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Simultaneous Acute Splenic Sequestration and Transient Aplastic Crisis in Children with Sickle Cell Disease

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Abstract

Acute splenic sequestration crisis (ASSC) is a hematological emergency in young children with sickle cell disease (SCD), characterized by worsening anemia and splenomegaly, usually with reticulocytosis and thrombocytopenia. Transient aplastic crisis (TAC) due to parvovirus B19 infection occurs in older children with SCD, and typically manifests as worsening anemia with reticulocytopenia and no splenomegaly. Five older children with SCD (4 HbSC, 1 HbSS on hydroxyurea) developed ASSC concurrent with TAC and had a severe clinical course. Our cases suggest that older children with SCD and acute parvovirus infection should be monitored closely for splenomegaly and multi-system dysfunction.

Keywords

Sickle cell disease; acute splenic sequestration crisis; aplastic crisis; parvovirus B19

INTRODUCTION

Two important complications of sickle cell disease (SCD) that most commonly occur in childhood include acute splenic sequestration crisis (ASSC) and transient aplastic crisis (TAC). ASSC usually occurs in children under 2-3 years of age and is characterized by an enlarged spleen with worsening anemia and trapping of circulating blood within the spleen; supporting laboratory values include reticulocytosis and thrombocytopenia [1]. ASSC is a major cause of morbidity in SCD and can result in severe anemia, hypovolemic shock, and even death [1-3]. The risk of developing ASSC is greatest for infants and toddlers with HbSS, who produce sickled erythrocytes but have not yet developed splenic infarctions and organ involution.

In contrast, TAC also causes severe anemia but usually in older patients and in association with acute human parvovirus (HPV) B19 infection [4]. In contrast to ASSC, the anemia observed in TAC is characterized by temporary absence of red cell production; reticulocytopenia is typical although mild neutropenia and thrombocytopenia sometimes occur as well [5,6]. Usually the distinction between anemia from ASSC or TAC is relatively

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easy based on age, history, physical examination, and laboratory values. Indeed, the diagnosis of ASSC usually requires the presence of reticulocytosis [1,2], while TAC requires reticulocytopenia [4]. However, scattered case reports describe ASSC occurring in conjunction with parvovirus B19 infection [7,8]. We report on 5 cases of ASSC with acute parvovirus infection, 4 occurring in older children with HbSC and 1 in a child with HbSS who began hydroxyurea therapy early in life. These cases suggest that older children with SCD and acute parvovirus infection should be monitored closely for the development of splenomegaly and multi-system dysfunction. Furthermore, generally accepted clinical and laboratory definitions of ASSC in SCD should be modified to include older patients and the presence of reticulocytopenia from acute parvovirus infection.

METHODS

We used the following criteria to diagnose ASSC: an enlarged tender spleen compared to previous assessment, drop in hemoglobin (Hb) concentration ≥2 gm/dL from baseline, and thrombocytopenia ($<150 \times 10^9$/L). There was no inclusion or exclusion based on the absolute reticulocyte count. The diagnosis of TAC required fever, reticulocytopenia, and positive parvovirus serology (elevated IgM titers acutely and subsequent positive IgG titers). With local IRB approval, we retrospectively reviewed the medical records of five pediatric patients with SCD hospitalized between October 2006 and May 2008, all of whom developed ASSC in conjunction with acute parvovirus B19 infection.

CASE REPORTS

Patient 1

A 3 year-old female with HbSS and no previous ASSC presented with five days of abdominal pain and fever. She was taking daily open-label hydroxyurea for 8 months, following a 2-year blinded treatment period with either hydroxyurea or placebo in the multicenter BABY HUG study (ClinicalTrials.gov # NCT00006400). She had left upper quadrant tenderness and an enlarged spleen, along with severe hypoplastic anemia (Table) requiring two blood transfusions. Post-transfusion, her spleen decreased in size and her blood counts improved. Two years later, she had a palpable spleen tip with recovery to baseline blood counts, and no further episodes of ASSC or TAC.

Patient 2

An 8 year-old female with HbSC presented with fever and pain in the lower back and thighs bilaterally. She had no previous ASSC or transfusions. While hospitalized for pain management, she developed progressive tender splenomegaly with falling blood counts suggesting ASSC but her reticulocyte count was very low. She received 2 transfusions and recovered. She has not had any further episodes of ASSC or TAC and her spleen remains palpable 2 cm below the left costal margin.

Patient 3

A 15 year-old female with HbSC presented with back and bilateral leg pain. She had multiple hospitalizations and several transfusions for previous acute chest syndrome, but no

history of splenomegaly or ASSC. Within 24 hours, she developed a pulmonary infiltrate and respiratory distress requiring intensive care and bi-level positive airways pressure. She quickly developed worsening anemia but without reticulocytosis; her spleen became very enlarged and serum creatinine rose to 1.5 mg/dL. She was transfused with a total of 45 mL/kg packed RBCs and platelets. She slowly recovered with improved pulmonary and renal function. One year later, her spleen is non-palpable and she has not had any repeat episodes of ASSC or TAC.

Patient 4

An 11 year-old male with HbSC presented with abdominal pain, decreased activity and appetite, and increasing scleral icterus. He appeared lethargic with massive splenomegaly medially to the umbilicus and distally into the pelvis with signs of cardiovascular collapse. Laboratory examination revealed hypoplastic anemia, severe electrolyte imbalance, and renal failure (creatinine 6.5 mg/dL). Within hours, he became obtunded requiring intubation and he received continuous veno-venous hemofiltration. He received a total of 40 mL/kg of pRBC and underwent erythrocytapheresis. The patient made a full recovery and later had his spleen removed electively to prevent recurrent splenic sequestration.

Patient 5

A 6 year-old male with HbSC presented with malaise, abdominal and leg pain, and fever. He had previous ASSC requiring transfusion 2 years earlier and subsequent baseline mild splenomegaly. He appeared somnolent with scleral icterus and massive splenomegaly, along with severe hypoplastic anemia. He received a total of 22 mL/kg of pRBCs and recovered. He underwent splenectomy one month later without complications.

DISCUSSION

Classical definitions of ASSC and TAC in children with SCD represent mutually exclusive diagnoses, since ASSC features anemia with splenomegaly and evidence of active erythropoiesis in younger patients[1,2], while TAC is characterized by hypoplastic anemia without splenomegaly in older patients[5]. However, unusual cases have been described where ASSC has occurred in association with acute parvovirus infection [7,8]. All five of our patients developed signs, symptoms, and laboratory features suggestive of concomitant ASSC and TAC, with enlarging splenomegaly, severe anemia and thrombocytopenia, but absent reticulocytes and serology consistent with acute parvovirus infection. Our patients were older than the usual at risk age for ASSC, due presumably to preservation of splenic organ function into late childhood and adolescence. This finding is not unusual for patients with HbSC disease and may be a long-term result of hydroxyurea therapy for patients with HbSS. Children who start hydroxyurea prior to autoinfarction of their spleen are at greatest risk for this complication, although some children with HbSS may actually recover splenic function during hydroxyurea therapy [9,10].

Notably, two of our patients developed multi-organ system failure during their hospitalization, both with HbSC disease and older than 10 years. A clinically severe course of TAC has been described previously in HbSC patients[11] and our cases confirm that

parvovirus infection in older children with HbSC may have increased morbidity. Children with HbSC appear to be more likely to develop ASSC and acute chest syndrome during TAC than children with HbSS[6]. In addition to constitutional symptoms and hypoplastic anemia, parvovirus can cause hepatitis[12,13], glomerulonephritis[14-16], and even central nervous system complications[17]. Two of our patients developed renal failure, due either to infection or compromised blood flow in association with massive splenomegaly. Despite the severe clinical course of our patients, with appropriate supportive therapy all recovered without long-term sequelae. Children in this clinical setting should be monitored closely for renal, hepatic, and CNS dysfunction.

Prospective studies investigating concurrent ASC and TAC from parvovirus B19 are needed. These studies should focus on the epidemiology of this rare event including: prevalence, identifying patients at risk, and age of presentation. Preservation of splenic function, either by hydroxyurea or transfusion therapy, may lead to increase numbers of cases of concurrent ASSC and TAC. Additionally, observing the morbidity and mortality of these concurrent conditions may help in identifying appropriate diagnostic workup and treatment.

Education about signs and symptoms of ASSC, as well as periodic splenic palpation by parents, should continue beyond infancy since the risk of ASSC may continue throughout childhood, particularly in children with HbSC or those with HbSS on therapy. Efforts to develop a parvovirus vaccine are ongoing and should continue, since acute parvovirus infection can lead to severe morbidity in this patient population.

REFERENCES

1. Kinney TR, Ware RE, Schultz WH, et al. Long-term management of splenic sequestration in children with sickle cell disease. J Pediatr. 1990; 117(2 Pt 1):194–199. [PubMed: 2380816]
2. Emond AM, Collis R, Darvill D, et al. Acute splenic sequestration in homozygous sickle cell disease: natural history and management. J Pediatr. 1985; 107(2):201–206. [PubMed: 4020541]
3. Powell RW, Levine GL, Yang YM, et al. Acute splenic sequestration crisis in sickle cell disease: early detection and treatment. J Pediatr Surg. 1992; 27(2):215–218. [PubMed: 1564621]
4. Ware R. Human parvovirus infection. J Pediatr. 1989; 114(3):343–348. [PubMed: 2537895]
5. Zimmerman SA, Davis JS, Schultz WH, et al. Subclinical parvovirus B19 infection in children with sickle cell anemia. J Pediatr Hematol Oncol. 2003; 25(5):387–389. [PubMed: 12759625]
6. Smith-Whitley K, Zhao H, Hodinka RL, et al. Epidemiology of human parvovirus B19 in children with sickle cell disease. Blood. 2004; 103(2):422–427. [PubMed: 14525777]
7. Mallouh AA, Qudah A. Acute splenic sequestration together with aplastic crisis caused by human parvovirus B19 in patients with sickle cell disease. J Pediatr. 1993; 122(4):593–595. [PubMed: 8463907]
8. Wethers DL, Grover R, Oyeku S. Aplastic crisis and acute splenic sequestration crisis. J Pediatr Hematol Oncol. 2000; 22(2):187–188. [PubMed: 10779041]
9. Hankins JS, Helton KJ, McCarville MB, et al. Preservation of spleen and brain function in children with sickle cell anemia treated with hydroxyurea. Pediatr Blood Cancer. 2008; 50(2):293–297. [PubMed: 17554794]
10. Hankins JS, Ware RE, Rogers ZR, et al. Long-term hydroxyurea therapy for infants with sickle cell anemia: the HUSOFT extension study. Blood. 2005; 106(7):2269–2275. [PubMed: 16172253]
11. Shao SH, Orringer EP. Case report: splenic sequestration and multiorgan failure as the presenting manifestation of hemoglobin SC disease. Am J Med Sci. 1996; 311(3):139–141. [PubMed: 8615389]

12. Al-Abdwani RM, Khamis FA, Balkhair A, et al. A child with human parvovirus B19 infection induced aplastic anemia and acute hepatitis: effectiveness of immunosuppressive therapy. Pediatr Hematol Oncol. 2008; 25(7):699–703. [PubMed: 18850484]
13. Pardi DS, Romero Y, Mertz LE, et al. Hepatitis-associated aplastic anemia and acute parvovirus B19 infection: a report of two cases and a review of the literature. Am J Gastroenterol. 1998; 93(3):468–470. [PubMed: 9517662]
14. Ieiri N, Hotta O, Taguma Y. Characteristics of acute glomerulonephritis associated with human parvovirus B19 infection. Clin Nephrol. 2005; 64(4):249–257. [PubMed: 16240895]
15. Tolaymat A, Al MF, MacWilliam K, et al. Parvovirus glomerulonephritis in a patient with sickle cell disease. Pediatr Nephrol. 1999; 13(4):340–342. [PubMed: 10454787]
16. Wierenga KJ, Pattison JR, Brink N, et al. Glomerulonephritis after human parvovirus infection in homozygous sickle-cell disease. Lancet. 1995; 346(8973):475–476. [PubMed: 7637482]
17. Wierenga KJ, Serjeant BE, Serjeant GR. Cerebrovascular complications and parvovirus infection in homozygous sickle cell disease. J Pediatr. 2001; 139(3):438–442. [PubMed: 11562626]

Table I

Characteristics of 5 children with SCD who presented with acute splenic sequestration crisis in association with acute parvovirus infection.

Patient	Genotype	Age (years)	Baseline Hb (gm/dL)	Lowest Hb (gm/dL)	Absolute Reticulocytes (X 10^9/L)	Reticulocytes (%)	Baseline Platelets (X 10^9/L)	Lowest Platelets (× 10^9/L)	Largest Spleen Size	Follow-up Spleen Size	Parvovirus IgM (positive >1.1)
1	HbSS on hydroxyurea	3	9.2	3.7	2	0.1	130	48	6 cm	0.5 cm	13.4
2	HbSC	8	Unknown*	4.3	5	0.2	Unknown*	108	4 cm	2 cm	14.7
3	HbSC	15	11.4	3.9	3	0.1	233	40	7 cm	Non-palpable	13.7
4	HbSC	11	10.3	3.9	8	0.4	130	85	10 cm	Splenectomy	13.3
5	HbSC	6	10.4	4.2	6	0.4	276	100	10 cm	Splenectomy	9.4

Spleen size refers to distance below the left costal margin.

* First presentation to our institution.