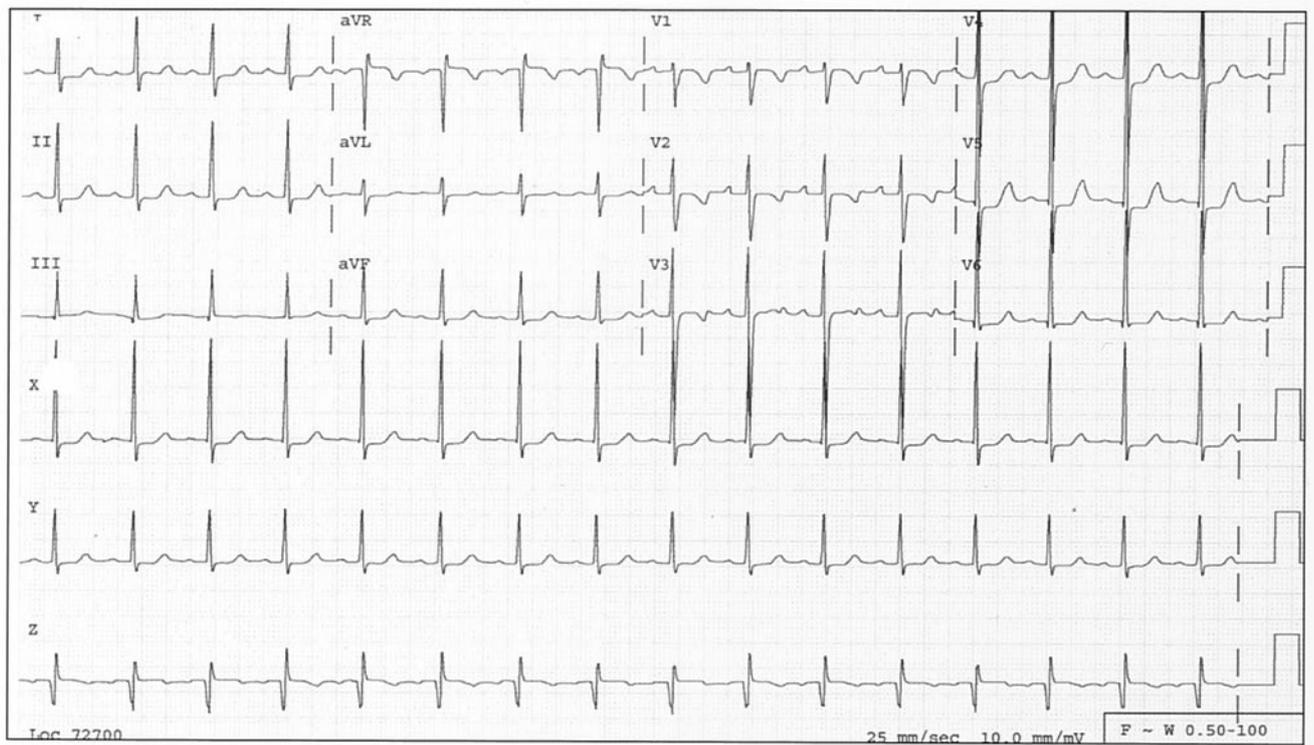


Fig 5. EKG at age 10.

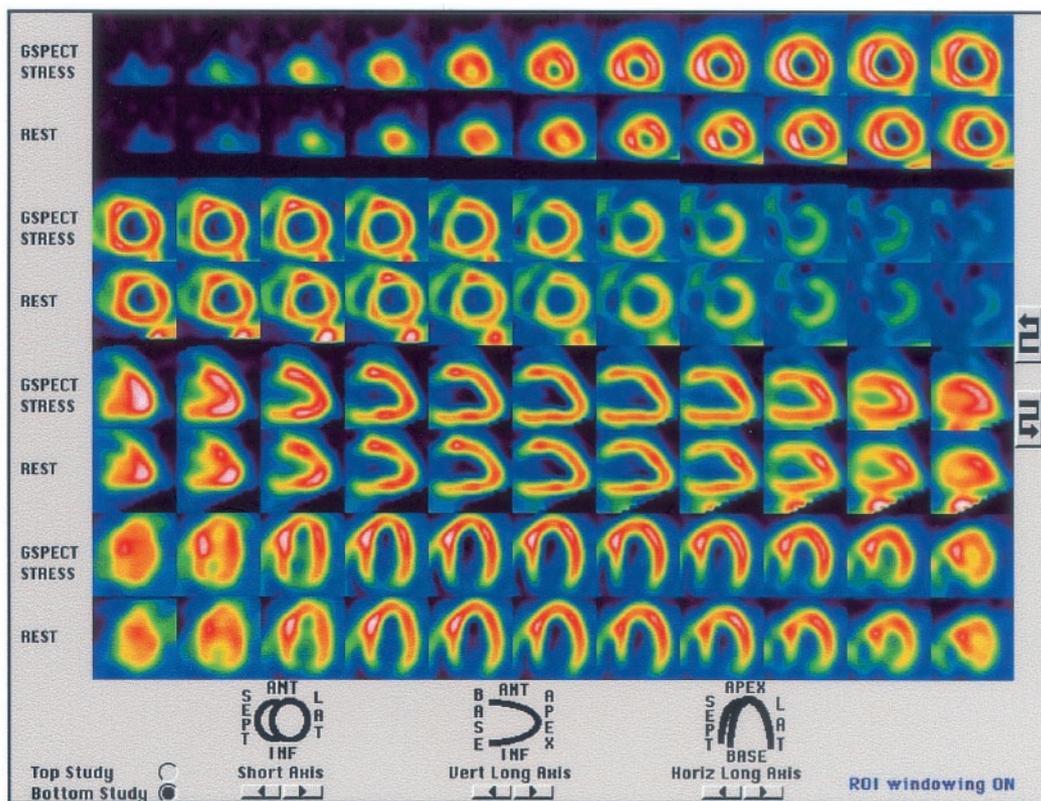


Fig 6. Cardiac perfusion stress test before discharge (age 16).

sickle cell disease. It is noteworthy that antiplatelet therapy remains unproved as well in sickle cell disease, and currently no evidence-based therapeutic regimen can be recommended for the treatment or prevention of cardiac complications of sickle cell disease.

However, experience drawn from stroke prophylaxis in sickle cell disease suggests initiating a hypertransfusion regimen with the goal of a hemoglobin S level of 30% or less for patients with sickle cell disease and signs of myocardial ischemia. Hy-

pertransfusion is known to prevent sickling and normalizes abnormal levels of pro- and anticoagulants in sickle cell disease, indicating decreased endothelial damage. This case and the previous case report suggest that aggressive support of cardiac function in conjunction with immediate exchange transfusion improves cardiac function probably as a result of improvement of microvascular circulation. Long-term prevention could include hypertransfusion, hydroxyurea administration, or bone marrow transplantation, but their roles remain to be demonstrated in the treatment of sickle cell disease-related complications.^{10,16–20}

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