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Partial splenectomy in children with sickle cell disease

Partial splenectomy was performed in 50 patients with sickle cell disease and acute splenic sequestration. Follow-up after surgery ranged from 2 to 14 years. During this period no recurrence of splenic sequestration crisis occurred and the quality of life of these children has improved.

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Acute splenic sequestration (ASS) is a well recognized complication in children with sickle cell disease (SCD) under 5 years old and a significant cause of morbidity and mortality.[1,2] The classical treatment of this crisis is total splenectomy but this procedure often carries the risk of fulminant septicemia.[3] For this reason we performed elective partial splenectomy in SCD patients with more than one episode of ASS.

We report the follow-up on the 50 children (Hb SS 43 and HbS/βthal 7) with SCD who underwent partial splenectomy. All had experienced more than one episode of ASS, defined as a fall in the hemoglobin (Hb) level of more than 2 g/dL from the baseline concentration, associated with an enlarged spleen and evidence of bone marrow erythroid activity.[1] Partial splenectomy was performed using a previously described technique.[4] Hematologic data were obtained in steady state according to standard methods.

Table 1. Clinical events in patients with SCD who had partial splenectomy.

Events	Before surgery Mean	Before surgery SD	After surgery Mean	After surgery SD	p
Hospitalizations	5.77	3.63	3.07	3.21	0.01
Transfusions	6.25	4.39	0.60	1.12	0.01
Infections	1.65	2.25	0.98	1.75	0.13

Table 2. Hematologic parameters in patients with SCD who had a partial splenectomy.

Tests	Before surgery N. patients	Before surgery mean	Before surgery SD	After surgery N. patients	After surgery mean	After surgery SD	P
Hemoglobin (g/dL)	49	6.0	1.3	50	7.7	2.0	0.01
Reticulocytes (%)	49	138.6	88.8	47	129.3	74.3	0.39
Leukocytes (10^9/L)	50	13.7	1.5	50	12.8	3.3	0.59
Platelets (10^9/L)	50	228.0	105.6	50	408.5	146.5	0.01
Pitted red cells (%)	20	4.9	1.7	33	3.7	2.9	0.07

To measure the functional capacity of the spleen, the percentage of pitted red cells was determined by the method of Pearson.[5] Splenic function was also evaluated by radionuclide scan with ^{99}Tc sulfur colloid. Student t test was used to compare clinical and hematological data before and after splenectomy. After the operation the children were followed at our clinic at intervals of one-to-three months. No prophylaxis was given prior to January 1989. Afterwards oral penicillin was given to all patients for 3 years after the operation. Pneumococcal vaccine was not used. The median age at the time of surgery was 3 years (1-9) and the median and mean duration of follow-up were 9 years (range 2-14), and 8.3 years (SD±3.7).

Immediate postoperative morbidity was limited to fever of unknown origin in 10 patients, wound infections in 5 and pneumonia in 3 children. No episode of ASS has been observed during the post-surgical follow-up. There was a significant reduction in requirements for blood transfusions and a decrease in the number of hospitalizations (Table 1). No patient died during the post-surgical follow-up. One patient developed overwhelming septicemia. Hematologic data before and after surgery are shown in Table 2. The mean hemoglobin concentration and platelet counts were significantly increased after surgery.

There was not significant difference in the percentage of pitted red cells before and after the operation. The postoperative spleen scans showed the presence of the splenic remnant in 13 of 20 children. Total splenectomy exposes the patient to the threat of overwhelming septicemia.[3] The incidence of this complication is higher in younger children with SCD (those less than five years of age) and reported to be about 7% with high mortality.[6] Our data show that preservation of a part of the spleen can provide protection against serious infections. Although in SCD there is a splenic dysfunction it is reasonable not to perform total splenectomy because reticuloendothelial activity persists, as demonstrated by the return of splenic function to normal by transfusion not only in young children[5] but also in adults.[7] Pitted red cell counts are a reliable marker for splenic function. The mean pitted red cell count in our patients

post-splenectomy was 3.5±4.3% which is higher than the values in normal subjects (below 2%) and much lower than those found in SCD patients after total splenectomy (more than 20%). These results imply significant preservation of splenic function in our patients. No recurrence of ASS occurred after the operation. Admissions to hospital and transfusion have been reduced and the quality of life of these children and their parents has improved. There were also increases in hemoglobin levels and platelet counts, and these findings may be explained by the fact that the children with the largest spleens and recurrent ASS also have hypersplenism. Only one case of severe infection occurred.[8] We believe that partial splenectomy is a good option for the treatment of ASS in SCD.

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Rituximab chimeric anti-CD20 monoclonal antibody treatment for refractory hemolytic anemia in patients with lymphoproliferative disorders

We administered rituximab monoclonal antibody to five patients suffering from a lymphoproliferative CD20-positive disease associated, at diagnosis or after starting treatment, with autoimmune hemolytic anemia (AIHA). After treatment with rituximab we observed an improvement of AIHA in all cases, and, in one case, improvement of the autoimmune thrombocytopenia associated with the AIHA. There were no relevant side effects.

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About 7-10% of lymphoproliferative disorders (LD) can be complicated by an autoimmune hemolytic anemia (AIHA). In some LDs, this condition is related to the production, by the neoplastic clone, of an antibody reactive against autologous red cell antigens, and is usually refractory to steroids and immunosuppressive agents.[1-3] Otherwise, the complication can be due to an imbalance in immune regulation. Often, an unknown, indolent LD can present with AIHA; alternatively, AIHA can precede a LD by a long time.

In this paper we present 5 cases of LD complicated by AIHA, that we treated successfully with an anti-CD20 monoclonal antibody (Rituximab-Mabthera®, Roche, Milan, Italy) resulting in a clinical improvement of both the AIHA and of the LD.

We treated 5 patients affected by LD with AIHA (Table 1): 2 had large-B cell non-Hodgkin's lymphoma (LBC-NHL); 2 had B-chronic lymphocytic leukemia (B-CLL) and 1 had B-prolymphocytic leukemia (B-PLL). At LD diagnosis all patients showed ≥ 27% of $CD20^+$ cells infiltration at cytofluorimetric analysis of bone marrow; in all cases, a warm autoantibody was detected. In 2 cases AIHA was the first sign of a LD, while in the other 3 patients it developed during the treatment of the LD. The diagnosis of AIHA was made as follows: decrease of the hemoglobin (Hb) levels, increase of serum lactate dehydrogenase (LDH) levels, increases of indirect and direct bilirubin levels and positivity of the direct and/or indirect antiglobulin test (DAT/IAT). Two patients had a low platelet count ($<100\times10^9$/L) before the rituximab treatment. An antiplatelet antibody was found in one of these two patients; in the other patient the serum test resulted negative. None of our patients had a monoclonal antibody related to production by the neoplastic clone. All patients received first line treatment for LD. Three were treated with CHOP (vincristine, cyclophosphamide and doxorubicin), 1 patient with MACOP-B (methotrexate, doxorubicin, cyclophosphamide, vincristine, bleomicin), and 1 patient with Codox-M (cyclophosphamide, vincristine, doxorubicin, cytarabine, methotrexate). The median time from chemotherapy to rituximab administration was 3 months (range 1-36).

Since none of the patients achieved a stable improvement of AIHA, all patients started immunotherapy with rituximab. The schedule of administration of rituximab was four courses of 375 mg/m^2/weekly. Response to treatment was evaluated by the improvement of the parameters of hemolysis, such as decrease in bilirubin, LDH, Hb levels, and negativization or improvement of DAT/IAT (Table 2). All patients showed a recovery from AIHA, already after the second administration of rituximab; in 3 cases AIHA recovery was associated with a complete remission (CR) of LD.

Only one patient suffered from an infusion-related reaction to rituximab, consisting in chills and fever. As of June 2002, 3 patients are still alive in 1st CR (median overall survival 8 months; range 8-20) and have not so far shown any relapse of the LD or AIHA.

Another patient, whose AIHA improved, had persistent