Chapter

Splenectomy in Liver Cirrhosis with Splenomegaly and Hypersplenism

Adianto Nugroho

Abstract

Spleen is a "mysterious" organ since with unique functions, and might be related to other pathology in the human body. Splenomegaly and hypersplenism can manifest following the development of portal hypertension in liver cirrhosis through fibrogenesis, immune and microenvironment dysregulation. Cirrhotic patients are generally considered as immunocompromised and prone to infections. Splenectomy in cirrhotic patients has produced concern over decrease immunity and elevated risk of infection, namely overwhelming post splenectomy pneumococcal sepsis. This review discus the splenectomy effect to the liver and how it can play a role in cirrhotic patients with portal hypertension without readily available access to liver transplantation.

Keywords: splenectomy, liver cirrhosis, hypersplenism, splenomegaly, liver transplantation

1. Introduction

The spleen is a unique organ with many functions, including its crosstalk with the liver in cirrhotic patients. This review aims to answer a clinical question "Should splenectomy be done in liver cirrhosis with hypersplenism and splenomegaly?".

2. The spleen

The spleen is an organ full of mystery, as stated by Galen. From the ancient times until the Renaissance, descriptions of the gross anatomy of the spleen were relatively accurate, yet the physiology of this organ remains incomplete and inaccurate. Even until today, much of spleen's function are still yet to be discovered [1].

Spleen comprised of two distinct compartments, both functional and morphological, namely red pulp and white pulp. The red pulp filters blood to remove foreign material and damaged erythrocytes. It also serves as iron, erythrocytes and platelets storages. With one fourth of body's lymphocytes stores in the spleen, it is the largest secondary organ which initiate immune response to blood-borne antigens [2]. It exerts important effects on local and systemic immune responses, which have the potential to affect different tissues and organs [3]. The white pulp, composed by periarteriolar lymphoid sheath (PALS), the follicles and the marginal zones, are the one responsible for this so called immune functions [2].

In addition, the spleen also produces opsonins, a substances that bind to the foreign antigen, which in turn enhance their uptake and phagocytosis by macrophages. Furthermore, the B-lymphocytes within the germinal centers of the spleen are also sites for the production of antibody activated by foreign antigen. The realization of this important immunological function has promoted the desire for splenic preservation [4].

3. Liver cirrhosis and the spleen

The association between the liver and spleen are shown in three different categories. Both organ, anatomically important in the portal circulation. Histologically, they share similar possession of reticuloendothelial structures, participating in substance exchange and cellular migration. And immunologically, both organs plays essential roles in immune homeostasis and pathogen clearance [2].

The first recorded encounter between spleen and cirrhosis could be trace back to Carl Freiderich Quittenbaum (1793–1852) of Rostock, Germany, who removed the spleen of a woman with cirrhosis and ascites "more from the patient's urgent entreaty rather than the surgeon's judgment." Unfortunately the woman lived only 6 h after the surgery [5].

The palpable spleen has long been considered as an obvious signs of liver cirrhosis, frequently occurs in parallel with hypersplenism, to be the major cause of cytopenia and thrombocytopenia. This condition are relatively sub-fatal, even in the absence of a bleeding varices. During the progression of liver cirrhosis, the spleen-derived immune cells and cytokines may travel into the injured liver via portal blood flow. Together with the portal hypertension and congestion, this will result in splenomegaly and hypersplenism. Furthermore, the chemokines, DAMPs like HMGB1, or exosomes, are also release into the circulation, which will trigger the activation and/or migration of splenocytes. This mechanism are known as the liver and spleen crosstalk pathways during liver cirrhosis [2].

Spleen size in patients with cirrhosis varies by the etiology of the disease. While in healthy adults, the size of the spleen in usually less than 12 cm, in cirrhotic patients it is relatively larger, as shown in the study by Kashani et al. This study revealed that the mean spleen size in the alcohol group (13.1 ± 2.5 cm) was significantly smaller than in the hepatitis C (15.0 ± 3.4 cm) and nonalcoholic steatohepatitis (15.2 ± 3.0 cm) groups (95% confidence intervals of the mean difference, 0.6 to 3.3 and 0.8 to 3.4 cm, respectively), sonographically [6].

4. Splenectomy effects to the liver

Cirrhotic patients are generally considered as immunocompromised, mainly due to the development of bacterial infection and community-acquired infections. Since the spleen is the largest lymphoid organs with large amount of T and B cells, macrophages, and dendritic cells, splenectomy in cirrhotic patients has produced concern over decrease immunity and elevated risk of infection, namely overwhelming post splenectomy pneumococcal sepsis.

However, a study by Hirakawa et al., showed the possibility of reducing suppressive cell fractions and enhancement of the effector cell population and functions by means of splenectomy, thus ameliorate the impaired immune status of cirrhotic patients [7].

Yamada et al. demonstrated that splenectomy improved hepatic functional reserves and nutritional metabolism, together with improvement in thrombocytopenia and

leukopenia in cirrhotic patients. Splenectomy is thought to induce a decrease in platelet pooling or breakdown in the spleen of thrombocytopenic patients, and as a result, increase blood platelet counts. Bilirubinemia secondary to hypersplenism, which is caused by an increase in bilirubin production, that overloads the capacity of the liver to metabolize bilirubin, are also reduced after splenectomy [8].

In a study by Ueda et al. of rats undergoing major liver resection with or without splenectomy, early stage splenic red pulp TGF-β1 production and secretion into the portal blood exert an inhibitory effect on liver regeneration. Splenectomy reversed this inhibition and enhanced the regeneration of hepatocytes [9].

Study by Huang et al., unveiled serum cytokine profiles in HBV-related cirrhosis patients with PH and hypersplenism, indicating a potential role of the hypertensive spleen in the progression of liver disease. Furthermore, the changes in cytokine levels following splenectomy maybe potential advantageous to reduce liver fibrosis and accelerate liver regeneration as well as reduce the risk of HCC [10].

Splenectomy also enhanced the repopulation of adoptively transferred bone marrow cell in cirrhotic liver and decreased collagen deposition through the upregulation of MM9 expression in transferred bone marrow cells, as suggested by Iwamoto et al. [11], and improved the efficiency of adipose tissue-derived mesenchymal cell transplant into the liver by enhancing liver SCF-1 and HGV expressions [12].

Considering all of the above mention mechanism, targeting spleen for the treatment of liver cirrhosis can be achieved through [2]:

- amelioration of cirrhosis' fatal complications such as bleeding esophageal or gastric varices
- efficiently improving liver function and the prognosis of esophageal varices
- increasing the efficacy of liver transplantation and improving the prognosis of HCC
- supplementary treatment for anti-HCV therapy in combination with interferons and other pharmaceuticals.

5. Technical and perioperative consideration for splenectomy in cirrhotic liver

Surgery in a patient with liver disease carries specific and higher risks, compare to those with normal populations. Perioperative care including assessment and optimalization is the key to a safe surgery. Many cirrhosis patients present themselves with a relative contraindications that preclude surgery.

The predictors for complications including Child-Pugh class B or C, ascites, etiology of cirrhosis other than PBC, elevated creatinine, preoperative infection, COPD, preoperative upper GI bleeding, invasiveness of surgical procedure, intraoperative hypotension, and ASA status 4–5. While the predictors of mortality including male gender, Child-Pugh class B or C, ascites, etiology of cirrhosis other than PBC, preoperative infection, ASA status 4–5 and respiratory surgery. The presence of 1 risk factors carries a 9.3% risk of complications, and this increase with the more numbers of risk factors. A total of 7–8 risk factors carries a 100% risk of complications [13].

Friedman proposed the following list of contraindication to elective surgery in patients with liver disease, including acute viral hepatitis, alcoholic hepatitis, acute liver failure, acute renal failure, severe coagulopathy, hypoxemia and cardiomyopathy [14].

Regarding the preferred method for splenectomy, recently laparoscopic has become technically feasible, safe and effective procedure for hypersplenism secondary to cirrhosis, and contributes to less blood loss, shorter length of stay and less impairment of liver function. However, this methods are generally more costly and might not readily available in every hospital. Thus the choice of splenectomy method must be personally selected for each patient, surgeon and hospital [15].

6. Splenectomy as a bridge to liver transplant

It is already a general consensus that liver transplantation is the preferred treatment options for patient with end stage liver disease. However, the waiting time for liver transplantation is also long due to the shortage of donor organs, even in living donor liver transplantation setting. Moreover, in some countries, liver transplantation still not a feasible option for all patients.

One among many alternatives is by doing a splenectomy prior to liver transplantation in patient with liver cirrhosis and subsequent splenomegaly-hypersplenism. A study by Kong et al., studied 833 patient patients underwent liver transplantation, of which 88 patients had splenectomy before liver transplantation. They found that postoperative infection and 90-days mortality in the splenectomy and non-splenectomy group were not statistically difference. Furthermore, the post-transplant thrombocytopenia and early allograft dysfunctions is significantly lower in splenectomy group compare to non-splenectomy group. They suggested that pre-transplantation splenectomy is recommended in cases with risky patients without appropriate source of liver for LT. Taking into consideration the possibility of more difficult operation due to adhesion when transplantation is being done. One thing to note is that as a "re-operation" the splenectomy is often as- sociated with more difficult dissection due to adhesions [16].

7. Summary

Splenectomy is beneficial in reversal of the pathologic process through live regeneration and pre-transplant splenectomy could be an alternative in patients without appropriate source of liver for liver transplantation. However, perioperative considerations should be thoroughly assessed to allow a safe surgery.

Conflict of interest

"The authors declare no conflict of interest."

Notes/thanks/other declarations

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Author details

Adianto Nugroho
Department of Surgery, HPB Section, Digestive Division, Fatmawati Central General Hospital, Jakarta, Indonesia

*Address all correspondence to: adiyusuf97@gmail.com

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