CASE REPORT

POST-SPLENECTOMY SEPSIS IN THALASSEMIC PATIENTS

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Abstract. Thalassemia is the commonest hemoglobinopathy in Malaysia. Patients with thalassemia major are transfusion dependent, and a large proportion of them will require splenectomy. As this particular group of patients is immunocompromized, overwhelming sepsis is a recognized complication. We report a series of three patients who all developed intra-abdominal abscesses following splenectomy.

INTRODUCTION

Thalassemia is a heterogenous group of genetic diseases in which there is defective synthesis of one or more globin chains. In Malaysia, the prevalence of carriers with beta-thalassemia is estimated to be 3 to 5%, with another 5% with Hb E and alpha thalassemia (Jamal, 2004). Both beta-thalassemia major and Hb E beta-thalassemia account for a significant bulk of the health problems in Malaysia.

Although the majority of Hb E beta-thalassemia patients present as thalassemia intermedia, they are also those who behave like thalassemia major clinically. In view of this, they would require a splenectomy. Amongst the recognized complications of splenectomy are thrombocytosis and overwhelming sepsis. The risk of post-splenectomy sepsis in thalassemia major is increased 30 fold compared to the normal population (Singer, 1973). Although encapsulated organisms are commonly responsible, there is now an emergence of gram-negative bacillary sepsis. Prompt recognition and treatment of overwhelming post-splenectomy sepsis is important as the mortality rate for such infections may reach 50% despite intensive supportive measures.

CASE REPORT

Patient 1

AZ is an 11-year old girl, diagnosed with Hb E beta-thalassemia since the age of one year. She has required an average of two to three monthly blood transfusions and had a splenectomy at six years of age. Both pneumococcal and hemophilus vaccines were given four weeks prior to surgery. AZ was prescribed prophylactic penicillin. Desferrioxamine was begun only at age 7 years due to financial constraints. Unfortunately, she developed cardiomyopathy a year later. A central venous catheter was inserted and continuous intravenous desferrioxamine was administered.

She presented at the age of nine years with features of diabetic ketoacidosis; this episode was complicated by *Klebsiella* septicemia. AZ was managed supportively with regular insulin and parenteral antibiotics. Two years later, she presented with acute gastroenteritis and dehydration. She developed overt heart failure, and a chest x-ray showed evidence of left lower lobe pneumonia. AZ required inotropic support and was commenced on intravenous cefotaxime and metronidazole. Unfortunately, her fever was persistent and she developed severe epigastric pain. Ultrasound of the abdomen revealed multiple loculated fluid collections within the abdominal cavity, particularly over the splenic fossa, and an abscess over the left lobe of the liver. Percutaneous drainage was performed, and the aspirated pus grew *Klebsiella* species, which was sensitive to amoxicillin, cefuroxime and ciprofloxacin. Following drainage, both her fever and abdominal pain resolved. AZ was treated with both ciprofloxacin and metronidazole for a total duration of one month.

Patient 2

SH is a 22-year old girl, diagnosed with Hb E beta-thalassemia since the age of two years. She has required an average of two to three monthly blood transfusions and underwent splenectomy at the age of 11 years. A pneumococ-

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cal vaccine was given prior to surgery and penicillin was started following surgery as prophylaxis. SH developed hepatitis C infection (genotype 1a) at the age of 19 years; the initial HCV RNA load was 3,307 IU/ml. She was treated with subcutaneous interferon and ribavirin, however, treatment was switched to pegylated interferon six months later as there was no response (RNA load 10,727 IU/ml) and after a year of therapy, the HCV RNA load declined to <600 IU/ml.

At 21 years, SH presented with four days history of high grade fever associated with diarrhea. Physical examination revealed that she had acute tonsillitis. Intravenous crystalline penicillin was initially started but as the fever did not resolve, intravenous cefuroxime and gentamicin were begun. SH developed localized right hypochondrium pain four days later and a clinical diagnosis of acute cholecystitis was made. Blood investigation showed leukocytosis (WBC 36.2 x 10^9/l with 77% neutrophils), and the liver function test was normal. Ultrasound of the abdomen confirmed that she had cholelithiasis and multiple hepatic abscesses. Following this, she was started on intravenous metronidazole and ciprofloxacin. Repeat blood cultures were all negative. SH was treated conservatively, for a total of four weeks with both metronidazole and ciprofloxacin. A repeat ultrasound showed resolution of the abscesses.

Patient 3

MF was diagnosed as having Hb E beta-thalassemia since the age of 3 years. He was only started on regular blood transfusions at age of 6 years, so his growth was affected. His hemoglobin then ranged from 6 to 8.4 g/dl and he required 4 to 6 weekly transfusions. He underwent splenectomy at the age of 11 years. Two months prior to surgery, he received both a pneumococcal and hemophilus vaccination. Following splenectomy, he was started on prophylactic penicillin. MF was started on desferrioxamine the same year; his serum ferritin then was 1,712. Following splenectomy, his transfusions declined to once in every 4 months.

He presented at 6 months following splenectomy with high grade fever, abdominal pain and vomiting. Clinically he was dehydrated and hypotensive; there were bilateral pleural effusion and ascites. There was hepatomegaly (4 cm) and tenderness over the right hypochondrium and lumbar region. He was resuscitated with intravenous fluids and a noradrenaline infusion was commenced. Both ceftriaxone and metronidazole were started. MF had leukocytosis, with a total white cell count of 27.5 x 10^9/l with 80% neutrophils and his liver function test was however normal. Ultrasound of the abdomen showed a hepatic abcess in segment 6. His temperature continued to fluctuate and after five days the ceftriaxone was changed to ciprofloxacin. Blood cultures grew *Klebsiella* species, which was sensitive to both cefuroxime and cefobid. MF was treated for a total of 2 weeks with ciprofloxacin and 4 weeks of metronidazole. Repeat ultrasound showed resolution of the abscess.

DISCUSSION

A major long term risk following splenectomy is overwhelming sepsis. In a literature review involving 19,680 post-splenectomy patients by Bisharat *et al* (2001), the overall incidence of infection following splenectomy was 3.2%, with a mortality rate of 1.4%. Of these, the incidence was highest in patients with thalassemia major (8.2%). The mortality rate in this group was also higher (5.1%). Not surprisingly, the mortality rate was highest in the pediatric population.

Encapsulated organisms, such as *Streptococcus pneumoniae* and *Haemophilus influenzae* are the commoner organisms involved, however, there is increasing evidence of overwhelming sepsis secondary to gram-negative bacilli. A possible explanation is that vaccination prior to splenectomy and the use of penicllin prophylaxis has successfully prevented the occurrence of streptococcal infection. Ghosh *et al* (2000) reviewed a series of 46 thalassemic patients who had undergone splenectomy. Amongst this particular group, all overwhelming infections were caused by gram-negative bacilli, such as *Klebsiella, Pseudomonas, Aeromonas* and *Campylobacter*. In another study by Ejstrud *et al* (2000), of 538 splenectomized patients, enterobacteria was the predominant organism (45%) following the post-operative period (the first 30 days following splenectomy). Jackson *et al* (1997) reported another case of a 35-year old man with Hb E beta-thalassemia who had fatal septicemia secondary to *Campylobacter jejuni*.

In our series, *Klebsiella* spp was cultured in both patients 1 and 3. Although there was no

positive culture in patient 2, there is still a possibility that the causative organism may be gram negative as the infection originated within the hepatobiliary tract. In patients with Hb E beta-thalassemia, cholelithiasis is a recognized complication. Gall stones are seen in up to 50% of these patients on ultrasonography. Ascending cholangitis may occur and this may be complicated by the development of hepatic abscesses. In view of this, the practise of performing elective cholecystectomy during surgery for splenectomy has been adopted in certain centers. However, in our series, none of the patients had undergone elective cholecystectomy.

Despite the apparent change in etiological organisms, preventative measures are still essential; immunoprophylaxis and chemoprophylaxis should still be carried out. Vaccination for both *Streptococcus* and *Haemophilus* is ideally administered between four to six weeks prior to surgery. As for penicillin prophylaxis, although the duration is still debatable, many clinicians, including the Hematology and Oncology Task Force (Davies *et al*, 2002) advocate its use for life. The risk of overwhelming post-splenectomy infection (OPSI) is highest during the postoperative period. However, in a study of 42 episodes of OPSI by Waghorn and Mayon-White (1997), OPSI was reported in a patient up to 59 years post-splenectomy. This finding would appear to favor the lifelong use of prophylactic penicillin, although one still needs to bear in mind the type of causative organism. In view of this recommendation, compliance to antibiotics is naturally a problem. Keenan *et al* (1999) showed that only 42% of splenectomized patients were compliant. Reinforcing patient education is, therefore, an important aspect of management. In our series, overwhelming sepsis was seen at 3 years, 11 years, and 6 months post-splenectomy in patients 1, 2, and 3, respectively. All three were on penicillin prophylaxis, although their compliance is debatable. Patient 2 received only a pneumococcal vaccination as the hemophilus vaccine was not readily available then.

OPSI should be considered as an emergency. It necessitates prompt treatment with broad spectrum parenteral antibiotics, particularly with the emergence of gram-negative sepsis. The choice of empiric therapy may vary with each center. Guidelines should be established for each center, taking several factors into account: local microbial and resistance patterns, possible occupational exposure and use/compliance to prophylactic antibiotics. In our series, all three patients were empirically administered broad spectrum antibiotics in the form of parenteral cephalosporins. In addition anaerobic coverage (metronidazole) was also given to patients 1 and 3. Following sensitivity reports, the antibiotics were then changed accordingly.

As the risk for overwhelming infection is lifelong, measures should be taken to keep its occurrence to a minimum. Certain reports have recommended re-vaccination with pneumococcal polyvalent vaccine after five years, based on the monitoring of antibody titers. Self-prescribed antibiotics may also be administered in certain groups of patients. Others have also suggested the use of intravenous immunoglobulin during such episodes. Although all these measures may be considered in the overall management, the most important measure is to remain vigilant and institute prompt treatment in cases with suspected OPSI.

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