Case Report

Stepwise partial splenic embolization for portal hypertension based on a new concept: Splanchnic caput Medusae

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A B S T R A C T

Management of splenomegaly with thrombocytopenia is important in the treatment of portal hypertension. We propose a new concept: “Splanchnic Caput Medusae” in which enlarged spleen is her face and portal collateral pathways are her snake hairs. We report 2 demonstrable cases who were treated based on this new concept. Case 1 with refractory esophageal varices and splenomegaly was treated by stepwise partial splenic embolization (PSE) and endoscopic injection sclerotherapy with ligation. Spleen/liver volume ratio changed from 0.33 to 0.10. Hepatic venous pressure gradient changed from 19 to 14 mmHg. Case 2 with mesenteric shunt and splenomegaly was treated by stepwise PSE and retrograde obliteration. Spleen/liver volume ratio changed from 0.70 to 0.05. Hepatic venous pressure gradient changed from 11 to 7 mmHg. In these 2 cases, 3D-CT reconstruction images after treatment revealed that spleen-portal system reversed almost to normal form. We conclude that splenomegaly and portal collateral pathways could be considered as “Splanchnic Caput Medusae” and have to be treated by stepwise PSE.

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Introduction

While control of bleeding from esophagogastric varices became easy by endoscopic treatment such as sclerotherapy or variceal ligation, splenomegaly is often left without being treated. Previous studies have reported splenic transforming growth factor beta 1 (TGF-β1) and endothelin production in liver cirrhosis and emphasized their critical roles in the development of liver fibrosis and portal hypertension [1,2]. Furthermore, some studies revealed that platelets associated with hepatocyte growth factor release have strong effect on

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promoting liver regeneration, and thrombocytopenia exacerbates liver fibrosis [3,4] (Fig. 1).

We have reported that partial splenic embolization (PSE) not only increases platelet count, but also reduces the splenic venous blood flow volume, portal venous pressure and spleen/liver volume ratio [5–7]. Management of splenomegaly with thrombocytopenia is important in the treatment of portal hypertension [8,9]. We propose a new concept: “Splanchnic Caput Medusae” in which enlarged spleen is considered as her face and portal collateral pathways as snake hairs (Fig. 2). In the proposed new concept: “Splanchnic Caput Medusae,” PSE is considered as the treatment of Medusae’s face. Here, we report 2 demonstrable cases who were treated based on this new concept.

Case report

Case 1: Refractory esophageal varices with splenomegaly

A 74-year-old female was referred to the department of surgery at our hospital for a refractory esophageal varices and splenomegaly with nonalcoholic steatohepatitis (NASH) related cirrhosis. Three months ago, she had undergone endoscopic variceal ligation for bleeding from esophageal varices. After 2 sessions of endoscopic injection sclerotherapy; the forms of esophageal varices were unchanged.

She had a past medical history of cerebral infarction, hyperlipidemia, and diabetes mellitus. She was on anticoagulant, lipid-lowering drug and oral antidiabetic.

On admission, her height was 154 cm, body weight was 61 kg, and body mass index was 25.7 kg/m². She did not have jaundice and her consciousness was lucid. Laboratory studies revealed hemoglobin 10.8 g/dL (normal range, 13.5-17.4); total leukocyte count 2380 /μL (3500 - 8000 /μL); platelet count 6.9 × 10⁴ /μL (12.3 - 33.1 × 10⁴ /μL); total bilirubin 1.4 mg/dL (0.3 - 1.3 mg/dL); albumin 3.9 g/dL (3.8 - 5.0 g/dL); aspartate transaminase 46 U/L (10 - 32 U/L); alanine transaminase 35 U/L (5 - 27 U/L); prothrombin time (PT) 78.0% (70 - 130 %); Mac-2 binding protein glycosylated isomers 4.75 COI (1+); α-Fetoprotein 2.7 ng/mL (0-20 ng/mL); protein induced by vitamin K absence or antagonist-II 13 mAUI/mL (<40 mAUI/mL); Hemoglobin A1c 6.5 % (4.6 - 6.2); total cholesterol 173 mg/dL (130 - 220 mg/dL); triglyceride 98 mg/dL (50-170 mg/dL); low density lipoprotein cholesterol 89 mg/dL (70 - 139 mg/dL); serum ammonia (NH3) 62 μg/dL (12 - 66 μg/dL). Retention rate of indocyanine green at 15 minutes was 13 % (<10 %). Child-Pugh score was 5 and the class was A. Hepatitis B surface antigen and hepatitis C virus antibody were negative. Antimitochondria antibody and antinuclear antibody were negative. These data indicated NASH related cirrhosis with thrombocytopenia.
Endoscopy confirmed large and tortuous esophageal varices (Fig. 3a). Abdominal ultrasonography and contrast-enhanced CT showed hepatosplenomegaly. Three-dimensional computed tomography (3D-CT) reconstruction images of the liver, spleen, and portal system demonstrated that the esophageal varices were supplied by the left gastric vein via the cardiac venous plexus (Figs. 4a and 5a). The spleen volume was 688 mL, the liver volume was 2073 mL and spleen/liver volume ratio [7] was 0.33 (Fig. 4a). According to “Splanchnic Caput Medusae” concept, enlarged spleen was regarded as her face and esophageal varices as her snake hairs.

Because the patient was elderly, stepwise PSE was attempted to minimize the side effects of PSE [5]. Hepatic venous cannulation was performed and hepatic venous pressure gradient (HVPG) was 19 mmHg (normal range, 1-5 mmHg). First PSE using gelatin sponge and microcoils was performed to control portal hypertension to reduce the HVPG (Figs. 6a and b). The HVPG immediately after first PSE was 18 mmHg. 3D-CT 6 days after first PSE revealed that the viable spleen volume decreased to 455 mL and corrected spleen/liver volume ratio was 0.26. Two months later, second PSE was attempted. The HVPG reduced to 14 mmHg and the viable spleen volume decreased to 178 mL and corrected spleen/liver volume ratio was 0.10 (Fig. 6c) One months after second PSE, platelet count increased to 12.5 × 10^4 /μL.

Four months after second PSE; endoscopic injection sclerotherapy with ligation (EISL) of esophageal varices was attempted [10]. 5% ethanolamine olate with iopamidol (5%HIO) 13ml in total was injected into the cardiac venous plexus and the root of the left gastric vein for 15 minutes under fluoroscopy [11] (Fig. 5b). Just after removal of the injection needle, 6 variceal ligation were added to stop the variceal blood flow. 3D-CT 1 week after EISL revealed sufficiently obliterated esophageal varices and cardiac venous plexus (Figs. 4 and 5). By portal view of 3D-CT before and after EISL, we can identify the esophageal varices, cardiac venous plexus and left gastric vein on endoscopic varicogram (Figs. 5a–c). Oblique view of 3D-CT after PSE and EISL revealed that spleen-portal system reversed almost to normal form (Fig. 4b). Endoscopy 2 weeks after EISL revealed distinct collapse of esophageal varices (Fig. 3b).

Case 2: Mesenteric shunt with hyperammonemia and splenomegaly

A 54-year-old female was referred to the department of surgery at our hospital for hypersplenism and hyperammonemia with primary biliary cirrhosis. She had a past medical history of endoscopic injection sclerotherapy for esophageal varices 5 years ago.

On admission, she did not have jaundice and her consciousness was lucid. Laboratory studies revealed hemoglobin 10.3 g/dL (normal range, 13.5-17.4); total leukocyte count 2510 /μL (3500 ~ 8000 /μL); platelet count 6.0 × 10^6 /μL (12.3 - 33.1 × 10^6 /μL); total bilirubin 0.7 mg/dL (0.3 - 1.3 mg/dL); albumin 4.1 g/dL (3.8 - 5.0 g/dL); aspartate transaminase 27 U/L (10 - 32 U/L); alanine transaminase 12 U/L (5 - 27 U/L); PT 88.0% (70 - 130 %); Mac-2 binding protein glycosylated isoforms 3.13 COI (2+) (<1.00). Her serum NH3 was at 170 μg/dL (12 - 66 μg/dL). Indocyanine green at 15 minutes was 13 % (<10 %). Child-Pugh score was 5 and the class was A. Anti-mitochondria antibody was positive (160 times) (normal range, < 20 times) and anti-nuclear antibody was positive (160 times) (normal range, < 40 times). Hepatitis B surface antigen and hepatitis C virus antibody were negative. These data indicated primary biliary cirrhosis with thrombocytopenia and hyperammonemia.
Endoscopy confirmed a mild grade of portal hypertensive gastropathy without esophageal varices. Abdominal ultrasonography and contrast-enhanced CT showed splenomegaly and large mesenteric shunt. 3D-CT reconstruction images of the liver, spleen and portal system demonstrated large mesenteric shunt which was supplied by the inferior mesenteric vein and drained into the left renal vein via the left ovarian vein (Fig. 7a). The spleen volume was 811 ml, the liver volume was 1181 ml and spleen/liver volume ratio was 0.70. According to “Splanchnic Caput Medusae” concept, enlarged spleen was regarded as her face and mesenteric shunt as her big snake hair. Stepwise PSE was also planned for this case to reduce the side effects of PSE and retrograde obliteration,[12,13]. 3D-CT reconstruction images after first PSE revealed that the viable spleen volume decreased to 348 ml and corrected spleen/liver volume ratio was 0.30. HVPGs before and after first PSE were 11mmHg. Three months later, first PSE was attempted. The viable spleen volume decreased to 237 ml and corrected spleen/liver volume ratio was 0.20. At this time, HVPG measurement was not performed.

Three months after second PSE, retrograde obliteration for mesenteric shunt was attempted by using microcoils, 40 mL 50% glucose, 3.0 mL absolute ethanol (Fig. 7b).

However, 3 days after retrograde obliteration, hematemesis from portal hypertensive gastropathy bleeding occurred. Third PSE was attempted to reduce portal venous pressure. HVPG changed from 9 to 7mmHg by third PSE.

Seven months after the treatment, her serum NH3 was at 67 μg/dL and platelet count was 29.0 × 10^9 /μL. 3D-CT reconstruction images revealed that corrected spleen/liver volume ratio was 0.05 and spleen-portal system reversed almost to normal form (Fig. 7c).

Discussion

We reported 2 demonstrable cases who were treated by stepwise PSE based on a new concept: “Splanchnic Caput Medusae” in which enlarged spleen was considered as her face and portal collateral pathways as her snake hairs. This concept is completely different from a classic concept of Caput Medusae, in which abdomen is her face and perinavel dilated subcutaneous veins are her snake hairs [14]. The classic Caput Medusae sign is frequently mentioned in medical books as a sign of portal hypertension but dilated superficial epigastric veins are rarely seen in clinical practice.

The classic Caput Medusae sign in portal hypertension comes from monster Medusae in Greek myth. Medusae was once a beautiful woman. She offended Athena, because Poseidon loved her in Athena’s shrine. Athena changed Medusae’s
Fig. 5 – Portal view of 3D-CT reconstruction images and endoscopic varicography in case 1. 5a. Portal view of 3D-CT reconstruction images before treatment shows that the esophageal varices are supplied by the left gastric vein via the cardiac venous plexus (arrow). 5b. Endoscopic varicography during EISL shows the esophageal varices, cardiac venous plexus, and left gastric vein (arrow). 5c. Portal view of 3D-CT reconstruction images after EISL shows the root of left gastric vein. The esophageal varices and cardiac venous plexus are obliterated (arrow).

Fig. 6 – Celiac arteriography and stepwise PSE in case 1 *PSE = partial splenic embolization, **Sp volume = spleen volume, S/L ratio = spleen and/or liver volume ratio, HVPG = hepatic venous pressure gradient. 6a. Celiac arteriography before stepwise PSE shows splenomegaly. 6b. Celiac arteriography after first PSE shows 30% embolization of spleen. 6c. Celiac arteriography after second PSE shows 70% embolization of spleen.
hairs into snakes and made her face so hideous monster. All who looked at her were turned to stone. Perseus beheaded Medusae and presented her head to Athena. Athena used the Medusae’s head on her aegis. The Parisian pathologist Jean Cruveilhier, 1791-1874, attributed the authorship of this clinical sign to Marco Aurelio Severino, 1580-1656, a Neapolitan surgeon. In 1632, Severino published the first textbook of surgical pathology, and described the appearance of dilated periumbilical veins resembled Caput Medusae. In the world of the art, Michelangelo Merisi da Garavaggio, 1573-1610 painted “Caput Medusae.” Peter Paul Rubens, 1577 – 1640, who was affected by Garavaggio, painted more terrible “Caput Medusae”. Severino, Caravaggio and Rubens are same generation, and they are thought to have been the cultural background that is easy to conscious of Caput Medusae in those days. For Severino in the 17th century, Cruveilhier in the 19th century, the classic Caput Medusae sign would be an important physical finding as endo-stage liver disease. However, nowadays, we can diagnose portal hypertension by various modalities before classic Caput Medusae sign appears. The classic Caput Medusae sign expresses only a part of portal hypertension. Here, we propose a new concept: “Splanchnic Caput Medusae” in which enlarged spleen is her face and portal collateral pathways are her snake hairs. This concept expresses the whole condition of portal hypertension. All who looked at monster Medusae were turned to stone. The liver located on the anti-side of spleen (face of Medusae) becomes hard like a stone in portal hypertension.

Spleen is a large, vascular lymphatic organ lying in the upper part of the abdominal cavity on the left side. In normal state spleen/liver volume ratio is 0.1, which is well balanced and beautiful when we see in 3D-CT reconstruction images (Figs. 4b and 7b). The spleen is a storage organ for red blood cells and platelets. Spleen acts as a blood filter, identifying and destroying effete red blood cells as well as participating in the immune defense of the body because of the large number of macrophages present in it [15].

During liver fibrosis, hepatic stellate cells and Kupfer cells act as the initial effectors of collagen deposition and inflammation modulation with the aid of the pro-fibrogenic cytokine TGF-β1 [16-18]. Previous studies have reported splenic TGF-β1 production in liver cirrhosis with hypersplenism, and emphasized its critical role in the development of hepatic fibrogenesis [1]. Splenic macrophages have been suggested as one source of TGF-β1. Endothelin contributes to stellate cell activation and fibrogenesis [19]. The spleen is one of the major sites of endothelin release in cirrhotic patients [2]. On the other hand, platelets associated with hepatocyte growth factor release have strong effect on promoting liver regeneration, and thrombocytopenia exacerbates liver fibrosis [3,4]. Therefore, we emphasize that the management of splenomegaly with thrombocytopenia is the core in the treatment of portal hypertension.

In liver cirrhosis, spleen/liver volume ratio increases [7]. PSE not only increases platelet count, but also reduces the splenic venous blood flow volume, portal venous pressure, and spleen/liver volume ratio [5,6]. Surgical techniques such as Sugiura procedure [20] and Hassab’s operation [21] are some of the accepted surgical treatments with splenectomy. We think PSE is more preferable than splenectomy for the treatment of splenomegaly, because spleen/liver volume ratio after
splenectomy becomes 0.0. It is thought that the spleen of adult humans maintains spleen/liver volume ratio to 0.1 in a process of the long evolution. An overwhelming post-splenectomy infection is a fatal infection occurring after splenectomy [22].

The treatment of severe splenomegaly is invasive and has a risk of complication such as fever, abdominal pain, and splenic abscess etc. [23]. Stepwise PSE can solve this problem. In our 2 cases, post stepwise PSE courses were uneventful. The aims of stepwise PSE are to gradually reduce splenic volume, spleen/liver volume ratio, portal pressure, increase platelet count and reverse the spleen-portal system to normal form like beautiful woman Medusae before transformation.

The spleen does not suddenly become huge in clinical practice unlike a Greek myth. Treatment at the stage of mild to moderate splenomegaly is recommended. We conclude that splenomegaly and portal collateral pathways have to be treated in a good balance using stepwise PSE based on a new concept: “Splanchnic Caput Medusae”.

Patient consent statement

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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