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BRIEF ARTICLE

Total embolization of the main splenic artery as a supplemental treatment modality for hypersplenism

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Abstract

AIM: To study the safety and feasibility of total embolization of the main splenic artery as a supplemental treatment modality for hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis.

METHODS: Fifteen consecutive patients with hypersplenism due to cirrhosis were enrolled in this study from January 2006 to June 2010. All patients underwent total embolization of the main splenic artery. Clinical symptoms, white blood cell (WBC) and platelet (PLT) counts, splenic volume, and complications of the patients were recorded. The patients were followed up for 1 and 6 mo, and 1, 2, 3 years, respectively, after operation.

RESULTS: Total embolization of the main splenic artery was technically successful in all patients. Minor complications occurred in 13 patients after the procedure, but no major complications were found. The WBC and PLT counts were significantly higher and the residual splenic volume was significantly lower 1 and 6 mo, and 1, 2, 3 years after the procedure than before the procedure ($P < 0.01$). Moreover, the residual splenic volume increased very slowly with the time after embolization. All patients were alive during the follow-up period.

CONCLUSION: Total embolization of the main splenic artery is a safe and feasible procedure and may serve as a supplemental treatment modality for hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis.

Key words: Liver cirrhosis; Hypersplenism; Coil embolization; Splenic artery

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INTRODUCTION

Partial splenic embolization (PSE) is a non-surgical procedure for hypersplenism resulting from hepatic disease and can thus avoid the disadvantages of splenectomy[1]. It has been shown that PSE can increase peripheral blood cell counts[2-5]. However, PSE often results in a number of complications, including daily intermittent fever, abdominal pain, nausea, vomiting, postemboliza-

tion syndrome, splenic abscess and rupture, pneumonia, refractory ascites, pleural effusion, and gastrointestinal bleeding[2-8].

Total embolization of the splenic artery is a safe and effective procedure for splenic artery aneurysms[9-13]. Moreover, stainless steel spring coils are used to embolize the main branch of splenic artery to increase the platelet (PLT) count before splenectomy[14]. To date, no report is available on the treatment of hypersplenism with total embolization of the main splenic artery. The present study was to study the safety and feasibility of total embolization of the main splenic artery for hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis.

MATERIALS AND METHODS

Patients

Fifteen consecutive patients (10 males and 5 females with a mean age of 50.07 ± 8.98 years, ranging 38-60 years) with hypersplenism due to cirrhosis were enrolled in this study from January 2006 to June 2010 and subsequently underwent computed tomography (CT) follow-up at our hospital. The causes of cirrhosis were hepatitis B virus (HBV) infection in 13 patients and hepatitis C virus (HCV) infection in 2 patients. The patients were diagnosed as hypersplenism based on their history, clinical laboratory tests, ultrasonography and CT. The protocol was approved by The Ethics Committee of Fudan University and the patients provided their written informed consent.

The inclusion criteria were those with hypersplenism, HBV/HCV-related active cirrhosis, neutropenia (neutrophil count $\leqslant 2.0 \times 10^9$ cells/L), thrombocytopenia (PLT count $\leqslant 50 \times 10^9$ cells/L) or both, and follow-up time > 2 years. Those with severe jaundice [serum total bilirubin (TB) level $\geqslant$ 81.4 μmol/L] or spontaneous bacterial peritonitis were excluded from the study.

Hypersplenism was classified as Child-Pugh class A in 10 patients, class B in 3 patients, and class C in 2 patients. The demographics of these patients are summarized in Table 1.

Endovascular techniques

Metallic coils and gelfoam were used as embolization materials, either alone or in combination. In general, the embolization coils used in this series were standard 0.089-cm (0.035-in.) fibered coils, microcoils (Tornado; Cook Inc., Bloomington, IN, USA).

Embolization was performed in all patients *via* the femoral artery. Selective angiography of the celiac trunk, splenic artery, and superior mesenteric artery was performed *via* the right femoral artery with a 5-Fr diagnostic catheter (Cook). Patency of the collateral arteries connected to the hilar splenic artery from the left gastric artery or from the gastroepiploic artery on a celiac arteriogram was monitored to avoid total splenic infarction. Total embolization of the main splenic artery was performed after confirmation of these connections.

All embolization procedures were performed by 2 experienced interventional radiologists. Details of the coiling procedures have been described previously[9,11,15]. Selective splenic artery, celiac, and superior mesenteric artery angiograms were performed to confirm occlusion of the main splenic artery and patency of the collateral arteries after embolization. Preoperative antibiotic prophylaxis was used routinely for 3 d. Following embolization, patients were monitored and antibiotics were continued after the procedure for several days to avoid infectious complications.

Follow-up protocol and postoperative outcome evaluation

All patients were followed up at our outpatient clinic. Peripheral blood cell parameters, including white blood cell (WBC), PLT, and red blood cell counts, were monitored at different time points prior to the procedure and on days 3, 14, and 30 after the procedure, then at 6-mo intervals during the 3-year follow-up period. To determine the effect of embolization on liver function, serum levels of aspartate aminotransferase, alanine aminotransferase, TB, and albumin were measured and prothrombin time was calculated at the same follow-up time points as above before and after the procedure. The procedure-related frequency and type of complications were recorded.

Abdominal CT scans were routinely performed before and 2 wk after the procedure, and then every 6 mo during the follow-up. Based on enhanced CT images, the pretreatment splenic volume and the post-embolization residual splenic volume were measured and compared on a workstation (Siemens Syngo MMWP VEZIA) using the volumetric analysis software. The infracted splenic volume (mL) was measured by subtracting the noninfarcted splenic volume from the pretreatment splenic volume. The splenic infarction rate was calculated by dividing the infarcted splenic volume by the pretreatment splenic volume (× 100%).

The procedure-related complications were divided into major and minor ones. Major complications associated with the procedure, including splenic abscess, splenic rupture, pneumonia, refractory ascites or pleural effusion, gastrointestinal bleeding, rupture of varices, and hepatic failure, were defined as complicated disease requiring surgical intervention or prolonged postoperative hospital stay time of more than 30 d. Minor complications, including abdominal pain, fever, vomiting, abdominal fullness, and appetite loss, were defined as those that lead to no consequential events and can be tolerated by the patients.

Statistical analysis

All data were expressed as mean ± SD. Changes in WBC and PLT counts after PSE were evaluated by paired *t* test. The variables between the 2 groups were compared by Mann-Whitney test, χ^2-test or Fisher's exact test when ap-

Table 1 Outcomes of total embolization of the main splenic artery in 15 patients

Pa./age (yr)/sex	Virus	Child-Pugh	WBC count ($\times 10^9$/L)						Platelets ($\times 10^9$/L)						Splenic volumn (cm^3)						Compli-cation	Follow-up (mo)	Out-comes
			Pre-EM	1 mo	6 mo	1 yr	2 yr	3 yr	Pre-EM	1 mo	6 mo	1 yr	2 yr	3 yr	Pre-EM	1 mo	6 mo	1 yr	2 yr	3 yr			
1/48/F	B	A	1.3	7.8	6.5	5.3	4.9	5.1	35	181	142	136	132	128	829	367	265	265	312	312	AP, F, V	52	Alive
2/52/M	B	B	1.8	9.8	5.3	5.6	5.6	4.4	24	191	156	148	145	139	768	258	326	326	326	367	F, V	48	Alive
3/60/M	B	A	1.6	8.6	6.5	6.3	4.2	6.4	33	233	185	157	132	142	869	369	328	328	328	305	AP, F	47	Alive
4/51/M	B	A	1.8	8.3	5.4	7.2	6.2	4.6	45	173	158	156	148	132	815	289	289	287	250	285	F, V	45	Alive
5/34/F	B	A	1.1	7.8	7.2	6.8	5.2	4.5	48	165	161	152	153	148	724	366	242	235	235	235	AP, V	41	Alive
6/49/M	B	C	1.4	8.6	4.8	4.6	4.4	4.8	43	144	43	139	132	123	698	278	278	278	278	278	AP, V	40	Alive
7/50/F	B	A	1.5	8.5	5.8	4.8	4.6	4.2	25	156	145	146	134	129	758	325	325	312	314	314		37	Alive
8/59/M	C	B	1.1	7.8	6.3	6.7	7.3	4.8	36	143	145	132	128	132	846	319	319	310	310	310	AP, F, V	36	Alive
9/28/M	B	A	1.5	9.6	6.0	5.1	5.2	5.3	48	213	167	164	156	147	687	247	247	247	249	276	AP, F,	36	Alive
10/55/M	B	A	0.8	7.3	6.9	5.6	5.4	4.5	32	121	125	131	128	124	784	305	305	298	320	320	AP, F, V	42	Alive
11/58/F	B	C	1.7	6.8	8.5	6.8	3.9	4.2	26	163	184	146	139	132	755	362	362	362	362	345	AP, F	38	Alive
12/46/M	B	A	0.9	5.3	4.8	3.8	4.5		48	146	135	141	136		732	247	285	285	285		AP, F, V	28	Alive
13/58/F	C	A	1.2	8.2	3.8	4.8	5.0		32	153	138	146	134		848	328	328	318	315		AP, F	30	Alive
14/55/M	B	B	1.4	8.3	5.2	4.5	4.4		35	164	176	163	165		683	361	356	346	327			26	Alive
15/48/M	B	A	1.6	8.8	6.3	6.2	6.4		38	241	220	168	137		752	298	305	315	315		AP, F	24	Alive

Pre-EM: Pre-embolization; AP: Abdominal pain; F: Fever; V: Vomiting; WBC: White blood cell.

propriate. All statistical analyses were performed using the SPSS package, version 13.0 (SPSS, Chicago, Illinois, USA).

RESULTS

Primary procedure results

Total embolization of the main splenic artery was technically successful in all patients, with no procedure-related complications. The mean postoperative hospital stay time was 8.40 ± 2.53 d (range, 5-15 d) after the procedure and the 30 d mortality rate was zero.

Minor complications occurred in 13 patients with no major complications found after the procedure. The most frequent side effects were abdominal pain, fever, and nausea. Prolonged fever, lasting over 15 d after the procedure, developed in 1 case. These side effects were controlled after conservative therapy.

Changes in peripheral blood cell counts after embolization

The outcomes of total embolization of the main splenic artery in 15 patients are shown in Table 1. All patients were assessed 1 and 6 mo, and 1, 2, 3 years after the procedure. The patients were followed up for 38.0 ± 8.32 mo (range, 24-52 mo). The mean WBC count increased from 1.4 (0.3) $\times 10^9$/L before the procedure to 8.1 (1.1) $\times 10^9$/L, 6.0 (1.2) $\times 10^9$/L, 5.6 (1.0) $\times 10^9$/L, 5.1 (0.9) $\times 10^9$/L, and 4.8 (0.9) $\times 10^9$/L, respectively, 1 and 6 mo, and 1, 2, 3 years after the procedure ($P < 0.01$).

The mean PLT count increased from 36.5 (8.3) $\times 10^9$/L before the procedure to 172 (34.1) $\times 10^9$/L, 152 (38.7) $\times 10^9$/L, 148 (11.6) $\times 10^9$/L, 140 (11.1) $\times 10^9$/L, and 134 (8.6) $\times 10^9$/L, respectively, 1 and 6 mo, and 1, 2, 3 years after the procedure ($P < 0.01$).

Changes in splenic volume after embolization

The mean splenic volume decreased from 769.87 (60.51) cm^3 before the procedure to 314.60 (44.52) cm^3, 304.0 (36.10) cm^3, 300.80 (35.20) cm^3, 301.73 (35.17) cm^3, and 306.00 (32.02) cm^3, respectively, 1 and 6 mo, and 1, 2, 3 years after the procedure ($P < 0.05$). During the follow-up, the residual splenic volume in these patients increased a very slowly. The mean infarction rate of the spleen was 60% (range, 59%-61%) 3 years after the procedure. No death occurred during the follow-up.

DISCUSSION

The results of his study show that total embolization of the main splenic artery with coils is a safe and feasible procedure for hypersplenism due to liver cirrhosis. The peripheral blood cell parameters including WBC and PLT counts increased significantly during the follow-up and the residual splenic volume increased very slowly after embolization.

Hypersplenism is a well-known complication of portal hypertension due to cirrhosis, which can result in thrombocytopenia and/or leukocytopenia. Splenectomy can eliminate hypersplenism-induced blood cell destruction, but the incidence of severe complications after splenectomy is 9.6%-26.6% whether laparoscopy or open splenectomy is performed[16-18]. In addition, splenectomy is often associated with an increased long-term risk of septic events[16-18].

Although PSE is an effective alternative to splenectomy to increase the peripheral blood cell counts[1-5], severe complications of PSE, such as splenic abscess, splenic rupture, pneumonia, refractory ascites or pleural effusion, and gastrointestinal bleeding[6-8], greatly limit its use. Furthermore, the complications of PSE are correlated with the infracted splenic volume. In addition, when 50% or less than 50% of the spleen is embolized, hypersplenism would relapse shortly after PSE[2,8]. Therefore, to ensure a sustained increase in PLT and leukocyte counts,

the splenic infarction rate should be greater than 50%[8], which, however, inevitably results in severe complications. To increase the PLT and leukocyte counts and reduce the rate of severe complications, total embolization of the main splenic artery was performed for hypersplenism due to liver cirrhosis in the present study.

The key procedure for reducing the severe complications and ensuring the sustained increase in PLT and leukocyte counts is to confirm the patency of collateral arteries connected to the hilar splenic artery from the left gastric artery or from the gastroepiploic artery. If these connections are absent or incomplete, total embolization of the main splenic artery should not be performed because the procedure may result in more severe complications.

When the main splenic artery is completely embolized, the main blood flow supplying the spleen is stopped, but the collateral arteries connected to the hilar splenic artery from the left gastric artery or from the gastroepiploic artery may provide a small amount of blood for the spleen to avoid complete infarction of the spleen. Thus, most of the spleen should be embolized with reservation of a partial normal spleen. Thus, the PLT and leukocyte counts increase after the procedure, and the occurrence of severe complications can be circumvented. In this study, the safety and feasibility of total embolization for hypersplenism of the main splenic artery were studied.

As compared with PSE, total embolization of the main splenic artery has the following advantages, including a low risk of procedure-related complications, persistent maintenance of normal WBC and PLT counts, and a very slow increase in residual splenic volume.

Although these results are encouraging, this study had the following limitations. First, it was not a comparative study and the number of patients was small with no control group. Future randomized multicenter trials comparing PSE with total embolization are needed to determine their long-term clinical efficacy and risk of complications. Second, total embolization could not be performed in patients with no or incomplete collateral arteries.

In conclusion, total embolization of the main splenic artery is a safe and feasible procedure for hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis and may serve as a supplemental treatment modality for it. Further clinical trials and expanded follow-up studies are needed to confirm its safety.

COMMENTS

Background

Partial splenic embolization (PSE) is a non-surgical procedure for hypersplenism resulting from hepatic disease, thus avoiding the disadvantages of splenectomy. However, after PSE, patients often experience complications, including daily intermittent fever, abdominal pain, nausea, vomiting, and postembolization syndrome.

Research frontiers

Total embolization of the splenic artery has been widely used in treatment of splenic artery aneurysms, but no report is available on treatment of hypersplenism with it. In this study, total embolization of the main splenic artery for hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis was studied.

Innovations and breakthroughs

Total embolization of the main splenic artery was devised for the treatment of hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis. All procedures were performed under fluoroscopic control. This is the first study reporting the treatment of hypersplenism with total embolization of the main splenic artery.

Applications

Total embolization of the main splenic artery is a safe and feasible procedure and may serve as a supplemental treatment modality for hypersplenism with thrombocytopenia or leukocytopenia accompanying liver cirrhosis with a low complication rate and a good mid-term clinical efficacy.

Terminology

Hypersplenism is a well-known complication of portal hypertension due to cirrhosis, which can result in thrombocytopenia and leukocytopenia.

Peer review

The finding in this study is interesting. Further study is needed confirm its safety in a much larger series of patients.

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