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PARTIAL SPLENIC EMBOLIZATION FOR THE TREATMENT OF HYPERSPLENISM

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Surgical removal of the spleen is a well established procedure which is indicated for various Hematologic disorders. As an alternative to surgical splenectomy, partial splenic embolization was done on 21 patients for secondary hypersplenism due to portal hypertension, manifested by splenomegaly, thrombocytopenia, leucopenia, and erythrocyte hemolysis. Within few days platelet and leucocytic counts rose significantly in all patients, and were maintained throughout the whole follow up period, hemoglobin levels did not significantly changed immediately after PSE, but returned to normal levels by 6 months after PSE. Splenic volume was decreased significantly after PSE. Transient procedural complications included abdominal pain and fever in all patients, 2 patients developed left basal pneumonia, and 2 patients developed bleeding from the puncture site. Given the safety, efficacy, and advantages of PSE, it should be considered a valid alternative treatment of hypersplenism and the treatment of choice for selected patients with hypersplenism caused by PHT.

Key wards: *Splenic embolization, Portal Hypertension, Hypersplenism, Splenic Volume.*

Abbreviations: *Partial Splenic Embolization (PSE), Portal Hypertension (PHT).*

INTRODUCTION

Splenectomy is the preferred treatment procedure in patients with primary hypersplenism, whereas in cases of secondary hypersplenism therapy should be directed to the underlying pathology [1]. With the awareness of the role and importance of the spleen in the immune system, conservative methods have gained prominence in the treatment of benign conditions of the spleen [2,3]. The alternative technique of partial splenic embolization (PSE) was therefore developed [4,5]. It resulted in ischemic necrosis of much of the functional spleen, followed by a decrease in splenomegaly and hypersplenism, while allowing preservation of adequate splenic tissue to prevent the occurrence of overwhelming infection. For patients with portal hypertension, this technique has the additional advantage over splenectomy of splenic vein preservation for possible future splenorenal shunt [6].

In our study we describe the outcome of PSE in patients with chronic liver disease and secondary hypersplenism.

PATIENTS AND METHODS

Patients:

This study was performed on 21 patients, with age ranged from 34-52 years (mean 43.2± 4.28 y), with hypersplenism caused by portal hypertension, selected from the inpatients of Internal Medicine and General Surgery Departments, Mansoura University Hospital during the period between January 1996 and January 2001.

All patients were selected to have advanced hepatocellular affection, hypersplenism, with platelet counts of 40 to 65,000/mm³ (mean 48,000/mm³), leucocytic count 1500 to 3100/ mm³ (mean 1980/mm³), and hemoglobin level 9.2 to 11.1 gm/L (mean 10.3 gm/L).

Exclusion criteria:

1- Patients with hypocellular or infiltrated bone marrow.

2- Patients with known collagen vascular or autoimmune disorders.

3- Patients with ischemic heart disease, hypertension, DM, renal failure, or malignant disease.

4- Patients with recent history of abdominal trauma or surgery.

Methods:

After written consent, all patients were subjected to the followings:-

1- Thorough history taking with special stress on bleeding tendency, variceal hemorrhage, repeated infections, and previous blood transfusion.

2- Thorough physical examination to evaluate the state of the liver, spleen, ascites, or manifestations of liver cell failure.

3- Laboratory investigations, including complete blood picture (CBC), complete liver function, serum creatinine, and bone marrow aspiration. (CBC, S albumin, S bilirubin, and prothrombin conc, were repeated 2 weeks, 2 months, and 6 months after doing PSE).

4- Abdominal CT was done before and 6 months after PSE to assess the splenic volume using the following formula: splenic volume = 30+0.58 (width x length x thickness)
The mean value of normal splenic volume in Prassopoulos et al study 1997 [7] was 214.6 cm^3, with a range from 107.2-314.5 cm^3, and he concluded that quantitative assessment of splenic volume might be of value in assessing mild variation in splenic size.

5- Embolization technique: The technique was similar to that done by Herrero et al 1994 [8]. The procedure was performed under sterile conditions with separate trays for the embolisation solution and the angiographic equipment, intravenous sedation and local anesthesia were used in all patients. All patients began antibiotic prophylaxis 6 hours before embolisation, and 5 days after. Modified Seldiger puncture of the right common femoral artery was performed followed by introduction of 5 F Cobra head catheter over guide wire, then selective catheterization of the celiac axis and splenic artery was performed. Splenic angiography was performed to show the arterial distribution in the spleen, the catheter was then advanced to the splenic hilum, distal to all pancreatic branches to minimize the risk of pancreatitis.

Controlled embolization of the peripheral splenic branches was performed using particles of polyvinyl alcohol sponge measuring 250 to 355µm (Boston Scientific corporation). During embolization the flow distribution and the extent of peripheral embolization were fluoroscopically visualized. After completing the embolization, angiography was performed to confirm approximately 50% infarction of the spleen [9] Fig (1,2). For pain control, paracetamol or pentazocine was given.

Statistical analysis:

The data were collected, and the analysis was done by using SPSS (statistical package for social science) program version 8, 1998. F test was used to compare between more than 2 groups. Student T test was used to compare between quantitative data of 2 groups.

RESULTS

Hospital stay: The hospital stay after PSE was 5 to 12 days (mean 8.7 days). All patients had significant generalized abdominal pain, for 3 to 7 days (mean 5.1days), which was will controlled by analgesics. After that pain tended to be localized in the left hypochondrium before resolving by 10 to 14 days after PSE. Fever occurred in all patients and lasted 2 to 21 days (mean 5 days), characterized by one or two daily spikes. Additional cultures of blood specimens were negative for bacteria and fungi. Two patients developed left basal pneumonia, with left pleural effusion which was resolved with conservative management. Two patients developed massive bleeding 6 hours after PSE from the femoral artery at the puncture site, and controlled well by compression.

Laboratory data (Table 1): Platelet counts responded promptly to PSE; counts which were <50,000/ mm^3 before PSE, after 2 weeks, they became >280,000/ mm^3, but no venous thrombosis occurred. Platelet counts were sustained at >200,000/mm^3 during longer follow up period of 6 month to 4 years (Fig. 3). Leucocytic counts also rose significantly after 2 weeks of PSE compared with counts before PSE. At follow up, leucocytic counts were within the normal range and were significantly higher than before PSE for all patients (Fig. 4). Hemoglobin levels did not significantly changed immediately after PSE but returned to normal levels by 6 months after PSE (Fig. 4). Coagulation studies, serum bilirubin, and serum albumin values were not altered significantly by PSE (Fig. 5,6). Serum alanine aminotransferase, and aspartate aminotransferase levels

were elevated immediately after PSE, and returned to normal levels after 2 months.

The spleen table (2): The average volume of the spleen of the 21 patients before PSE was 1585±250 mm³ (range 920 to 1920 mm³). The average splenic volume after PSE was 1211±235 mm³ (range 710 to 1750 mm³). Percentage decrease in splenic volume was 23.4% ± 5.4% (range 7.8 to 30.7%). Comparative analysis of splenic volume before and after splenic embolization showed highly significant decrease ($p<0.001$) (Fig 7,8).

Table (1): ***Laboratory Investigations Before and after PSE***

	Before	*2weeks*	*2 months*	*6 months*
Platelet counts (1000/mm³)	48.762 (±16.5)	293.470 (±34.3)	251.230 (±23.5)	235.330 (±26.7)
TLC(/ mm³)	3.1 (±0.7)	10.5 (±3.6)	7.6 (±1.6)	6.3 (±1.1)
Hemoglobin (gm/dl)	10.2 (±1.9)	10.9 (±1.6)	11.1 (±1.1)	13.7 (±1.2)
Prothrombin conc. (%)	47.66 (±12.2)	52.21 (±17.5)	55.29 (±11.5)	53.24 (±19.5)
Serum albumin (gm/dl)	2.83 (±0.52)	2.72 (±0.6)	2.91 (±0.71)	2.88 (±0.5)
Bilirubin (mg/dl)	1.89 (±0.32)	2.17 (±0.67)	1.53 (±0.43)	1.77 (±0.53)

Table (2): ***Splenic volume before and after PSE***

	Before PSE	*After PSE*
Splenic volume (cm³)	1585±250 mm³	1211±235

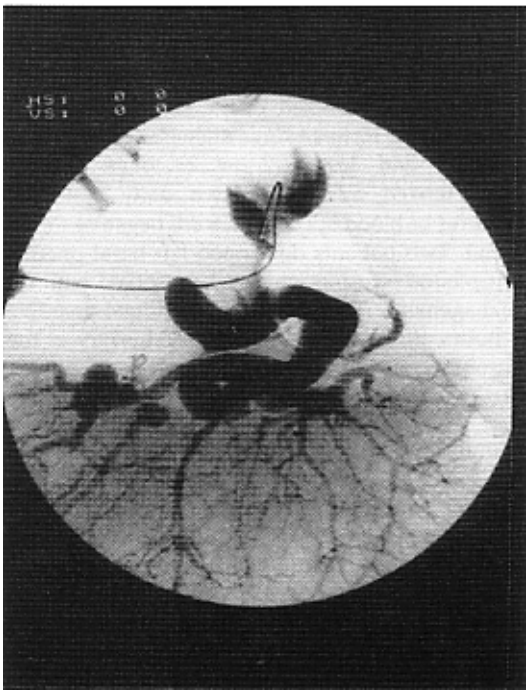

Fig .(1) :

a- ***Pre-embolization angiography . Markedly dilated tortuous splenic artery***

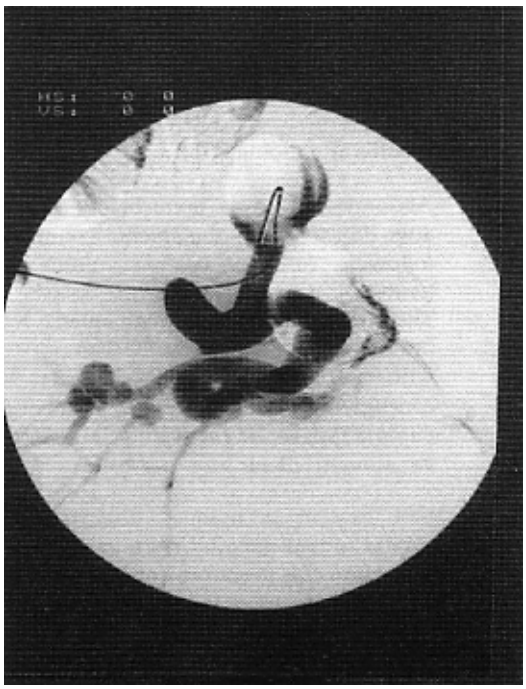

Fig .(1) :

b- ***Post-embolization angiography. Marked reduction in vascularity more in upper part.***

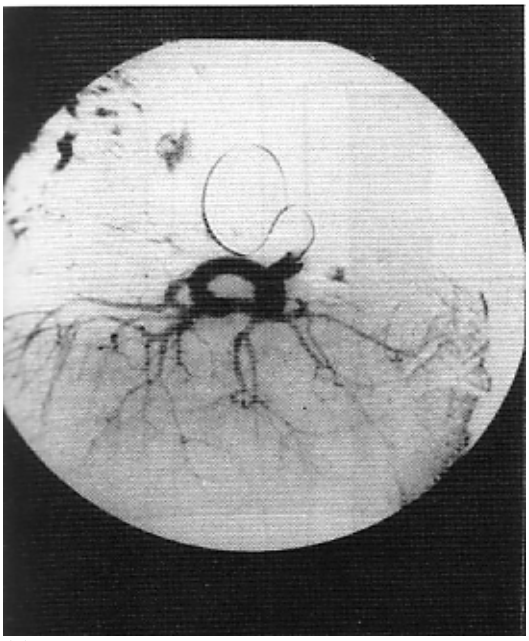

Fig .(2) :
a- *Pre-embolization angiography.*

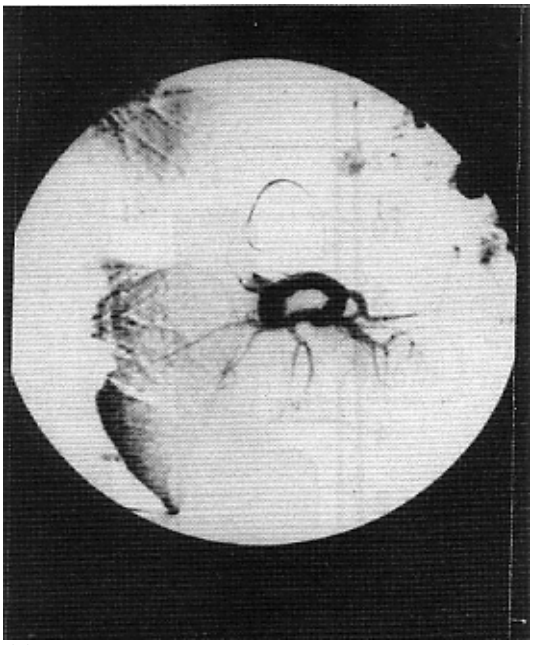

Fig .(2) :
b- *Post-embolization angiography Marked reduction in vascularity, more in lower part.*

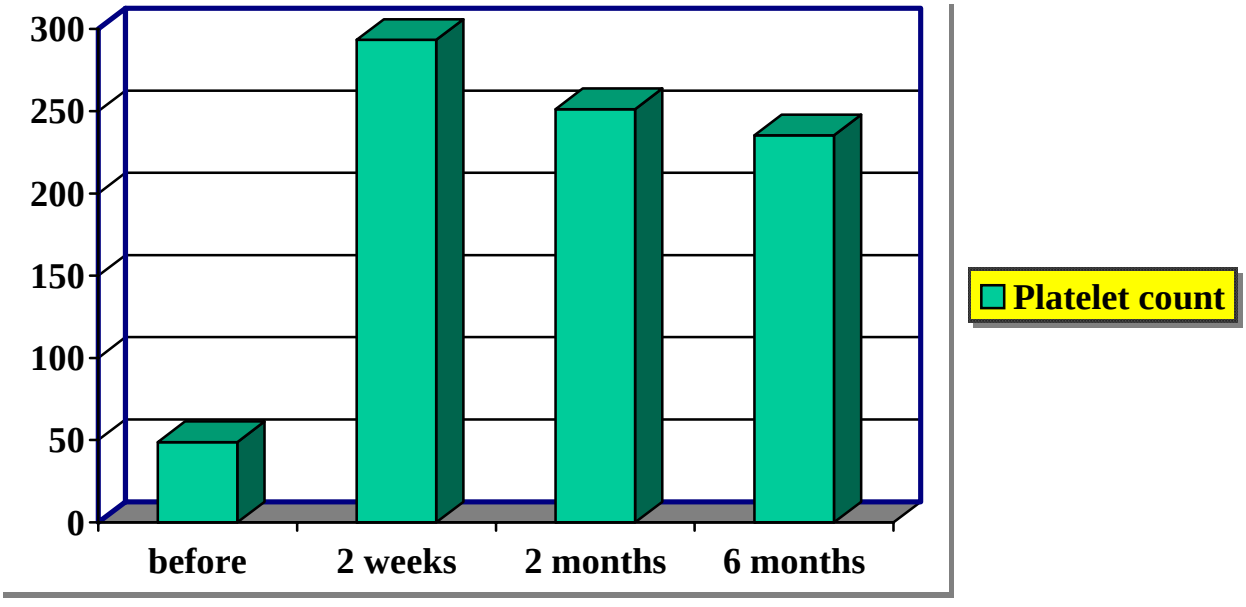

Fig. (3): Platelet counts (1000/mm^3) before and after PSE

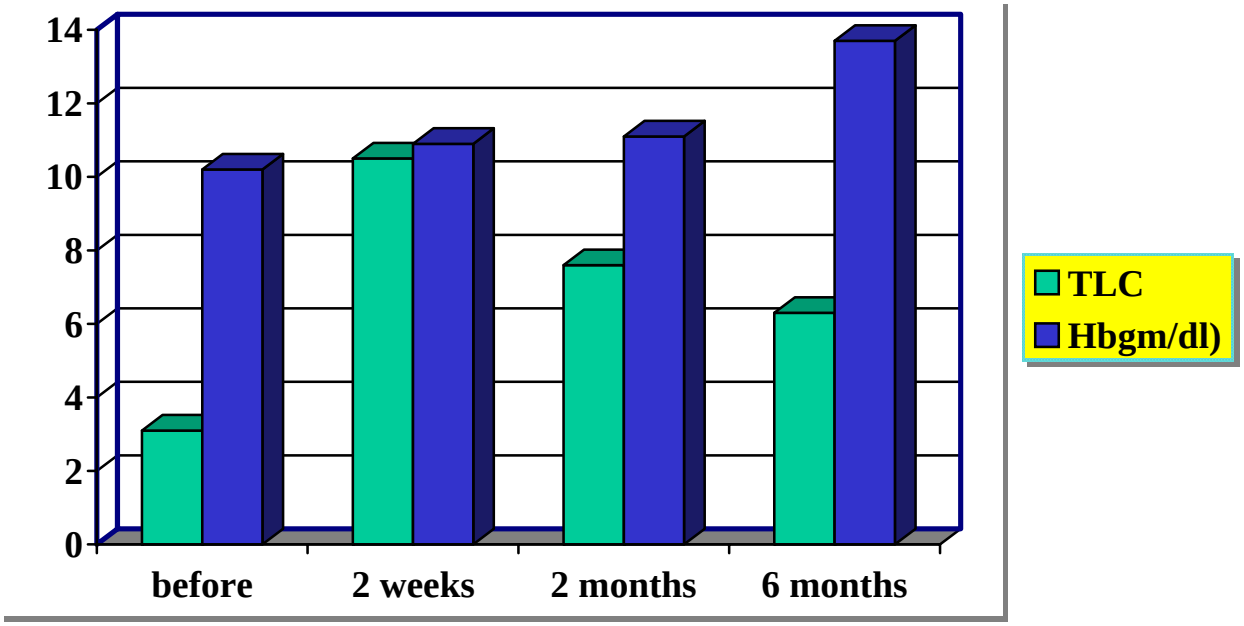

Fig.(4) : TLC((mm³), and Hb(gm/dl) before and after PSE

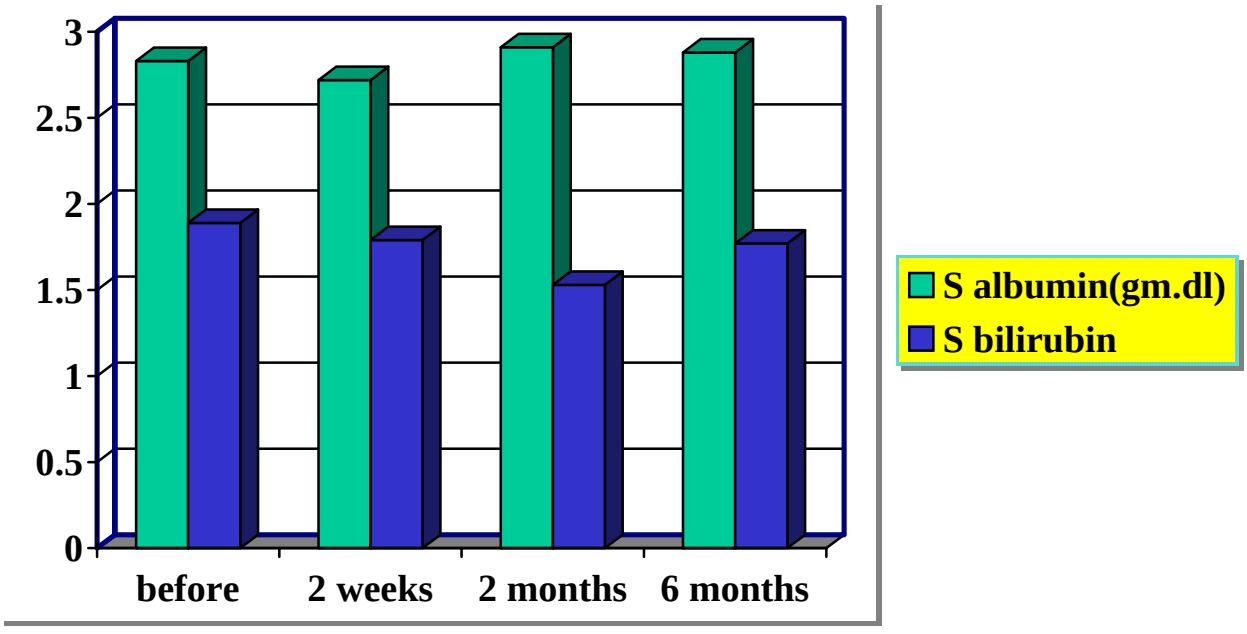

Fig. (5) : S albumin & Sbilirubin before and after PSE

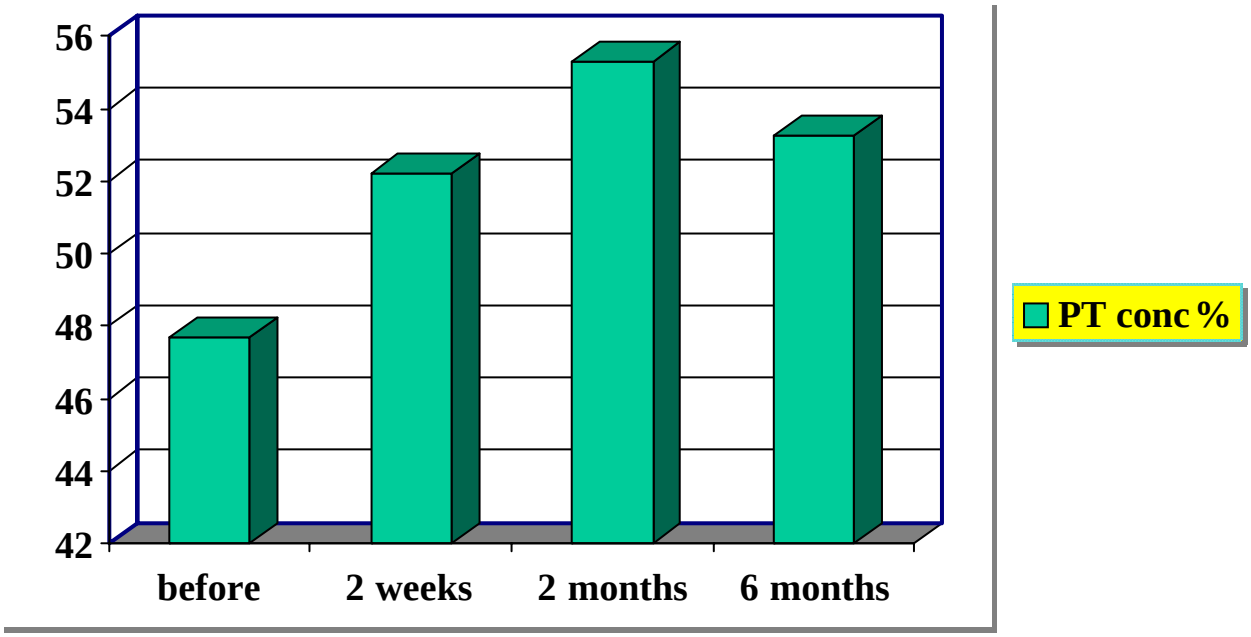

Fig. (6) : Prothrombin conc% before and after PSE

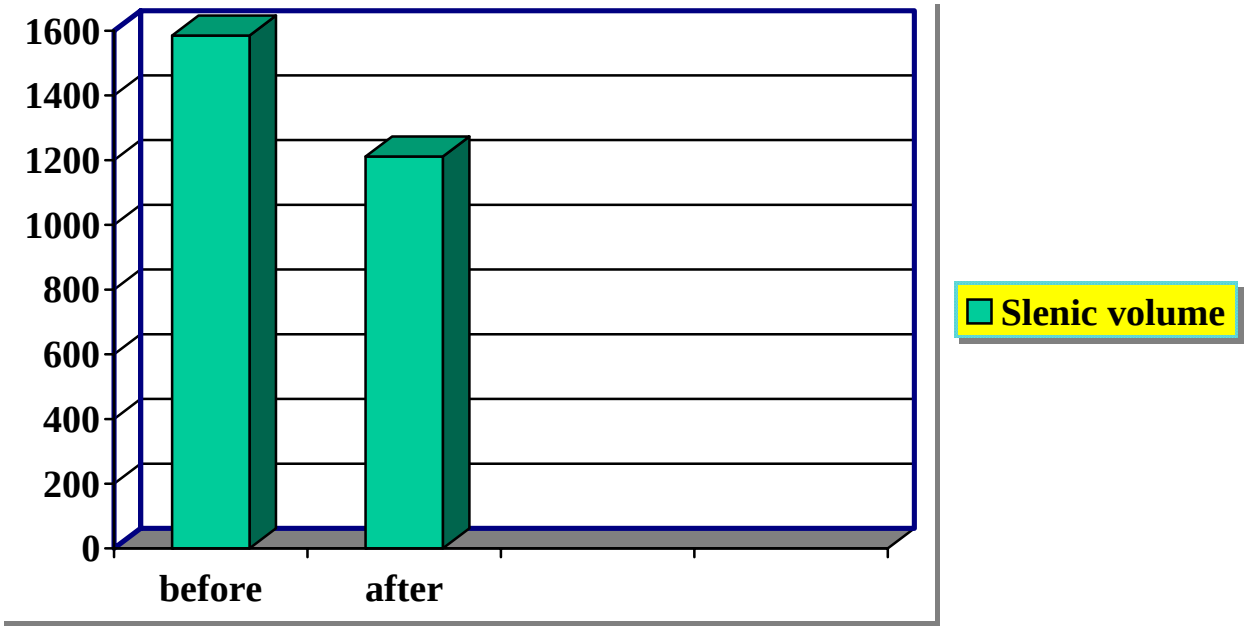

Fig. (7) : Splenic volume before and after PSE

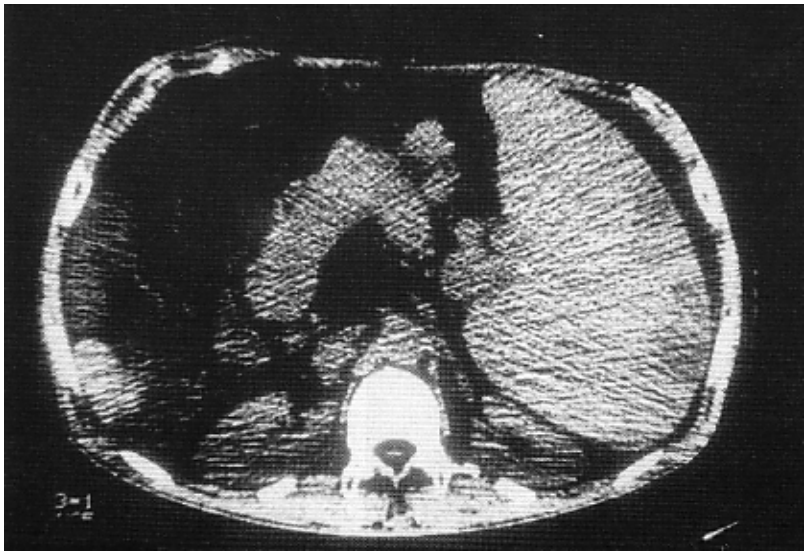

Fig . (8) : Post-embolization CT, shows multiple, small hypodense areas of subcapsular infarctions.

DISCUSSION

Splenomegaly is a frequent finding in patients with liver disease. It is usually asymptomatic but may cause hypersplenism. Thrombocytopenia is the most frequent manifestation of hypersplenism and may contribute to portal hypertension related bleeding [10]. Although surgical splenectomy constitutes effective treatment of hypersplenism, it has major drawbacks: it does not control variceal bleeding, except in the rare circumstances of left-sided PHT; it jeopardizes future shunt options by removal of the splenic vein; and for liver transplant candidates, it makes the definitive surgery more difficult. In addition, splenectomy carries significant postoperative morbidity and long-term risk of overwhelming infection in 1 to 2% of patients [11]. So there is consensus that total splenectomy should be avoided whenever possible in favor of more conservative and surgical approaches [12].

Initial attempts at splenic embolization aimed at total medical splenectomy, but resulted in multitude of serious complications, including death [13]. More recently better results have been obtained by means of modified techniques aimed at partial splenic embolization, combined with sterile technique and coverage with intravenous antibiotics before and after PSE [14].

The clinical course in our patients- fever and abdominal pain after PSE- was similar to that described by Sharma et al 1995, and Sangro et al 1993 [4,5].

Approximately 30% of total platelets are pooled in normal spleen, this rate increases with the development of splenomegaly, and the increased pool size is thought to result in a marked decrease of platelet counts in peripheral blood. Aoki et al 1993[15], investigated platelets kinetics in patients with liver cirrhosis using 111 indium-tropolone labeled platelets, and they reported platelet counts had a positive relationship to the life span of a platelet, but had a negative relationship to platelet associated IgG (PA-IgG) and volume of the spleen.

In our study, platelet counts were significantly increased following PSE ($p<0.001$). Sakata et al 1996 [16], proved an increase in platelet count, and a decrease in PA-IgG and suggested an improvement in the immunological mechanism following PSE, but they were unable to suggest reasons why WBC counts increase, and why there was not a strong efficacy for RBCs.

Recently the discovery of the specific cytokine thrombopoietin, which is predominantly produced by hepatocytes, the missing link hepatocellular function and thrombopoiesis was found [17].

Splenic volume in patients with hypersplenism is variable. In our study, there was a significant decrease in splenic volume after PSE, and the percentage of decrease was 23.4% ($p<0.001$). Watanabe et al, 1996 [18] observed that the spleen enlarged to 110% to 138% of the pre-PSE volume 1 to 2 weeks after PSE, probably owing to necrosis and edema of the surrounding splenic parenchyma. Marked expansion of the splenic capsule could result in rupture. Accordingly, patients should be strictly protected against blunt trauma to the upper abdomen for approximately

4 weeks after PSE. Then the splenic size decreased gradually, owing to resorption of the necrotic tissue.

Neither splenectomy nor splenic embolization predictably decreases portal pressure, because a compensatory increase in superior mesenteric venous flow often occurs when splenic arterial blood flow is decreased. However reversal of Thrombocytopenia may contribute to hemostasis, and decreased bleeding after PSE may occur by this mechanism [19].

Given the safety, efficacy, and advantages of PSE, it should be considered a valid alternative treatment of hypersplenism and the treatment of choice for selected patients with hypersplenism caused by PHT. Among other advantages, it is relatively easy to perform, has minimal morbidity, the splenic vein is preserved, and a portion of the splenic parenchyma remains intact to carry on the immunologic roles.

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