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Hypersplenism Caused by Portal Hypertension due to Abnormal Liver Function

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Abstract
Portal hypertension refers to a range of complications that arise from elevated pressure in the portal vein system, which can be caused by various factors. The primary causes of portal hypertension are cirrhosis induced by viral hepatitis and non-cirrhotic factors such as Budd-Chiari syndrome, portal cavernous transformation, and regional portal hypertension. Patients with portal hypertension experience increased blood flow and resistance in the portal vein, leading to enlargement of the spleen and increased splenic function. This, in turn, can result in a decrease in blood cells and an overgrowth of bone marrow hematopoietic cells, leading to complications like anemia, bleeding, and infection. The treatment for splenomegaly induced by portal hypertension involves both medical and surgical approaches, with surgical treatment being the primary method. This article provides an overview of the common treatment options for splenomegaly caused by portal hypertension.

Keywords: Hypersplenism, Hypertension, Liver

1. Introduction

Portal hypertension is a prevalent issue, with higher rates in developing nations compared to Western European countries. The incidence is particularly high in Asia, specifically in India and Japan. Noncirrhotic portal hypertension accounts for approximately 25% of global cases, but in Japan, the number of new cases has significantly decreased to only 11 annually. In North America and Europe, NCPH is considered a rare condition, making up only 3-5% of portal hypertension cases (Dhiman et al., 2002; Sarin et al., 2007) .

The diagnosis of NCPH primarily involves ruling out other potential causes of portal hypertension and liver diseases. This includes confirming clear signs of portal hypertension, conducting appropriate serological tests, liver biopsies, and radiological examinations to exclude chronic liver diseases like viral hepatitis, fatty liver, alcoholic liver disease, autoimmune hepatitis, primary biliary cirrhosis (PBC), and Budd-Chiari syndrome. Portal hypertension is characterized by an increase in portal pressure (> 10 mmHg) and can be caused by liver cirrhosis or noncirrhotic diseases in portal and hepatic veins (Schouten, Garcia-Pagan, Valla, & Janssen, 2011; Schouten, Verheij, & Seijo, 2015). When portal hypertension occurs without liver cirrhosis, NCPH becomes a consideration. The prognosis for NCPH is generally more favorable than that of cirrhosis, and noncirrhotic diseases are a common

cause of portal hypertension in developing regions, especially in Asia (Rajekar, Vasishta, Chawla, & Dhiman, 2011). NCPH encompasses a wide range of diseases with origins either within or outside the liver. Typically, the lesions in NCPH are vascular and can be classified based on the location of blood flow resistance. In many cases, these conditions are associated with damage to endothelial cells, thickening of the inner lining of blood vessels, blockages due to blood clots, or scarring within the portal system of the liver effects by portal hypertension (Sarin & Kumar, 2006).

2. Etiology of Portal hypertension

The development of portal hypertension in humans is believed to be caused by a combination of increased resistance in the hepatic vascular bed, known as "backflow," and a hyperdynamic splanchnic circulation, referred to as the "forward flow" theory. This condition can be classified into prehepatic, intrahepatic, and posthepatic forms, each with its characteristics and contributing factors. The main cause of certain types of pre- and intrahepatic portal hypertension is an increase in splanchnic blood flow. Intrahepatic portal hypertension can be further categorized into presinusoidal, sinusoidal, or post-sinusoidal types, although not all diseases fit neatly into these classifications. The contribution of each factor to elevated portal pressure in liver cirrhosis varies depending on the underlying cause, Recent studies have focused on spleen stiffness as a potential indicator of portal hypertension, as it can be measured using non-invasive imaging techniques like transient elastography and acoustic radiation force impulse imaging. Some research suggests that spleen stiffness may predict the presence of varices or ascites in individuals with portal hypertension. In an experimental model of cirrhosis with portal hypertension, there was a positive correlation between portal pressure and spleen size, highlighting the complex factors involved in this condition (Vadlapudi et al., 2024).

3. Risk Factors

Portal hypertension does not have any well-defined risk factors, however, cirrhosis, which is the primary cause of portal hypertension, is associated with a multitude of risk factors. Some common risk factors that contribute to the development of cirrhosis include intravenous drug use (IVDU), tattooing or piercing in unsanitary conditions, needlestick injuries, blood transfusions before 1992, viral hepatitis infections, and engaging in unprotected sexual intercourse. These risk factors can significantly increase the likelihood of developing cirrhosis, which in turn can lead to the development of portal hypertension. It is important for individuals to be aware of these risk factors and take necessary precautions to prevent the onset of cirrhosis and subsequent complications such as portal hypertension (Metwally, Essam, Atwa, Awad, & Abdelsameea, 2022).

4. Pathophysiology of Portal hypertension

The main cause of portal hypertension in cirrhosis is an increase in resistance to blood flow within the liver. This resistance is primarily due to structural changes associated with fibrosis/cirrhosis and constriction of blood vessels within the liver. Research has shown that vasoconstriction within the liver alone accounts for at least 25% of the overall increase in resistance. It is important to note that changes in certain types of liver cells, such as hepatic stellate cells and liver sinusoidal endothelial cells, play a crucial role in increasing resistance and have been extensively studied. Once portal hypertension develops, collateral vessels form as alternative pathways for blood from the digestive organs. However, these vessels also contribute to an increase in blood flow within the portal vein, worsening the already elevated portal hypertension. Additionally, cirrhosis is characterized by dilation of arteries in both the splanchnic and systemic circulations, further increasing blood flow to the portal vein. Therefore, simply reducing the formation of collateral vessels would not effectively alleviate portal hypertension. It is crucial to inhibit arterial dilation in the splanchnic circulation to decrease blood flow to the portal vein. This combined approach is essential in the treatment of portal hypertension. This section provides a detailed analysis of the mechanisms underlying the formation of collateral vessels and arterial dilation in the splanchnic and systemic circulations in cirrhosis with portal hypertension (Buob, Johnston, & Webster, 2011; Iwakiri, 2014).

5. Complication of Portal hypertension

Internal bleeding can be a severe consequence of esophageal varices, which are enlarged veins located at the lower end of the esophagus. These varices develop due to portal hypertension, where blood flow is obstructed in nearby veins in the esophagus and stomach. When varices burst, they can lead to life-threatening internal bleeding, particularly at the junction of the esophagus and stomach, resulting in sudden and forceful vomiting of blood. In addition to the risk of internal bleeding, individuals with esophageal varices may also experience fluid buildup in the stomach, leading to feelings of fullness, rapid weight loss, and malnutrition. The accumulation of fluid can cause discomfort and hinder mobility, as the pressure on the diaphragm may result in breathing difficulties. These symptoms can significantly impact the quality of life for affected individuals. Furthermore, complications associated with esophageal varices can extend to kidney and lung problems, further exacerbating the health risks posed by this condition. Kidney problems may arise due to the body's inability to effectively regulate fluid levels, while lung problems can occur as a result of pressure exerted by the accumulated fluid. These additional health issues underscore the seriousness of esophageal varices and the importance of timely medical intervention to manage and treat this condition effectively (Simonetto, Liu, & Kamath, 2019).

6. Treatment Strategies

The initial approach to managing hepatopulmonary syndrome involves the administration of oxygen therapy, while hepatorenal syndrome is typically treated with dialysis. Hepatic encephalopathy is addressed through the use of specific medications, and excess fluid from ascites is removed via paracentesis, which also allows for testing for peritonitis. In cases where there is a need to redirect blood flow through the portal venous system and alleviate pressure, two different shunt procedures may be considered. These procedures aim to provide relief by altering the circulation of blood within the body. Treatment options for portal hypertension-induced splenomegaly are somewhat limited within the realm of internal medicine. The focus is primarily on managing the underlying condition and providing symptomatic relief. Antiviral therapy is often recommended for patients with liver cirrhosis resulting from viral hepatitis B, as it can help improve liver function and reduce liver fibrosis, ultimately easing symptoms associated with hypersplenism (Li et al., 2017). However, when patients with cirrhosis following hepatitis C receive interferon therapy, it can further decrease their white blood cell and overall blood cell count. In addition to treating the underlying disease, there are various methods that can be used to reduce blood cell count. Common treatments include infusing blood products, using erythropoietin, recombinant human granulocyte colony-stimulating factor, recombinant human thrombopoietin, and administering platelet-raising capsules to stimulate blood cell production. Furthermore, certain medications have shown positive therapeutic effects in treating splenomegaly caused by portal hypertension. These medications include those that clear and remove blood stasis, improve blood circulation, and unblock collaterals, among others. The choice of these medications should be based on clinical considerations (Pozzato, Marzano, Botta, Anania, & Uslenghi, 1998).

Following a comprehensive internal medicine treatment, early splenic hyperactivity can be relieved without resorting to surgical intervention if the root cause can be effectively managed. However, in cases where the primary disease treatment fails to yield satisfactory results, the spleen may experience significant compression from neighboring organs, leading to severe bleeding and posing challenges for treatment. In such instances, surgical treatment is advised to control recurrent infections and mitigate severe damage to blood cells (Merkel, Gatta, Arnaboldi, & Zuin, 1985; Yoshida et al., 2023).

7. Surgical Treatment

Splenectomy is typically recommended when other treatment options have failed to provide relief or when the enlarged spleen is causing severe symptoms such as pain, anemia, or low platelet count. The surgery can be performed through open surgery or laparoscopic techniques, depending on the individual's specific condition and overall health. During a splenectomy, the surgeon carefully removes the spleen while taking care to preserve surrounding organs and tissues. After the surgery, patients may experience some discomfort and require a period of recovery before returning to normal activities. It is important for individuals who have undergone a splenectomy to receive vaccinations against certain infections, as the spleen plays a crucial role in the immune system's response

to bacteria and viruses. While splenectomy can effectively treat splenomegaly and its associated symptoms, Overall, splenectomy remains a valuable option for individuals with severe splenomegaly who have not responded to other forms of treatment (Al-raimi & Zheng, 2016).

8. Complete splenectomy

Splenomegaly, or an enlarged spleen, can be effectively treated through complete splenectomy. This treatment approach encompasses various methods, including traditional open splenectomy, laparoscopic splenectomy, and da Vinci robot-assisted splenectomy. Over time, these procedures have become more standardized, particularly the traditional open splenectomy, which is now commonly performed in local hospitals worldwide. In cases where patients have both portal hypertension and splenomegaly, splenectomy is often accompanied by additional procedures such as periportal vascular dissection or portal body shunting. These additional measures, such as splenic cavity and splenic kidney shunting, are implemented to prevent and manage upper gastrointestinal bleeding (Miko et al., 2017). Emphasizing the importance of removing any potential accessory spleen during a splenectomy is crucial to prevent splenomegaly recurrence post-surgery. However, there is a risk of OPSI after complete spleen removal, so it is recommended to avoid this in adolescent patients with immature immune systems if possible. Complications such as portal vein thrombosis and abdominal fluid accumulation can occur after a splenectomy, highlighting the need for careful consideration and risk assessment before proceeding with the procedure.

Laparoscopic and robot-assisted splenectomies offer advantages over traditional open surgery, including reduced trauma, less blood loss, shorter hospital stays, and lower complication rates. As a result, these techniques are becoming increasingly popular in the field of splenectomy (Morgan & Tomich, 2012).

9. Partial splenectomy

Scholars have made significant advancements in understanding the role of the spleen, leading to a widespread agreement within the medical community to minimize the risk of developing overwhelming post-splenectomy infection (OPSI) (Sinwar, 2014). Therefore, it is crucial to prioritize the preservation of splenic function by utilizing various methods such as regular partial splenectomy and autologous splenic transplantation. Recent studies have shown that the spleen, similar to the liver, has distinct blood supply segments and avascular zones between them. This understanding of the spleen's anatomy serves as the foundation for regular partial splenectomy, which involves removing specific portions of the spleen based on the distribution pattern of blood vessels.

It may choose to perform splenectomy (complete removal of the spleen), lobectomy (removal of a lobe), or hemisplenectomy (removal of half of the spleen) depending on the distribution of blood vessels. These surgical techniques aim to preserve the essential functions of the spleen while addressing specific medical conditions or injuries (Zouki & Fry, 2024). However, the widespread adoption of partial splenectomy is hindered by the challenge of accurately identifying blood vessel distribution in the spleen during surgery. This procedure, compared to complete splenectomy, presents difficulties in controlling bleeding and carries a higher risk of postoperative bleeding. These factors contribute to the limited use of partial splenectomy due to the associated risks and complexities involved. To address the limitations of partial splenectomy and the potential decrease in immune function, experts suggest autologous splenic transplantation. This involves transplanting healthy splenic tissue into different areas of the body, such as the omental sac, splenic bed, and retroperitoneum. Various techniques, including semi splenic transplantation with a vascular pedicle, splenic slice transplantation, and splenic cell transplantation, can be utilized for autologous splenic transplantation. Research indicates that autologous splenic transplantation has the potential to partially preserve the immune function of the spleen. However, further investigation is needed to fully understand the effectiveness and implications of this transplantation method. By examining the advantages and limitations of autologous splenic transplantation, researchers can contribute to improved surgical outcomes and enhanced patient care in cases where splenectomy is necessary (Y. Zhang et al., 2024). It is important to highlight that when dealing with patients who have splenomegaly caused by portal hypertension, the treatment objective should not solely focus on reducing the enlargement of the spleen. It is equally crucial to consider the prevention and management of upper gastrointestinal bleeding as part of the overall treatment plan (Chaouch et al., 2024). In the case of patients with portal hypertension induced hypersplenism,

blindly performing partial splenectomy and autologous splenic transplantation may provide short-term relief from splenomegaly. However, it is important to note that this approach does not completely address the issue as residual splenic tissue can still develop splenomegaly over time. Moreover, the resulting splenic hyperdynamic circulation can further worsen portal hypertension. Therefore, it is crucial to exercise caution and carefully select the appropriate candidates for partial splenectomy, excluding adolescents and individuals with underdeveloped immune function, in order to effectively manage portal hypertension and its associated complications (Cianci et al., 2016).

10. Spleen lung fixation surgery

It is suggested by Japanese researchers Akita et al., the technique of spleen lung fixation surgery emerged as a potential surgical intervention for the management of Budd-Chiari syndrome (Akita & Sakoda, 1980). Our facility has implemented enhancements to a procedure referred to as modified spleen lung fixation surgery, a technique that has gained popularity in treating different forms of portal hypertension. This surgical method hinges on establishing collateral circulation between the spleen and lungs using the patient's own blood vessels to alleviate pressure in the portal vein and avert gastrointestinal hemorrhaging by incorporating splenic artery ligation and partial splenectomy into the surgical process, there is a notable improvement in reducing splenomegaly to a certain extent. These modifications have proven to be effective in enhancing the overall outcome of the surgery and in addressing the complications associated with portal hypertension (Bell-Allen, McNamara, Bull, Lewin, & O'Rourke, 2024). The recent clinical study revealed that patients suffering from portal hypertension experienced a notable rise in white blood cell count, hemoglobin levels, and platelet count twelve months post undergoing a modified splenic pulmonary fixation surgery, effectively alleviating their splenic hyperfunction. However, the primary objective of enhancing spleen lung fixation surgery is to mitigate portal hypertension and lower the chances of gastrointestinal bleeding, despite the relatively high risks associated with this procedure. It is crucial to meticulously adhere to the indications and contraindications, as opting for this surgery solely to address splenomegaly may not be a prudent decision (Merchant & Kotawala, 2024).

11. Partial splenic embolization

Partial splenic embolization (PSE) is a procedure that involves using vascular intervention to block specific branches of the splenic artery, leading to partial ischemic necrosis of the spleen. This results in a decrease in splenic volume and blood flow, ultimately reducing splenic function.

The main objective of partial splenic embolization is to address the decrease in white blood cells and platelets seen in conditions like liver cirrhosis and splenomegaly. By reducing splenic function through embolization, PSE aims to improve blood cell counts and alleviate symptoms associated with these medical conditions by strategically blocking branches of the splenic artery, partial splenic embolization provides a long-term treatment option for individuals with liver cirrhosis and splenomegaly. By decreasing spleen function, PSE can help manage complications and enhance quality of life for these patients in the future (Ozturk et al., 2016). Studies have indicated that pharmacological splenic embolization (PSE) has the potential to not just alleviate splenomegaly in individuals diagnosed with liver cirrhosis, but also lower portal vein pressure, mitigate the risk of upper gastrointestinal bleeding, and exhibit minimal negative impacts on liver function (Liu et al., 2024). The splenic embolism plays a crucial role in determining the therapeutic effect of PSE. Therefore, the key to achieving successful outcomes lies in effectively controlling the area of embolism. Studies have shown that when the embolic area exceeds 30%, there is a noticeable and significant increase in platelet levels in the short term. This highlights the importance of carefully managing the extent of embolism to maximize the desired therapeutic effects of PSE (Talwar et al., 2020). In order to ensure the prolonged efficacy of splenic embolization, it is crucial that the embolic area exceeds 50%. Studies have shown that when the embolic area surpasses 70%, there is a notable rise in the occurrence of postoperative complications. As a result, experts suggest maintaining the embolic area within the range of 50% to 70% to optimize outcomes and minimize risks associated with the procedure (Ahuja, Farsad, & Chadha, 2015). In Cai Mingyue et al. (Cai et al., 2016) discovered that various factors such as embolism proportion, non-infarcted spleen volume, and cholinesterase level play crucial roles in determining the effectiveness of partial splenic embolization (PSE) in treating thrombocytopenia resulting from liver cirrhosis and

splenomegaly to optimize treatment outcomes and minimize potential complications, a strategic approach involving staged and repeated splenic embolization procedures can be implemented to gradually reduce the size of the spleen. In recent years, PSE has emerged as a promising therapeutic option for managing severe splenomegaly and upper gastrointestinal bleeding associated with portal hypertension. Clinical evidence supports the safety and efficacy of PSE, positioning it as a viable alternative to surgical splenectomy in certain cases (Ueda et al., 2023).

Radiofrequency ablation (RFA) induces necrosis in local tissue by utilizing radiofrequency current, with splenic RFA specifically targeting splenic tissue to decrease splenic volume and alleviate splenomegaly. This is achieved through the combination of central region coagulation necrosis and surrounding tissue infarction, resulting in the desired therapeutic outcomes for patients with splenic-related conditions (Putnik & Ilic, 2023). Microwave ablation is primarily a method that utilizes microwave magnetic fields to desiccate and coagulate tissues. Studies have indicated that percutaneous microwave ablation plays a crucial role in enhancing white blood cells and platelets in individuals suffering from splenomegaly. The process involves the application of microwave energy to the targeted tissue, leading to the destruction of abnormal cells through heat generation. This technique has shown promising results in the treatment of various medical conditions, including liver tumors and renal cell carcinoma by utilizing microwave ablation, medical professionals can precisely target specific areas within the body, minimizing damage to surrounding healthy tissues. This minimally invasive procedure offers patients a faster recovery time and reduced risk of complications compared to traditional surgical methods (Beermann, Delle, Magnusson, & Casswall, 2021). However, it is crucial to recognize that both RFA and microwave ablation therapy pose a risk of splenic rupture and bleeding. This risk is heightened by the fragile nature of spleen tissue and the hemodynamic characteristics of the spleen, which undergoes significant circulation changes during portal hypertension. Therefore, it is essential to proceed with caution and closely monitor for these potential complications throughout the puncture procedure and beyond (Assal et al., 2017; Martins et al., 2015).

12. Combine Therapy

A technique known as high intensity focused ultrasound (HIFU), low-energy ultrasound is concentrated on specific tissue by means of an ultrasound focusing transducer. This concentrated ultrasound generates a thermal effect that rapidly elevates the temperature of the targeted tissue, resulting in coagulation and necrosis within the focal region. In comparison to other treatment methods such as radiofrequency ablation (RFA) and microwave ablation, HIFU offers a non-invasive approach to treating various conditions (X. Zhang et al., 2022). Studies have indicated that HIFU (High-Intensity Focused Ultrasound) demonstrates both safety and efficacy in the treatment of splenomegaly, particularly in elderly individuals with compromised liver function or underlying health conditions. Nevertheless, the precision of ultrasound ablation can be influenced by variables like focusing accuracy and respiratory movements, thereby limiting its application in the context of splenomegaly to an exploratory phase. The effectiveness and safety of this treatment modality necessitate further investigation through the lens of evidence-based medicine (Zhu et al., 2014).

The sensitivity of splenic tissue to radiation can lead to degeneration, necrosis, and fibrosis of spleen cells when local radiotherapy is used, resulting in a decrease in spleen volume and function. This can provide relief from splenomegaly, with studies showing that local radiotherapy has a similar therapeutic effect on splenomegaly induced by portal hypertension as interventional surgery. It effectively reduces blood cell levels and minimizes adverse reactions and treatment costs for patients. Another method for treating splenic hypertrophy is through percutaneous local injection of anhydrous ethanol into the spleen, which can help reduce splenic hyperactivity by inducing bacterial necrosis and fibrosis. However, like local radiotherapy, the use of anhydrous ethanol injection poses challenges due to limited clinical research. The safety and effectiveness of this treatment method require further investigation, emphasizing the importance of caution and careful consideration when choosing treatment options in clinical practice (Bolognesi, Merkel, Sacerdoti, Nava, & Gatta, 2002).

13. Transjugular intrahepatic portosystemic shunt (TIPS)

The procedure called Transjugular intrahepatic portosystemic shunt (TIPS) involves the use of X-ray imaging to guide an interventional radiologist in placing a stent in the liver. This method is considered less invasive than open surgery, making it a safer option for patients with specific liver conditions during the TIPS procedure, a pathway is created in the liver using a needle, allowing the doctor to connect the portal vein to one of the hepatic veins. This connection helps redirect blood flow in the liver, reducing pressure in the portal vein and improving overall liver function to ensure the pathway remains open and functional, a stent is carefully inserted and positioned by the interventional radiologist. The stent helps maintain the openness of the pathway, allowing for continuous blood flow between the portal vein and hepatic veins, Although TIPS is generally effective in managing certain liver conditions, there is a small risk of stent malfunction over time. If the stent becomes blocked or displaced, additional interventions may be necessary to address the issue and restore proper blood flow in the liver (Yu, Rao, Fergus, Lorenz, & Zangan, 2024).

14. Distal splenorenal shunt (DSRS)

The distal splenorenal shunt (DSRS) is a surgical intervention that could potentially offer a superior option for certain individuals. It is essential for patients to meet specific health criteria to ensure a safe surgery and recovery process, but the long-term benefits of disease management may outweigh the risks. By rerouting the splenic vein away from the liver and redirecting it to the left kidney vein, the procedure effectively decreases blood flow and pressure in both the liver and spleen, potentially leading to improved health outcomes (Rehman & Nazir, 2019).

15. Conclusion

The management of splenomegaly caused by portal hypertension is increasingly using techniques like radiofrequency ablation, microwave ablation, and high-intensity focused ultrasound due to advancements in research and technology. These methods have shown promising outcomes and potential for future use as minimally invasive treatments. Traditional surgical and internal medicine approaches still play a significant role, and a personalized approach is important for each patient. Portal hypertension is commonly seen in patients with cirrhotic alcoholic fatty liver disease or non-alcoholic fatty liver disease. However, evidence suggests that it can also develop in non-cirrhotic NAFLD patients. The primary cause is an increase in intrahepatic vascular resistance due to fibrosis and microcirculation damage. The diagnostic method HVPG may underestimate portal pressure in NAFLD patients, and some may experience liver decompensation even with an HVPG below the traditional threshold. Obesity can affect the accuracy of LSM in diagnosing portal hypertension.

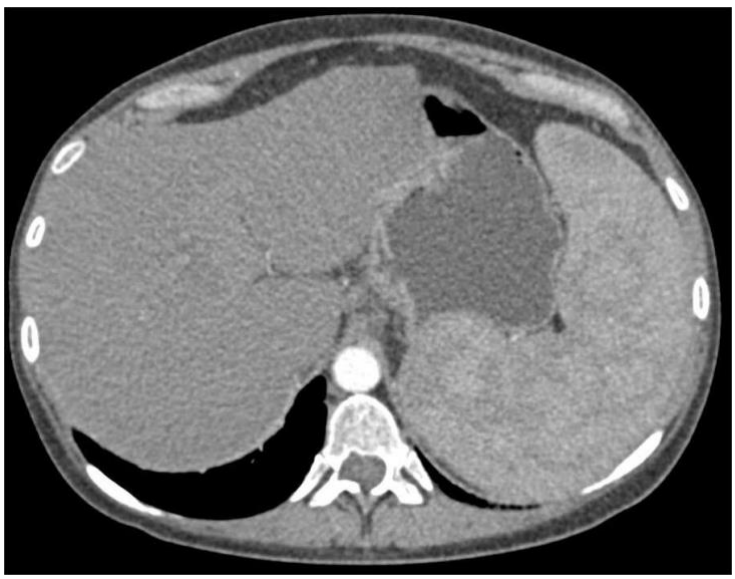

Figure 1: Hypersplenism due to portal hypertension

In figure 1 CT scan showed the hypersplenism due to portal hypertension.

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