Indications and outcomes of splenectomy for hematological disorders

Abstract: Background and Aim: Splenectomy is a frequent component of the diagnosis and treatment of hematological disorders. The aim of this study was to define the indications and outcomes of splenectomy for benign and malign hematological disorders.

Materials and Methods: One hundred and two patients with hematological disease who had splenectomy at Hacettepe University Hospital between the years of 2010 and 2018 were evaluated.

Results: A total of one hundred and two patients were included in this study. The median age was 52 (20-82) years at the time of splenectomy. Most of the patients were female (57.9%). The median follow up time was 11.0 (0.03-87.9) months after splenectomy. Splenectomy was performed to diagnose thirty patients (29.4%). Seventy-two patients underwent splenectomy for the treatment of hematological disease (70.6%). Twenty-seven patients (90%) were diagnosed with various lymphomas. Two patients (6.7%) were diagnosed with hairy cell leukemia and one patient (3.3%) was diagnosed with large granular lymphocytic leukemia.

Conclusion: In conclusion, an improvement in medical therapy, especially with monoclonal antibodies, the indications and outcomes of splenectomy for hematologic disorders have changed extremely in last years. Nevertheless, splenectomy has an important role for diagnosis and treatment of benign and malign hematological disorders.

Keywords: Hematological disorders; splenectomy; idiopathic thrombocytopenic purpura

1 Introduction

Spleen is a lymphoid organ that has hematopoietic and immune functions. Splenectomy is a frequent component of the diagnosis and treatment of hematological disorders. Benign and malign hematological disorders compose the major indication for elective splenectomy [1]. Splenectomy is a standard and effective treatment modality for patients with recurrent, refractory, or chronic diseases for which drug treatment fails or is unable to cure [2]. After the failure of medical therapy, splenectomy is indicated for the red blood cells disorders and a variety of thrombocytopenic disorders. Splenectomy is also successful in reversing hypersplenism in myeloproliferative disorders. In the treatment of leukemia and lymphoma, indications and benefits of splenectomy are limited [3]. The aim of this study was to define the indications and outcomes of splenectomy for benign and malign hematological disorders. Herein we report a retrospective study of our experience with patients who underwent splenectomy for the diagnosis and/or treatment of benign and malign hematological disorders.
2 Materials and methods

2.1 Study design and data collection

This study has been performed in a retrospective manner. Demographic data of the patients and treatment regimen were obtained from hospital database. As a result of application standards of the hospitals of Hacettepe Medical School, it has been recognized from the patient records that all of the studied patients had given informed consents at the time of hospitalization and before the administration of relevant diagnostic/therapeutic standards of care. Patients gave informed consent for the procedure.

Ethical approval: All of the ethical considerations had been strictly followed in accordance with the 1964 Helsinki declaration.

2.2 Patients and disease characteristics

One hundred and two patients with hematological disease who had splenectomy at Hacettepe University Hospital between the years of 2010 and 2018 were evaluated. The inclusion criteria were: patients ≥18 years of age with splenectomy for hematological benign or malign disorders. Our preparation protocol for elective splenectomy required all patients to have received polyvalent pneumococcal vaccine, meningococcal vaccine and Haemophilus influenzae vaccine, at least 3 weeks before splenectomy. All patients were covered prophylactically with oral penicillin after splenectomy.

2.3 Statistical analysis

Statistical analyses were performed using the SPSS software version 25. The variables were investigated using visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk’s test) to determine whether they are normally distributed or not. Statistical comparisons were made using Chi-square for categorical data. Student t-test (for two independent samples) was used for comparison of continuous numerical data. Values of \( p < 0.05 \) were considered statistically significant.

3 Results

3.1 Patient characteristics

A total of one hundred and two patients were included in this study. Median age was 52 (20-82) years at the time of splenectomy. Most of the patients were female (57.9%). Median follow up time was 11.0 (0.03-87.9) months after splenectomy. Splenectomy was performed to diagnose thirty patients (29.4%). Seventy-two patients received splenectomy for the treatment of hematological disease (70.6%) as shown in Figure 1. All patients who underwent diagnostic splenectomy were diagnosed (100%). Twenty-seven patients (90%) were diagnosed with various lymphomas as shown in Figure 2. Two patients (6.7%) were diagnosed with hairy cell leukemia (HCL) and one patient (3.3%) was diagnosed with large granular lymphocytic (LGL) leukemia. The baseline clinical and demographic characteristics of patients are listed in Table 1.

3.2 Response to splenectomy

Hemoglobin levels of the patients with autoimmune hemolytic anemia, thalassemia, sickle cell anemia and hereditary spherocytosis increased after splenectomy as shown in Figure 3. Of thirty-nine patients with idiopathic thrombocytopenic purpura (ITP) thirty-eight (97.4%) patients responded to splenectomy (PLT level >100x10^9/L) and only one patient (2.6%) did not respond to splenectomy. Thrombocyte levels before and after splenectomy are shown in Figure 4. Three patients with HCL, two patients with LGL leukemia, two patients with myelofibrosis (MF) had complete remission after splenectomy. Three patients had partial response after splenectomy and one patient died after splenectomy. Splenectomy was performed for the diagnosis in the majority of patients with lymphoma (69.2%). After splenectomy, six patients were diagnosed with follicular lymphoma (FL), two patients with diagnosed hepatosplenic T cell lymphoma (HSTCL), one patient with peripheral T cell lymphoma (PTCL), nine patients with diffuse large B cell lymphoma (DLBCL) and nine patients with splenic marginal zone lymphoma (SMZL). Twelve patients (30.8%) with lymphoma were submitted for splenectomy for the treatment of the disease. After splenectomy one patient with Hodgkin lymphoma, two patients with DLBCL and two patients with PTCL had complete remission. However, following splenectomy two patients with DLBCL and two patients with PTCL had progressive disease. One patient with FL had complete...
remission, and one patient with FL had partial response after splenectomy. In fifteen patients (14.7%) post-splenectomy infection developed. Hematoma was observed in one patient (0.9%) and thrombosis was observed in three patients (2.9%) after splenectomy. Five patients (4.9%) died due to complications within 2 months post-splenectomy and four patients died because of infectious complications. One patient died after splenectomy because of thrombosis.

The mean ages of the patients who underwent splenectomy showed statistically significant difference according to the diagnosis (p<0.001). The gender of the patients who underwent splenectomy was similar according to the diagnosis (p=0.77). Pre (p<0.001) and post-splenectomy (p<0.001) hemoglobin (HB) levels, pre-splenectomy white blood cells levels (WBC) (p=0.003), pre (p<0.001) and post-splenectomy platelet (PLT) (p=0.001) levels were statistically significant different according to the diagnosis as shown in Table 2. Only post-splenectomy WBC levels were not statistically significant different in all patients with various hematological disorders (p=0.15).

| Parameters | Splenectomy for diagnosis | Splenectomy for treatment |
|------------|---------------------------|---------------------------|
| N (%)      | 30 (29.4%)                | 72 (70.6%)                |
| Gender (male/female) | 15/15 (50%/50%)          | 28/44 (38.9%/61.1%)       |
| Age (range) | 56 (27-82)                | 46 (20-80)                |
| ECOG PS    |                           |                           |
| ECOG PS 0  | 23 (76.6%)                | 58 (80.5%)                |
| ECOG PS 1  | 3 (10%)                   | 3 (4.1%)                  |
| ECOG PS 2  | 4 (13.4%)                 | 5 (6.9%)                  |
| ECOG PS 3  | 0                         | 6 (8.3%)                  |
| Charlson comorbidity index |               |                           |
| 0          | 6                         | 34                        |
| 1-2        | 14                        | 22                        |
| 3-4        | 9                         | 13                        |
| ≥5         | 1                         | 3                         |
| Hematological disease (%) |               |                           |
| Lymphoma   | 27 (90%)                  | 12 (16.6%)                |
| Hairy cell leukemia | 2 (6.7%)     | 1 (1.4%)                  |
| Large granular lymphocytic leukemia | 1 (3.3%) | 1 (1.4%)                  |
| Hereditary spherocytosis | 0           | 1 (1.4%)                  |
| Idiopathic thrombocytopenic purpura | 0           | 39 (54.2%)                |
| Autoimmune hemolytic anemia | 0           | 9 (12.5%)                 |
| Sickle cell anemia | 0           | 1 (1.4%)                  |
| Thalassemia | 0                         | 2 (2.8%)                  |
| Myelofibrosis | 0                        | 6 (8.3%)                  |
| Splenectomy related complications (%) | |                           |
| Hematoma    | 0                         | 1 (1.4%)                  |
| Infection   | 5 (16.7%)                 | 10 (13.9%)                |
| Thrombosis  | 0                         | 3 (4.2%)                  |
| Splenectomy related mortality (%) | 0           | 5 (6.9%)                  |

Abbreviations: N: number of the patients; ECOG PS: ECOG Performance Status
Discussion

Splenectomy plays a role in the diagnosis and treatment of many hematological diseases. With the improving of the advent of monoclonal antibody treatment, the indications and outcomes of splenectomy for benign and malignant hematological diseases have changed in recent years [1]. Nevertheless, splenectomy has its place in hemoglobinopathies and hemolytic diseases. It improves thrombocytopenia in refractory ITP, can reverse symptoms linked to splenomegaly secondary to MF, and can be used for diagnostic and treatment purposes in lymphoproliferative diseases [1].

In this study, we retrospectively evaluated patients who underwent splenectomy for hematological diseases. Most patients had splenectomy for the treatment of hematological disease. Fewer patients had splenectomy for diagnosis of hematological disease. All patients who underwent diagnostic splenectomy were diagnosed.

Post-operative complications such as hematoma, thrombosis and infection were observed in nineteen patients. Post-operative mortality was observed in five patients who underwent splenectomy for the treatment.

Cases of splenectomy for various hematological diseases have been analyzed in the past literature. Kojouri et al. reported a 66% complete response rate after splenectomy. A complete response was defined as the achieve-
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ment and maintenance of a normal platelet count (at least $100 \times 10^9/L$) without additional ITP treatment [4]. Patel et al. reported the effect of splenectomy in patients with ITP refractory to medical treatment and AHA. In the ITP group ($n=45$), 91% of the patients had complete response within a median period of 51 days and in the AHA group ($n=15$), 93% of the patients had complete response within a median period of 172 days after splenectomy [5]. Two other studies showed that splenectomy is a potent treatment modality for symptomatic patients with SMZL [6, 7]. Subbiah et al. showed that all patients with LGL in their analyses had hematologic response and achieved transfusion independence after splenectomy [8]. Another study showed that a significant continuous fall in annual blood transfusion requirement and a rise in platelet counts occurred post-splenectomy in thalassemia patients [9].

Infection is a common complication of splenectomy, as the spleen has a major role in eradicating infections from the body. Bisharat et al. reported that the incidence of infection after splenectomy was 3.2% with a mortality rate of 0.9% [10]. Our study had a few limitations. Firstly, the study was retrospective and secondly the diagnosis of the patients were heterogeneous. Additionally, the sample size was small. In conclusion, an improvement in medical therapy, especially with monoclonal antibodies, the indications and the outcomes of splenectomy for hematologic disorders have changed extremely in last years. Nevertheless, splenectomy has an important role in hemoglobinopathies and hemolytic diseases, as it improves thrombocytopenia in refractory ITP, can reverse cytopenia and symptoms related to splenomegaly secondary to MF, or can be used for diagnostic purposes or for splenomegaly in lymphoproliferative diseases.

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### Table 2. Demographic characteristics and laboratory results of 102 patients with hematological disorders who underwent splenectomy

| Parameters | Lymphoma | HCL | LGLL | HS | ITP | AIHA | SCA | Thalassemia | Myelofibrosis | P |
|------------|----------|-----|------|----|-----|------|-----|-------------|---------------|---|
| N          | 39       | 3   | 2    | 1  | 39  | 9    | 1   | 2           | 6             | <0.001 |
| Ages±SD    | 57±15    | 53±8| 33±6 | 61 | 40±14 | 59±15 | 31  | 36±10       | 63±11         | <0.001 |
| Sex (M/F)  | 18/21    | 2/1 | 0/2  | 0/1| 15/24 | 4/5  | 1/0 | 1/1         | 2/4           | 0.77 |
| Pre-splenectomy HB (g/dL)±SD | 10±1.9 | 11.1±1.7 | 9.8±1.7 | 8.9 | 12.7±2.1 | 8.1±2.2 | 10.1 | 8.1±1.5 | 8.6±1.0 | <0.001 |
| Post-splenectomy HB (g/dL)±SD | 10.3±1.9 | 10.8±2 | 12.3±0.2 | 9.9 | 12.5±1.9 | 11.5±1.5 | 12.6 | 10.1±1.8 | 9.9±2.1 | <0.001 |
| Pre-splenectomy WBC (10^9/L)±SD | 5.7±1.2 | 7.5±9.1 | 1.3±0.6 | 6.3 | 10.6±4.0 | 6.8±2.8 | 11.4 | 9.3±4.3 | 6.9±6.6 | 0.003 |
| Post-splenectomy WBC (10^9/L)±SD | 11.4±6.3 | 5.9±4.3 | 13.1±10.3 | 18.7 | 14.3±6.8 | 11.7±3.6 | 9.2 | 22.4±2.1 | 15.8±14.2 | 0.15 |
| Pre-splenectomy PLT (10^9/L)±SD | 140±143 | 85±19 | 166±48 | 150 | 47.4±44.4 | 229±109 | 67  | 246±65 | 61.6±47.5 | <0.001 |
| Post-splenectomy PLT (10^9/L)±SD | 470±291 | 438±71 | 556±123 | 226 | 372±178 | 491±302 | 425 | 1270±217 | 278±417 | 0.001 |
| Splenectomy related mortality (%) | 4 (3.9%) | 0 | 0 | 0 | 0 | 0 | 1 (0.9%) | 0.12 |

Abbreviations: N: number of the patients; HB: hemoglobin; WBC: white blood cell; PLT: platelet
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