Acute splenic sequestration crisis in children with Sickle Cell Disease

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ABSTRACT

Objective: The aim of this study was to demonstrate the clinical experience with acute splenic sequestration crisis in children with sickle cell disease, followed in Madina Maternity & Children's Hospital, Madina Al-Munawara, Kingdom of Saudi Arabia.

Methods: A retrospective review of hospital case notes of all children with acute splenic sequestration in sickle cell disease, was carried out in the Pediatric Hematology unit at Madina Maternity & Children's Hospital between 1993 through to 2000.

Results: One hundred and twenty children with sickle cell disease were registered and followed in Madina Maternity & Children's Hospital. Out of these, 8 had acute splenic sequestration crisis with a prevalence of 7%. Seven were Saudi and one was non-Saudi (Sudanese), 7 had sickle cell anemia and one had Sickle β-Thalassemia. The female to male ratio was 3:1, 2 patients presented with associated painful crisis. In 50% of the patients, the spleen was not palpable before the attack of acute splenic sequestration crisis. All patients had major splenic sequestration with circulatory collapse, 4 patients (50%) had recurrence and 3 (37.5%) had splenectomy carried out at the age of 2 years. The steady state hematological data did not show any risk factor for acute splenic sequestration crisis and none of our patients died.

Conclusion: We conclude that acute splenic sequestration crisis is of relatively high prevalence in the western region of the Kingdom of Saudi Arabia, and is of severe type. Management measures recommended are, prevention of sickle cell disease through health education, reduction of consanguineous marriage, implementation of premarital and neonatal screening programs for hereditrary blood disease, regular follow-up and education of parents to palpate the spleen in an established sickle cell case.

Keywords: Acute splenic sequestration crisis, sickle cell disease.

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Acute splenic sequestration crisis (ASSC) is a sudden pooling of a large amount of blood into the spleen leading to an acute splenomegaly, profound anemia with a decrease of at least 2g/dl from the steady-state hemoglobin concentration, and in severe cases hypovolemic shock, and death may occur. With the recent decline in mortality from pneumococcal sepsis, ASSC has become a leading cause of death in children with Sickle cell disease (SCD). The over all incidence of ASSC is variable, ranging from 7.5% to 30%,[1-2] the incidence of ASSC in the eastern province of Saudi Arabia is 2% and its of minor type occurring in older children.[3-5] Acute splenic sequestration has been reported as early as 5 weeks of age,[6] and also in adults',[7] and is often associated with viral or bacterial infection. There are no clear risk factors for ASSC, however hemoglobin F level (HBF) at 6 months of age was somewhat lower in children who developed the crisis.[2] Madina Region is located in the western province of Saudi Arabia, it is one of the major pockets of sickle cell gene, besides the eastern province and Tehamat Asir

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Region.[8] The Madina Maternity & Children's Hospital (MMCH) is a 400 bed hospital with 200 bed pediatric section. It is the main referral hospital for the Madina Region. The age limit for pediatric admission is 13 years and the approximate number of children served by the hospital is 350,000 in an estimated population of 800,000. The purpose of this study was to demonstrate our clinical experience with ASSC in SCD patients and to compare our data with other available studies.

Methods. All the children with SCD followed in the Pediatric Hematology unit at MMCH from 1993 to 2000 known to have ASSC during this period, were included in the study. Acute splenic sequestration was defined as a decrease of at least 2 g/dl from the steady state hemoglobin concentration, evidence of increased erythropoiesis such as markedly elevated reticulocyte count and acutely enlarging spleen. The major attacks are associated with a greater drop in hemoglobin, reaching a level of less than 2 g/dl and hypovolemic shock, while the minor attacks are characterized by moderate increase in spleen size with a drop in the hemoglobin level of 2 to 3 g/dl from steady state. The diagnosis of SCD was based on cellulose acetate electrophoresis at alkaline pH 8.4 (Helena Laboratories 1530 Lindbergh Drive, Beaumont, Texas United States of America). Eight patients had ASSC, all were followed for a minimum of 12 months. The medical records of these patient were studied retrospectively, the following variables were studied, age at onset, sex, nationality, clinical signs of shock, splenic size before and after crisis, associated crisis or illness, steady state leukocyte count, hemoglobin, platelet counts, hemoglobin electrophoresis, management undertaken, recurrence and mortality.

Results. Acute splenic sequestration crisis occurred in 8 out of 120 children with SCD, indicating a prevalence rate of 7%. Seven were Saudi and one was Sudanese, 5 patients (63%) presented below the age of 2 years. The lowest age of a patient was 2 months and the highest age was 6 years, with the mean age of 2.5 years. Females were affected more than males 75% versus 25%. Seven patients (87.5%) had homozygous (HbSS) disease and one (12.5%) had sickle B-Thalassemia. In 4 patients (50%) spleen was not palpable before ASSC. All patients had major attacks with circulatory collapse. Acute painful crisis was associated only with 2 patients (25%), all patients received blood transfusion at presentation and 3 patients (37.5%) had splenectomy at 2 years of age, 4 patients (50%) had recurrence and there was no mortality. Table 1 summaries the hematological data during steady state.

Discussion. This study is the first in Madina region that highlights the experience of one of the most serious complications of SCD, that is considered a major cause of mortality and morbidity in the first 5 year of life.[9] Although we report 8 cases of ASSC in children over a 7 year period, this does not represent all the cases in this region, as some cases might have been referred to local hospitals, or may not have been diagnosed. To our knowledge there has only been a few reported cases of ASSC in children with SCD in the Kingdom of Saudi Arabia.[3-4] We found a relatively high prevalence of ASSC among our patients (7%) as compared to other studies (2%).[3] The majority of our patients (87.5%) were Saudis. The age group mostly affected was below 2 years of age (63%) as reported, by others,[10] and this is the age after which the spleen develops

Table 1 - Steady state hematological data.

Age	WBC C x 10^9/L	HB G/dl	PLT x 10^9/L	Retic %	HBA %	HBF %	HBS %	HB A2 %
2 Months	11	11	284	(5)	-	(30)	(66.5)	(3.5)
4 Months	8	10.5	165	(5)	-	(25)	(72)	(4)
1 Year	12	8.8	272	(6)	-	(30)	(67)	(3)
5 Years	20	6	410	(7)	-	(10)	(86)	(4)
6 Years	5	7.5	241	(6)	-	(15)	(82)	(3)
1 Year	10	8	300	(4)	-	(30)	(67)	(3)
5 Years	15	9	290	(5)	-	(30)	(67)	(3)
9 Months	14	8	200	(8)	-	(5)	(92)	(3)

WBC=white blood cell, C=count, HB=hemoglobin, PLT=platelet, Retic=reticulocyte, HBA=hemoglobin A_1, HBF=hemoglobin F, HBS=hemoglobin F, HBA2=hemoglobin A_2

acute infarction and subsequent fibrosis. However, it does occur in older age and adults especially in those with other forms of SCD whose spleen remains enlarged into adult life such as sickle cell B-Thalassemia and HbSC disease.[11-12] The youngest patient in our study was 2 months old, consistent with other studies,[13] however it has been reported as early as 5 weeks of age.[6] The majority of our patients were female, the reason for female predominance is unknown. Eighty seven and a half percent of our patients had homozygous (HbSS) SCD, consistent with other studies.[2,9] All our patients had major ASSC with hypovolemic shock in contrast to Salamah et al,[4] who reported all their cases with minor ASSC. This is consistent with the finding that SCD in children in the eastern region of Saudi Arabia is clinically mild,[3] this is attributed to the high level of HbF and the frequently associated a-thalassemia.[14,15] The majority of our patients (75%) although having a high level of HbF (15%-30%), had major ASSC, indicating that SCD with high levels of HbF is not always benign, particularly in the western region of the Kingdom of Saudi Arabia, a finding consistent with Acquaye et al.[16] The sickle cell genes in western Saudi Arabia were of Benin Haplotypes[17,18] suggesting that these genes had their origin in Western Africa and probably imported from Africa through migration of Muslims to the holy city of the Kingdom of Saudi Arabia over the years. The cause of ASS in SCD is not known, however an association with intercurrent viral or bacterial infection is often present. Only 25% of our patients had associated painful crisis. None of our patients had associated acute chest syndrome (ACS), in contrast to Emond et al[2] who reported 20% of his patients with ACS. In 4 patients (50%), spleen was not palpable before ASSC, similar presentation was reported by Casey et al.[19] This emphasizes the need for a high index of suspicion for splenic sequestration, and the utility of ultra-sonography in documenting splenomegaly as it is considered reliable and accurate.[20] Recurrence of ASSC was 50% in our study consistent with other studies.[9] Three patients (37%) underwent splenectomy, the other 5 patients (63%) were treated with short-term blood transfusion, in 2 out of them, parents refused splenectomy and 3 were below 2 year of age. The role of splenectomy in major attacks is well established.[21,22] However the age at which splenectomy should be carried out is still a controversial issue, due to risks of post-splenectomy infection. The spleen in SCD is frequently dysfunctioning after 6-9 months of age, as progressive hyposplenism in SCD has been demonstrated by an increase in pitted red blood cell counts, as early as 8 months of age.[23] Based on that, Powell et al,[22] recommended splenectomy after the first major episode of ASSC and reasoned that removal of a poorly or non functioning spleen does not add increased susceptibility to infection. Although chronic blood transfusion is an alternative mode of therapy of ASSC to prevent recurrence, particularly in infants younger than 2 years of age, it usually reduces splenic size, restores function and prevents sequestration, thus avoiding splenectomy in the very young child. Rao and Gooden[24] showed that the time gained from short term transfusion 1-3 year therapy was beneficial in reducing the risk of recurrence of ASSC and temporarily reversing splenic dysfunction; in contrast Kinney, et al[1] showed that a short term transfusion program to prevent recurrent splenic sequestration is of limited benefit. In our study. those who had ASSC under the age of 2 years were maintained on short term transfusion until 2 years of age when splenectomy was performed. Grover and Weathers,[25] recommend long term transfusion therapy for a child with ASSC under 3 years and prompt splenectomy after the first episode of ASSC in the child 5 years of age and older. We agree with others that splenectomy should be considered after 2 minor attacks of ASSC,[5,26] however for a major attack we recommend prompt splenectomy after the first episode in the child 2 years of age and older, and short term transfusion for the patient under 2 years of age. Although recurrence of ASSC can be prevented by chronic blood transfusion, however in situations like ours with poor compliance of patients and limitation of blood availability with increasing risk of blood transfusion complication, partial splenectomy might be a suitable form of therapy for children under 5 year of age, as it has been recommended for children with ASSC as a means of preventing recurrence and preserving splenic function.[27-29] None of our patients developed hypersplenism following ASSC, by contrast Topley et al[9] described that hypersplenism is higher in children developing minor or major episodes of ASSC. None of our patients died or developed overwhelming post-splenectomy septicemia during follow-up period. In a Jamaican study,[9] the mortality rate for the first attack was (12%) and for those who survived the first episode was 20%. The steady-state hematological data (Table 1), did not show clear risk factors for occurrence of ASSC.

In conclusion, prevalence of ASSC in children with SCD is relatively high in the western region of Saudi Arabia, we also conclude, prior splenomegaly is not a good predictor for occurrence of ASSC. We recommend the prevention of SCD and other hemoglobinopathies in the Kingdom of Saudi Arabia by genetic counselling through health education, reduction of consanguineous marriages and implementation of premarital screening for hereditary blood disease. We also recommend, neonatal screening for early diagnosis of SCD in the area with high prevalence of SCD, regular follow up, early education of parents on how to palpate the spleen, recognize sudden enlargement and an appropriate action for obtaining rapid evaluation and treatment.

Patients who have major episodes of ASSC should have splenectomy shortly after the event at the age of 2 years and more, and if the age is below 2 years, then the patient should be maintained on short term blood transfusion to keep HbS level below 30% until splenectomy is performed.

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