Long term outcome of splenectomy in Immunethrombocytopenia (ITP)

ABSTRACT

ITP is a chronic illness with frequent mucosal bleed. Though the first line treatment is corticosteroids, relapse is frequent which necessitates splenectomy. Response to splenectomy is usually good initially; however over the years relapses are frequent. Drugs then used are azathioprine, mycophenolate mofetil, anti D globulin, TPO-receptor agonists, rituximab, cyclosporine etc. Ultimately there is a small subset of patients who may require a small dose of prednisolone life long.

Introduction

Splenectomy is an effective therapy for steroid-refractory or steroid dependent immune thrombocytopenia (ITP). However, spleen produces opsonin, a substance which is critical for the optimal killing of invasive micro-organisms by white blood cells) . Thus In the absence of spleen, individual is prone for life-threatening infections.

For decades, splenectomy was the standard of care for steroid-refractory ITP patients. However, with the availability of rituximab and the thrombopoietin receptor agonists (TPO-RAs), scenario has changed.

Efficacy of splenectomy for ITP

In most of patients with ITP, platelet counts increase immediately postsplenectomy, and patients achieve durable remission.[1,2,3] In a systematic review of case series published between 1966 and 2004, 1731 (66%) of 2623 adults maintained a complete response after a median follow-up of 29 months.[4]

Postsplenectomy relapses occur in 20% to 30% of patients, within the first 24 months.[5] however, they respond to alternative treatment. A small proportion of patients experience high morbidity and mortality. [5]

Both the 2011 American Society of Hematology (ASH) [6]and the International Working Group Consensus report [7] recommend splenectomy as a second-line therapy for ITP. ASH guidelines, however, give splenectomy a higher recommendation.

Complications associated with splenectomy can be infections. The risk of overwhelming bacterial sepsis in asplenic patients is well recognized [7] With presplenectomy vaccination, this risk has been reduced from ~7.16 per 100 person-years to 2.3 per 100 patient-years [8].

Pondicherry experience, India [9]

AIM: Splenectomy is the accepted second-line treatment in chronic immune thrombocytopenic purpura after corticosteroids fail. Splenectomy has a success rate of 50-60% in achieving complete remission. However, true long-term outcome is unknown since most of the follow-ups are around five years, according to other given publications. This retrospective review of adult patients with chronic ITP analyses true long term outcome of splenectomy over a long period and also examines for predictors of response to splenectomy.

METHODS: We retrospectively reviewed the medical records of 49 patients who had undergone splenectomy for chronic ITP from 1982 to 2015 [Range 2 - 396 months (33 years)] in a premier institute in south India. The mean follow-up period was 75.71 months.

RESULTS: Response to splenectomy gradually declined from 83.3% (five out of six patients) at one year to 25% (one out of four patients) when observed beyond 15 years, following splenectomy. Out of several factors studied like age, gender, initial response to steroids (pre-operative) and post-operative platelet count, there was no factor found to be statistically significant to predict long term remission. However, patients with post-splenectomy relapse could be managed with a significantly lower dose of prednisolone of 16.7 mg/day compared to their pre-splenectomy average requirement of 47.5 mg/day.

CONCLUSION: Although splenectomy normalizes platelet count acutely, sustained long term remission decreases with passage of time, to an extent only one-third of patients may remain in remission by 10 years of surgery. Further, there was no factor which could predict response to splenectomy.

A review by Vesely SK et al [10]

In a systematic review by Vesely SK et al, 90 articles with 656 splenectomised patients treated with 22 therapies were studied. Azathioprine,

cyclophosphamide, and rituximab had the most reported complete responses, but they were reported in only 41 to 109 patients. Reported complete response rates ranged from 17% to 27%, but 36% to 42% of patients had no response with these 3 treatments. Most reports described only platelet count responses; bleeding outcomes were reported in only 63 patients (10%). Only 111 (17%) of the 656 eligible patients had pretreatment platelet counts of less than 10×10^9 cells/L.

Authors concluded that evidence for the effectiveness of any treatment for patients with idiopathic thrombocytopenic purpura and persistent severe thrombocytopenia after splenectomy is minimal. Potentially effective treatments must be evaluated by randomized, controlled trials to determine both benefit and safety.

Review by Bell et al [11]

Long-term outcome of splenectomy for idiopathic thrombocytopenic purpura:

Idiopathic thrombocytopenic purpura (ITP) is an illness of primary acquired thrombocytopenia occurring in the absence of marrow failure. Splenectomy was first used as a treatment for ITP in 1913. However, with the realization that opsonin (critical for the optimal killing of invasive micro-organisms by white blood cells) is manufactured only in the spleen, spontaneous splenic removal was reevaluated and questioned. Splenectomy has a success rate that remains nearly identical (about 50% to 60%) whether it is performed soon after diagnosis or several months or years later.

Perspective: deciding on splenectomy

In general, it is advised splenectomy should be deferred at least for a year after onset of illness, since there may be spontaneous remission.

There are several situations in which splenectomy should be considered.. Patients may present with severe ITP characterized by profound thrombocytopenia, bleeding, a poor or transient response to corticosteroids and IVIg, and a suboptimal response to TPO-RA. Splenectomy is performed for express relief.

Conclusion

ITP is a benign recurrent bleeding disorder which responds to steroids initially very well. However, relapses are common which warrant consideration of splenectomy later. Nevertheless long term effect of splenectomy may not be very satisfying in all cases; and patients may require subsequent treatment with oral drugs like rituximab, TPO-R agonists, cyclosporine, low dose steroids etc.

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