Refresher Course

The Outcomes Following Splenectomy For Thalasemic Children

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Indications for Splenectomy

Splenectomy is indicated in the management of patients who have severe thalassemia, increasingly require blood transfusions, have massive splenomegaly with hypersplenism causing leukopenia, thrombocytopenia or who suffer from recurrent severe pain due to infarction caused by the massive spleen size.[1,2] Modell et al[3,4] observed the annual blood requirement among patients with thalassemia major and suggested that the spleen be removed if the observed requirement exceeded that predicted by more than 50 percent. However, the decision to remove the spleen must take several factors into consideration. The spleen serves both as a scavenger of increasing red cell destruction and as a redistributor of iron. It acts as a storage depot of sequestering and releasing iron.[1] Because the spleen acts primarily as a storage depot for excess iron, premature removal could theoretically be detrimental.[1] However, the iron storage property of the spleen has to be balanced with the iron loading effect that is developed by frequent transfusions due to hypersplenism.[5] The benefits of splenectomy for the balance of iron are realised if the transfusion requirement exceeds 200 to 250 mL of packed red cells/ kg/ year.[5,6]

Haemoglobin H disease usually does not require a specific therapy. Although splenectomy may be of value in Haemoglobin H associated with severe anaemia and splenomegaly,[7] splenectomy for the condition may be followed by a higher incidence of thromboembolic phenomenon than that which occurs in splenectomised children with B thalassemia.[8]

Surgical Outcome

In an experienced unit, the hospital mortality of splenectomy is now less than 1 percent.[9] The most common postoperative complication is bleeding. If bleeding fails to subside when coagulation defects have been corrected, the abdomen must be re-explored, which is necessary in 1.6 percent of cases.[9] The other complications include fever, mild pancreatitis, chest or wound infection and intra-abdominal abscess.[2]

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Recurrence of the severe symptoms, requiring splenectomy, may occur because of a retained accessory spleen. Accessory spleen is noted in approximately 25 percent of autopsy cases in the following locations: the hilum of the spleen, tail of pancreas, omentum, or in the lienorenal or gastrosplenic ligaments of the spleen. In cases where the accessory spleen is left inside after splenectomy, it may show hypertrophy and clinically manifest as hypersplenism. This phenomenon can occur as late as 25 years after splenectomy.[10,11] Because of the possibility that these conditions will occur, partial splenectomy[12] and splenic embolization for thalassemia major are not advised. In partial splenectomy, the protective effect of the remaining spleen could not be exactly determined.[12] Apart from the possibility of symptomatic recurrence, splenic embolization can also result in several complications including fever and pain, perisplenic fluid collection, pleural effusion, splenic rupture and splenic abscess formation.[13]

Perioperative Anaesthetic Outcome

"Post-transfusion Hypertension, Convulsion and Cerebral haemorrhage Syndrome" (HCC Syndrome) may occur following blood transfusion in thalassemic patients.[14-16] Although HCC syndrome is well recognised, the cause of perioperative hypertension that occurs in splenectomised patients who do not receive any transfusions is still unknown. This association between thalassemia and hypertension could be the result of vasodilator nitric oxide (NO) being trapped by haemoglobin.[17] Since intraoperative and postoperative hypertension may lead to more serious neurological complications, careful haemodynamic monitoring must be considered for all thalassemic children undergoing general anaesthesia for splenectomy.[18] The reduction of the circulatory volume with furosemide cannot prevent hypertension occurring during the perioperative period.[19]

Pulmonary complications following splenectomy are not uncommon. Pulmonary atelectasis resulting from hypoventilation of the left lower lobe may be treated effectively by chest physiotherapy.[2] Pulmonary micro-thromboembolism is also another serious complication found in thalassemic patients following splenectomy.[20]

Haematological Outcome

The major haematological effect of splenectomy is an increase in platelet counts, which can be observed during the first two weeks after the operation.[21] Platelet counts greater than $10^6/mm^3$ and sometimes exceeding $10^9/mm^3$ are often seen. The correction of anaemia by transfusions usually results in the suppression of platelet production.[22] Because the spontaneous platelet aggregation can occur,[23,24] and because it may exacerbate thromboembolic problems following splenectomy,[25-27] the use of low dose aspirin or dipyridamole has been proposed.[25] However, in many large series, none of thalassemic children developed acute thrombosis. There are no definite guidelines for antiplatelet therapy after splenectomy except in rare cases in which thrombocytosis persists.[27]

Red cell survival usually increases immediately after splenectomy.[28] The blood films of splenectomised patient show a number of red cell changes that persist for many years. Those changes include the presence of Howell-Jolly bodies, nucleated red cells, reticulocytosis and target cells.[2] White cell counts of 15,000 to 20,000/ mm^3 are common and the differential count is usually normal.[1]

Mean haemoglobin levels rise following splenectomy.[29] Most patients achieve a moderate, but significant, reduction in blood transfusion requirement to the predicted 200 mL of packed red cells/ kg/ year[3,4,29] and remain stable over many years.[30]

Immunological Outcome

The major long-term concern in splenectomised patients is the risk of serious infection. It was first noted in 1919 that splenectomised rats showed decreased resistance to infection.[31] In 1952, attention was focused on that problem in humans.[32] Such infections may be fulminant with disseminated intravascular coagulation, multiple organ failures, and severe hypoglycaemia preceding rapid death. The term "overwhelming postsplenectomy

infection"(OPSI) has been used to describe this clinical syndrome. Because the removal of the spleen may blunt the primary immune response to encapsulated organisms, delay of splenectomy until older than five years is preferable.[1]

The incidence of OPSI is currently reviewed by Holdsworth et al.[33] From 5,902 splenectomies, the overall incidence of severe infection was 2.9 percent, with a death rate of 1.5 percent. The incidence of the infection in children under the age of 16 years was 4.4 percent, with a mortality rate of 2.2 percent, whereas in adults the figures were 0.9 percent and 0.8 percent, respectively. The highest incidences of severe infection and death were observed in infants (15.67 percent and 6.7 percent respectively), but the risks were also high in children under five years, at 10.4 and 4.5 percent, respectively. Patients undergoing splenectomy for Hodgkin's disease or for thalassemia have higher incidences of infection and death than patients who are splenectomised for other conditions.[2,33]

The majority of the serious infections in splenectomised patients are due to encapsulated bacteria. The most common of those is *Streptococcus pneumonae* (pneumococcus), which is responsible for 50-60 percent of cases. *Haemophilus influenzae* type b and *Neisseria meningitidis* account for another 25 percent. The remainder is caused by *Escherichia coli*, other species of Streptococcus, *Staphylococcus aureus*, Klebsiella species, Salmonella species and *Pseudomonas aeroginosa.*[33,34] Vaccination against these organisms, which is now currently available for the pneumococcus, *H influenzae*, and the meningococcus, is recommended for all patients undergoing splenectomy,[35-37] ideally at least two weeks prior to surgery in order to ensure an optimum antibody response.[38]

The current pneumococcal vaccine (Pneumovax III) is polyvalent and contains purified capsular polysaccharides from the 23 most prevalent serotypes of *Streptococcus pneumonae*. Although the vaccination in young children or immunocompromised patients produces less positive responses than from healthy adults, a level of protection is still afforded by this vaccine. However, the safety and efficacy for children under two years of age remains to be established.[38] Antibody levels in children receiving vaccination after splenectomy are lower than those with intact spleens.[39] The levels of the specific antibody decline overtime and current guidelines suggest re-vaccination every 5-10 years.[38] However, there are well-documented cases of pneumococcal infection occurring in patients who have been immunised.[40]

It is also recommended that children undergoing splenectomy should receive *H. influenzae* type b (HIB) vaccine preoperatively if they have not already been immunised.[2,41,42] The vaccine may be given at the same time as Pneumovax.

The current meningococcal vaccine (Mengivac) provides protection against only meningococcus group A and C strains. Because the majority of meningococcal infections are caused by the group B strain, effective protection against this pathogenic meningococcus cannot be obtained from this vaccine. It is therefore unclear whether children undergoing splenectomy should be routinely vaccinated with this vaccine.[2]

Because of the uncertain protection provided by the current vaccines, prophylaxis antibiotics are also recommended for splenectomized patients.[40,43,44] The recommended antibiotic is penicillin. Although amoxycillin has also been recommended by some authorities, in view of increasing reports of pneumococcal resistance to penicillin[45] and broader antibacterial spectrum drugs, it still may not cover *H. influenzae* reliably. Erythromycin should be offered to children allergic to penicillin. How long penicillin prophylaxis should be continued is still debated.[2,45] The fact that the continued risk of OPSI appears to be lifelong supports the policy for lifelong penicillin prophylaxis.

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