Original Article

Indications for Splenectomy among Children with Sickle Cell Disease in Kuwait

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Kuwait Medical Journal 2002, 34 (1): 33-35

ABSTRACT

Objective: Acute splenic events are a common cause of morbidity in sickle cell disease. These events include acute splenic sequestration, hypersplenism, infarction and abscess formation. This study was carried out to document the following: age, Hb genotype, indications for splenectomy, pre- and post-operative care and complications among children with sickle cell disease in Kuwait.

Setting: The Pediatric and Surgical Departments of Mubarak Al-Kabeer and Al-Amiri Hospitals in Kuwait.

Patients and Methods: A combined retrospective and prospective study of all SCD patients that had splenectomy over a 7-year period (1994 – 2000).

Results: Sixteen SCD patients, aged 4 to 12 years, made up of 8 β˚thal, 6 SS and 2 SD, had splenectomies during the study period. The indications were hypersplenism (HS) in 9 (56.3%) and recurrent acute splenic sequestration (ASS) in 7 (43.8%). Of the 9 cases of HS, 7 (77.8%) were Sβthal and only 2 (22.2%) were SS. Of the 7 ASS cases, 4 (57.1%) were SS, 2 (28.6%) were SD and only 1 was Sβthal. The mean age (5.2 ± 1.5 years) of the ASS patients was significantly ($P<0.05$) lower than that of the HS patients (8.9 ± 2.9 years). They all had open laparotomy and there were no complications. They have been followed for 1 to 6 years post surgery. All are doing well and none has required further transfusions.

Conclusion: The two common acute splenic complications among Kuwaiti SCD patients are HS and ASS and both respond well to splenectomy. ASS is much more common among SS patients while HS is found mainly in Sβthals.

KEYWORDS: Sickle cell disease, splenectomy

INTRODUCTION

Most sickle cell disease (SCD) patients in Kuwait carry the Saudi Arabia/India β^S-globin gene haplotype and, as such, have elevated Hb F levels and their disease is relatively mild[1-3]. Functional asplenia and autosplenectomy do not occur in early childhood and in previous studies we showed that up to 75% of our patients (aged 4 to 16 years) retain full or partial spleen function[4,5]. The implication of this is that the spleen remains viable and is, therefore, available for other acute events, which may be a cause of morbidity in these patients.

The common acute splenic events in SCD include acute splenic sequestration crisis (ASS), hypersplenic syndrome (HS), massive infarction, and abscess formation[6-9]. ASS is defined as a fall in hemoglobin level of >2 g/dl, with evidence of marrow compensation (increased reticulocyte count) and an acutely enlarged spleen[6,7]. It tends to be recurrent and is a common cause of mortality in SCD. HS, on the other hand, occurs in a chronically enlarged spleen (>4 cm below the costal margin) and results in low Hb level (usually <6.5 g/dl), low platelets (<200 x 10^9/l) and increased reticulocytes[8,9]. The children end up being transfused repeatedly with all the consequent problems. Both ASS and HS are indications for splenectomy in SCD. The present report is a combined retrospective and prospective study of SCD patients who had splenectomy between 1994 and 2000.

PATIENTS AND METHODS

All the patients attending the pediatric hematology clinics in Mubarak Al-Kabeer and Al-Amiri Hospitals in Kuwait, who had splenectomies between 1994 and 1997 were studied retrospectively. All such cases since 1997 have been studied prospectively. The following were noted on all patients: the size of the palpable spleen below the left costal margin, indication for splenectomy, usual CBC pre-op, frequency of transfusions, what pre-operative care was given, any post-operative complications and post-operative CBC. The Hb genotype was verified in all patients and the percent Hb F level was determined using cation-

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exchange high performance liquid chromatography (HPLC)[10]. The β^S-globin gene haplotype was determined using allele-specific oligonucleotide hybridization to identify haplotype-specific mutations in the 5' flanking and IVS-II regions of the $^G\gamma$ and $^A\gamma$-globin genes as previously described [2,11]

RESULTS

Sixteen SCD patients had splenectomies in the study period. They were made up of 11 males and 5 females aged 4 to 12 years with a mean of 7.3 ± 3.0 years. The Hb genotypes were 8 Sβ^0Thal, 6 SS and 2 SD. There was no significant difference in the mean ages of the SS and Sbthal groups.

Nine (56.3%) patients had HS, while 7 (43.8) had recurrent ASS and one patient had both. There was no case of massive splenic infarction or abscess. Of the 9 cases of HS, 7 (77.8%) were Sβthal and 2 (22.2%) were SS. Among the ASS, 4 (57.1%) were SS, 2 (28.6%) were SD and only 1 (14.3%) was SβThal. The mean age (5.2 ± 1.5 years) of the ASS patients was significantly lower ($P<0.05$) than that of the HS patients (8.9 ± 2.9 years).

The patients with ASS had had at least two episodes for which they were admitted and required blood transfusion. Their range of Hb at presentation was 4.1 to 7.0 with a mean of 4.9 ± 1.0 g/dl. Two of the HS patients were transfusion dependent while the others were transfused sporadically. The range of Hb before each transfusion in this group was 3.7 to 8.2 with a mean of 7.7 ± 0.7 g/dl. In preparing these patients for surgery, the aim was to decease the Hb S concentration to < 30% and raise the total Hb to ≥ 10 g/dl. This was achieved by top-up filtered RBC transfusions over 2 to 3 weeks in 12 patients, while 4 patients had exchange blood transfusion. All the patients had pneumococcal and Hib vaccines at least two weeks before the surgery. Prophylactic penicillin was started two days before surgery.

The surgical technique was open laparotomy in all the patients; a laparascopic technique was introduced after the current study period. A meticulous search for splenules was carried out at surgery. The patients were given routine post-op care with special emphasis on adequate hydration and antibiotic coverage (IV ampicillin), which was started a day before surgery and continued till discharge from hospital when oral penicillin was started at a dose of 125 mg or 250 mg twice daily depending on age (the lower dose for those < 5 years). None of the patients had any crisis in the immediate post-op period and were discharged on the 3rd or 4th day. They are all still being followed in the outpatient clinic and are doing well. None has required further transfusions and the mean Hb 3 months after surgery in the whole group was 10.1 ± 0.9 g/dl. They are all on penicillin prophylaxis either orally twice daily or monthly intramuscular injection of long-acting penicillin (benzathine penicillin).

All the spleens removed at surgery were subjected to histopathological examination. All showed congested red pulps and hyperplasia of the reticulo-endothelial cells. Siderotic nodules (Gamna-Gandy bodies) were seen in eight. Hemosiderin deposits were reported in four patients (1 SS, 3 Sβthal) who had received multiple blood transfusions. One 11-year-old SβThal patient with hypersplenism also showed multiple infarcts.

DISCUSSION

Splenic complications constitute a significant cause of morbidity in SCD[8,9,12]. Splenomegaly occurs early, within the first two years of life, in many patients because of extramedullary hemopoiesis and congestion. Even then, the spleen may show evidence of sub-optimal phagocytic function, a situation referred to as functional asplenia or hyposplenia. The recurrent infarction that characterizes the disease produces progressive fibrosis culminating in autosplenectomy usually within the first decade. The enlarged spleen also quite often produces enhanced destruction of blood cells causing hypersplenism. The other common acute splenic events in these patients include sequestration crisis, massive infarction and abscess formation[13].

The mild nature of SCD among most Gulf Arab patients ensures the spleen remains viable until an older age. Therefore, a variety of acute splenic events may be encountered. The two indications for splenectomy in this series are HS and ASS. However, the former is much more common among SbThal patients, while SS and SD tend to present with ASS. This is not surprising since persistent splenomegaly is more a feature of Sbthal than SS patients, especially among our patients. The cause of ASS is not known but it is common in early childhood among SCD patients. Thus the mean age of the ASS patients in this study was significantly less than that of the patients with HS. ASS also tends to be recurrent and in this series, the patients had 2-4 episodes each before splenectomy was done.

Since many of the patients present with moderate to severe anemia pre-operatively, it is necessary to transfuse them to bring their Hb to acceptable levels, usually ≥ 10 g/dl. More importantly, it is desirable to reduce the Hb S concentration to ≤ 30% to prevent vaso-occlusive crisis or acute chest syndrome during or soon after surgery. This was easily achieved by repeated top-

up packed RBC transfusion over a period of two to three weeks. Alternatively, exchange blood transfusion was done in some of patients.

The choice of surgery in this series was open laparotomy. The post-op period was uneventful in all cases and no complications were recorded. The patients were discharged usually on the third or fourth post op day. The main long-term complication of splenectomy is predisposition to severe bacterial infections, especially in the first few months but may be life-long[14,15]. For this reason all our patients were vaccinated against pneumococcus and *H. influenzae* type B, at least two weeks before surgery. Post-op, they were put on prophylactic penicillin, either orally or by monthly intramuscular injection. So far we have not had any episode of overwhelming sepsis in any of them.

The main benefit of the operation has been the fact that none of the patients has required further transfusion since the surgery. The patients with hypersplenism also always became much more active in the weeks and months after the surgery. They were more out-going and many showed a spurt in linear growth as found in other studies[16]. All these can be attributed to the increase in Hb levels.

One other surgical option in these patients is laparascopic splenectomy, which reduces the length of hospital stay, post-op pain and scarring[17,18]. This has recently been introduced in our center on selected patients. Also partial splenectomy has been tried in some other centers in an effort to preserve enough splenic tissue to provide adequate immune surveillance and prevent the bacteremia that may otherwise occur[19,20].

In conclusion, the two common acute splenic complications among Kuwaiti SCD patients are HS and ASS and both respond well to splenectomy. ASS is much more common among SS patients while HS is found mainly in SβThals.

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