Case Report

Splenectomy in Primary Immune Thrombocytopenia (ITP)

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Abstract

Splenectomy represents an effective second-line therapy for the treatment of primary immune thrombocytopenia (ITP). The objective of surgery is to stop the bleedings by eliminating the organ responsible for the clearance of antibody-coated platelets. We evaluate the efficacy of laparoscopic splenectomy versus open splenectomy for primary immune thrombocytopenia in patients with severe refractory thrombocytopenia. We studied 56 patients with ITP hospitalized in the Clinic of Hematology from Craiova (Romania) between 2003-2012. All patients were diagnosed with ITP, other causes of thrombocytopenia having been ruled out. All patients were initially treated with corticosteroids ± immunoglobulins as first line therapy and vinca alkaloids and splenectomy as second-line therapy. Indications for splenectomy were bleedings and low platelet count (<30×10⁹/l) after corticosteroids/immunoglobulin/vincristine. Eleven patients from 56 had indications for splenectomy: Three patients received open splenectomy and eight laparoscopic splenectomy. Seven patients obtained a very good response after splenectomy, three patients obtained a good response and one no response after splenectomy. After three years from splenectomy, two patients relapsed (one due to accessory spleen). In conclusion, in our small cohort of patients, laparoscopic splenectomy seemed preferable to open splenectomy, reducing the level of patient discomfort, the postsurgical complications and the hospitalization period.

Keywords: Primary immune thrombocytopenia; Laparoscopic splenectomy; Open splenectomy

Introduction

Primary immune thrombocytopenia (ITP) is an autoimmune mediated disorder characterized by isolated immune mediated thrombocytopenia (ITP) with a peripheral blood platelet count less than 100 × 10⁹/l in the absence of any obvious initiating and/or underlying causes of thrombocytopenia [1-3]. In ITP pathogenesis two mechanisms of thrombocytopenia are involved: increased platelet destruction immune-mediated by autoantibodies and impaired platelet production. In the pathogenesis of disease dendritic cells, B cells, T helper cells and regulatory T cells are involved [4-6]. The activity of B cells and T helper cells is under control of regulatory T cells. The B cells that escape the T cells regulatory surveillance produce auto-antibodies directed against specific glycoproteins of platelet specific surface (GP IIb/IIIa and/or GP Ib-IX) and also against antigens present on megakaryocytes. The effects of these events are: early platelet destruction and phagocytosis by macrophages from spleen and liver and decreased platelet production. Deficiency of regulatory T cells probably determines the persistance of immune reaction [7].

The new consensus of the therapeutic modalities of ITP recommended as first line therapy at newly diagnosed patients with ITP are corticosteroids (prednisone, prednisolone, methylprednisolone, dexamethasone) which increase platelet count and have a direct effect on blood vessels, or high dose IV immunoglobulins. Second line therapy is surgical (splenectomy) or medical, including immunosuppressive/immunomodulatory agents (azathioprine, cyclophosphamide, vinca alkaloïds, cyclosporine, rituximab) or thrombopoietin receptor agonist (romiplostin and eltrombopag). Third line therapy includes the thrombopoietin receptor agonist as the only salvage therapy single or in combination with chemotherapy, alemtuzumab or stem cell transplantation [8-13].

Patients and Method

We studied 56 patients with ITP (informed consent obtained) hospitalized in the Clinic of Hematology from Craiova (Romania) between 2003-2012. All patients were diagnosed with ITP according to the guidelines of European/American Society of Hematology and other causes of thrombocytopenia were ruled out. Pseudothrombocytopenia (caused by EDTA dependent platelet agglutinines), drug-induced thrombocytopenia (patients with recurrent episodes of thrombocytopenia after drugs administration), HIV, hepatitis C infections, systemic lupus erythematous, lymphoproliferative disorders (immune-mediated thrombocytopenia, positive specific tests), thrombotic thrombocytopenia purpura (absence of microangiopathic anemia, fever, neurological and renal symptoms), congenital/hereditary thrombocytopenia (young patients who did not respond to treatment of ITP) were excluded.

At all patients, there were determined: patient/family history, physical examination, complete blood count and reticulocyte count, peripheral blood smear, bone marrow examination, quantitative immunoglobulin level; tests for H.pylori, HIV, HCV, antiphospholipoid antibodies, antithyroid antibodies/thyroid function, antinuclear antibodies, bleeding time, serum complement were made.

All patients were initially treated with corticosteroids (prednisone 1 mg/kg/day for several days to several months or high-dose dexamethasone 40 mg/day × 4 days ), two of them with high-dose intravenous immunoglobulin (IVlg) 1g/kg, 2 infusions over 2 days; one received Danazol orally at a dose of 200 mg three times daily; one received Azathioprine 150 mg/day and three slow perfusions with Vincristine.
The majority of patients responded to medical treatment, but 12 of them had refractory ITP. For the patients with bleedings (recurrent epistaxis, genitourinary hemorrhage, melena, gingival hemorrhage, ecchymoses) and low platelet count (<30×10^9/l) after corticosteroids/immunoglobulin/vincristine therapy indicated the need for splenectomy. One patient with ITP and diabetes mellitus received eltrombopag 50 mg/day. Three patients received open splenectomy and eight laparoscopic splenectomy. At least 2-4 weeks before surgery the patients received prophylactic polyvalent vaccines and oral high dose dexamethasone (40 mg/day for 4 days). The response after splenectomy was measured by the platelet count as following: very good response: platelet count >150×10^9/l, good response: platelet count between 150 - 50×10^9/l; no response: platelet count < 50×10^9/l. After discharge from surgical clinic, the patients were follow-up in the Clinic of Hematology.

**Results**

Of the 56 patients with ITP hospitalized in the Clinic of Hematology from Craiova, 11 patients (19.64%) were splenectomized; mean age was 36 years, F/M ratio = 2.66 (Table 1). Five patients had associated diseases: diabetes mellitus (two cases), ischemic heart disease (one case), arterial hypertension (two cases). All patients presented bleedings: recurrent epistaxis (four patients), genitourinary hemorrhage (two patients), melena (two patients), gingival hemorrhage (two patients), ecchymoses (one patient). The mean platelet count was 18×10^9/l. All patients received corticosteroids (prednisone/high-dose dexamethasone); in addition, two patients received IVIg and three vincristine, with no response. The patients with platelet count < 20×10^9/l received peripheral platelet transfusions. Three patients had undergone open splenectomy and eight laparoscopic splenectomy. Response after splenectomy was: very good in 7 cases (63.63%), good in 3 cases (27.27%) and no response in one case (9.10%). Two patients had postoperative complications: one - urinary tract infection (with open splenectomy) and one subphrenic abscess (with laparoscopic splenectomy). After a period of 2-4 years, two patients with splenectomy (18.18%) relapsed (one due to accessory spleen).

**Discussion**

Splenectomy represents an effective second-line therapy for the treatment of ITP with a rate of 70-90% of hematologic response at 2-4 years, two patients with splenectomy (18,18%) relapsed (one after laparoscopic splenectomy and one open splenectomy), one had a partial response (after open splenectomy), one did not respond after laparoscopic splenectomy.

At three years after splenectomy, eight patients showed a complete response (six with laparoscopic splenectomy and one with open splenectomy), one had a partial response (after open splenectomy), two patients relapsed (one after laparoscopic splenectomy and one after open splenectomy) and one no response (after laparoscopic splenectomy). In one case with relapse, surgical reintervention was made and an accessory spleen was discovered; in another case the patient received thrombopoietin receptor agonist with a favourable evolution.

In conclusion, the splenectomy should be considered a second line therapy in patients with refractory ITP at medical treatment. In our small cohort of patients, laparoscopic splenectomy seemed to be preferable to open splenectomy because it decreased blood loss, the

Table 1: Characteristics of patients splenectomized for refractory ITP.

<table>
<thead>
<tr>
<th>No</th>
<th>Age/sex [years]</th>
<th>Duration of disease [months]</th>
<th>First therapy</th>
<th>Plt count before splenectomy [×10^9/l]</th>
<th>Bleedings</th>
<th>Type of splenectomy</th>
<th>Response after splenectomy</th>
<th>Complications</th>
<th>Response at 3 years</th>
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<td>P, Dex</td>
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<td>very good</td>
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<td>CR</td>
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<tr>
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level of patients’ discomfort, the postoperative complications and the hospitalization period.

References


