AN UNUSUAL PRESENTATION OF INTRAHEPATIC ARTERIOPORTAL FISTULA WITH MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

Memduh Şahin[1], Harun Erdal[2], Kıvılcım Eren Erdoğan[3], Güldal Yılmaz[4], İbrahim Doğan[2], Selahattin Ünal[2]

[1]Mersin State Hospital Gastroenterology Department, Endoscopy Unit, Mersin

[2]Gazi University Gastroenterology Department, Ankara

[3]Çukurova University Pathology Department, Adana

[4]Gazi University Pathology Department, Ankara

ABSTRACT

Arterioportal fistula (APF) is a rare disorder of the mesenteric vasculature Patients with arterioportal fistula may present with complications, including portal hypertension (gastrointestinal bleeding and ascites), heart failure or intestinal ischemia. Furthermore, membranoproliferative glomerulonephritis (MPGN) subsequent to portosystemic shunts have been reported. In this paper, we report on a case of arterioportal fistula complicated with membranoproliferative glomerulonephritis and treated with an endovascular embolization procedure. A rapid improvement and complete resolution of ascites were observed following the treatment.

Keywords: *Glomerulonephritis, arterioportal fistula, embolization.* ***Nobel Med 2016; 12(3): 77-81***

MEMBRANOPROLİFERATİF GLOMERÜLONEFRİT İLE BİRLİKTE GELİŞEN SIRADIŞI BİR İNTRAHEPATİK ARTERİOPORTAL FİSTÜL VAKASI

ÖZET

Amaç: Arterioportal fistüller nadir olarak gözlemlenen mezenterovasküler sistemin bozukluklarından birisidir. Arterioportal fistül gelişen vakalar portal hipertansiyon (gastrointestinal kanama ve asit), kalp yetmezliği ve intestinal iskemi gibi komplikasyonlarla ortaya çıkabilmektedir. Bununla birlikte daha önce literatürde portosistemik şant vakalarında bildirilen membranoproliferatif glomerülonefrite bağlı akut böbrek yetmezliği olgumuzda tespit edilmiştir. Makalemizde membranoproliferatif glomerülonefrit ile komplike olan ve başarılı bir şekilde endovasküler embolizasyon yöntemi ile tedavi edilen arterioportal fistül vakası bildirilmektedir. Yapılan tedavi sonrası asit tablosunda hızlı düzelme ve iyileşme süreci gözlenmiştir.

Anahtar kelimeler: Glomerülonefrit, arterioportal fistül, embolizasyon. **Nobel Med 2016; 12(3): 77-81**

INTRODUCTION

Arterioportal fistula (APF) is a rare disorder of the mesenteric vasculature. This condition is characterized by a direct communication between the mesenteric arteries and portal venous system.[1] Although APF may remain as an asymptomatic clinical entity, patients may undergo a complicated disease course and may present with portal hypertension, heart failure or intestinal ischemia, resulting from APF.[2] Congenital causes of APF are extremely are and hereditary telangiectasia (Osler-Weber-Rendu syndrome, Ehler-Danlos syndrome), arteriovenous malformations, cavernous hemangiomas or biliary atresia may be associated with APF. Secondary causes of APF include trauma, iatrogenic injuries (during percutaneous liver biopsy, splenoportography, gastric and hepatobiliary surgery, etc.), hepatocellular carcinoma, cirrhosis and vasculitis syndromes such as Behçet disease.[1,2] Small, low-flow APFs may result from hepatocellular carcinoma or cirrhosis or iatrogenic injury in particular and may remain "silent". However, a large, high-flow APFs may cause severe portal hypertension and is a rare but treatable cause of portal hypertension. Whether symptomatic or asymptomatic, early recognition is of vital importance for early intervention to prevent further complications.[1-4]

Membranoproliferative glomerulonephritis (MPGN) refers to a general pathogenic pattern of glomerular injury, rather than a histopathologic description of a single disease.[5] Cases of MPGN secondary to portosystemic shunt have been reported in the medical literature.[6-8]

Herein, we report a case of APF complicated by ascites and MPGN. In our patient, iatrogenic APF manifested by a chain of extensive complications and the patient improved following endovascular coiling.

CASE

A 67 year-old male patient referred to our hospital due to massive ascites of unknown etiology. He had developed ascites one year ago and had a history of coronary bypass surgery and an exploratory laparoscopic surgery for an abdominal mass 2 years ago (histological examination result of the mass was reported as benign inflammatory lymphadenopathy and later on the mass resolved spontaneously). Although he was on diuretics for one year, no regression was reported in the amount of ascites that led to severe abdominal distention. Urinalysis revealed proteinuria (1 g/daily) along with asymptomatic hematuria. Histological examination of a kidney biopsy during previous hospitalizations revealed mesangial proliferation and capillary wall thickening and the patient was diagnosed with MPGN. Enzyme immunoassay identified immune complex deposits in the basement membrane (Figure 1). Based on the medical history of the patient and clinical/laboratory investigations, dysproteinemic, autoimmune (lupus nephritis, Sjögren's syndrome or rheumatoid arthritis) or inflammatory disorders (hepatitis C, endocarditis, parasitic infections etc.) that might lead to MPGN were eliminated as possible diagnoses (Figure 1).

Physical examination of the patient revealed ascites and abdominal distention without tenderness. Laboratory studies indicated a mild anemia (hemoglobin, 10.2 g/dL) and thrombocytopenia (platelets, 87.3x103/ml), an impaired kidney function (creatinine, 2.7 mg/dl) and hypoalbuminemia (3.2 gr/lt). Bilirubin concentration was elevated (1.2 mg/dL). Alanine aminotransferase and aspartate aminotransferase levels were within normal limits. Ascites workup did not reveal any abnormal cytological findings, albumin gradient indicated that the fluid was transudate in nature and cultures were negative. Tuberculosis tests on ascitic fluid (adenosine deaminase, tuberculosis polymerase chain reaction and culture) were also negative. There was no serological evidence of hepatitis B or C infections.

CT scans of the abdomen revealed a massive amount of ascites, mild hepatic lobulation and a dilated inferior vena cava secondary to a decompensated heart failure.

A percutaneous liver biopsy was performed to eliminate possible causes of a chronic liver disease. Histological examination of the biopsy specimen revealed sinusoidal dilatation and congestion and Zone 3 findings secondary to the inadequate venous outflow. In addition, focal portal-central septations in the biopsy specimen were consistent with mild fibrotic changes (Figure 2).

Computed angiography scans of the liver displayed heterogeneous liver parenchyma. The study revealed a decreased contrast flow in the segment 8 of the liver during the arterial phase and a contrast leak into the middle segment of the portal vein. This finding was found to be consistent with a proximal arterioportal shunt. The largest diameter of the portal vein was measured as 13.5 mm. A conventional angiography displayed a low-flow fistula between the right hepatic artery and a branch of portal vein. No esophageal varices were observed during the upper gastrointestinal endoscopy. After determining the location of the fistula, microcoil embolization of the shunt was performed in two sessions and the repeat angiogram revealed no residual arterioportal flow (Figure 3,4,5).

Following the procedure, portal vein dilation and ascites markedly regressed and kidney functions improved during the next two weeks of inpatient treatment. The patient has been followed up for 6 months and creatinine levels were found to be below 1 mg/dL without proteinurea in the routine follow up visits. Following the endovascular coiling procedure, heart function was improved and hypovolemic symptoms and heart failure-related respiratory distress were resolved. Cardiac ejection fractions were within normal limits in repeat echocardiograms and the platelet count was 160000/mm^3 at the 6th month follow up visit. No recurrence was observed during the outpatient follow up.

DISCUSSION

APF is one of the rare causes of portal hypertension and may be complicated by heart failure and intestinal ischemia. The persistence of an APF may result in prolonged ischemia of the liver with decreased perfusion pressure leading to decreased flow of highly oxygenated blood. The size of the fistula and the flow rate are of paramount importance. The variations in these parameters correlate with a spectrum of clinical manifestations from asymptomatic condition to heart failure or variceal bleedings.[1] The patient reported in this paper developed a wide range of complications. Complaints started four months after a laparascopic procedure. The high flow shunt caused heart failure and kidney failure. Unexpectedly, as confirmed by the histological studies, MPNG was the underlying

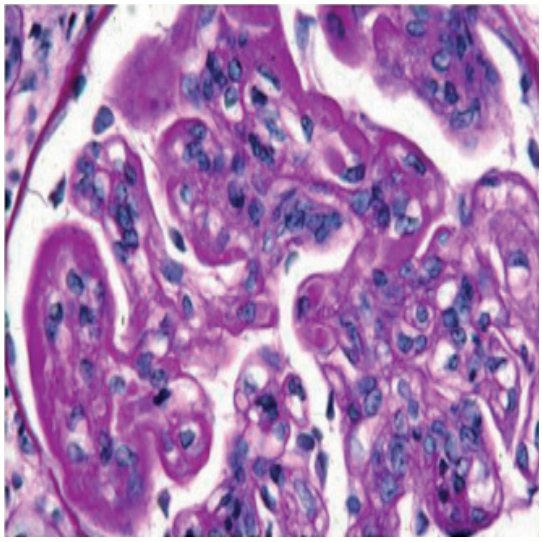

Figure 1. The glomerulus of the patient with membranoproliferative glomerulonephritis

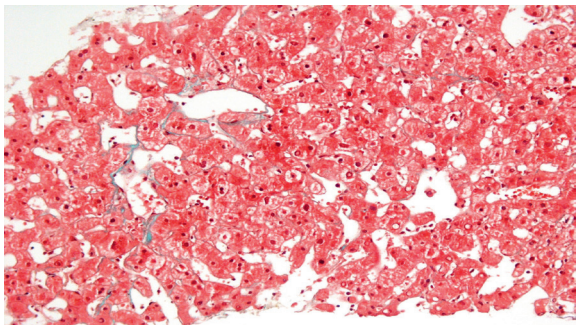

Figure 2. Sinosoidal fibrosis around the central vein with congestion (trichrome x200)

cause of kidney failure. MPGN may occur as a form of shunt nephritis. The main feature of our case was the development of MPGN after the clinical presentation of APF which was also unexpected. In our case, complete cure was achieved after performing interventional radiology procedures.

Basically, there are two treatment modalities for APF. Currently, interventional radiology procedures are preferred over surgery. A wide range of materials may be used in the transarterial coil embolization, including N-butyl cyanoacrylate, gel foam, steel coils, guide wire core, detachable balloons, and amplatzer occlusion device, as well as many other materials.[2,9] Donovan et al. studied morphological and venous flow changes following the development of arterioportal fistula.[10] In this study, they observed highly vascularized and slightly enlarged portal areas. In addition, intrahepatic portal venous dilatation was also detected. In experimental models of arterioportal fistula, portal venous wall thickening, fibrosis in the portal triad, sinusoidal dilatation and fatty infiltration have been reported.[11,12] The mildly elevated bilirubin level was not associated with elevated alanine aminotransferase and aspartate transferase levels in our patient. Liver biopsy revealed a moderate focal portal fibrosis and sinusoidal dilatation.

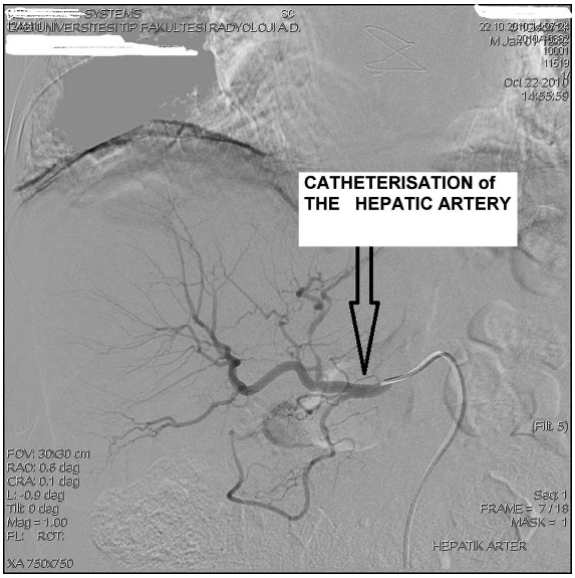

Figure 3. Catheterisation of the hepatic artery

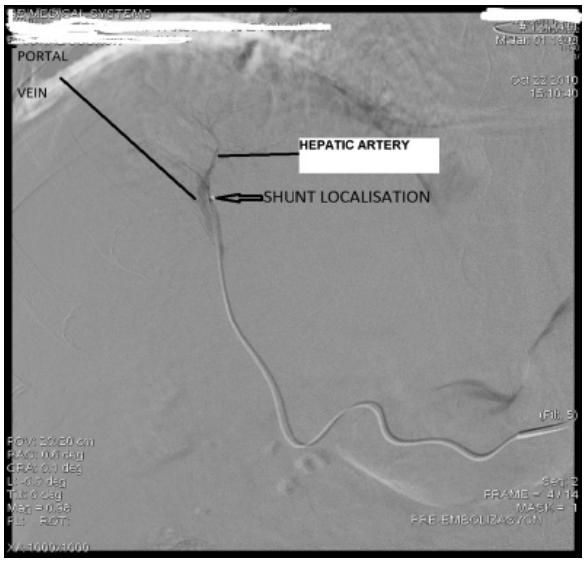

Figure 4. The arterioportal fistula image

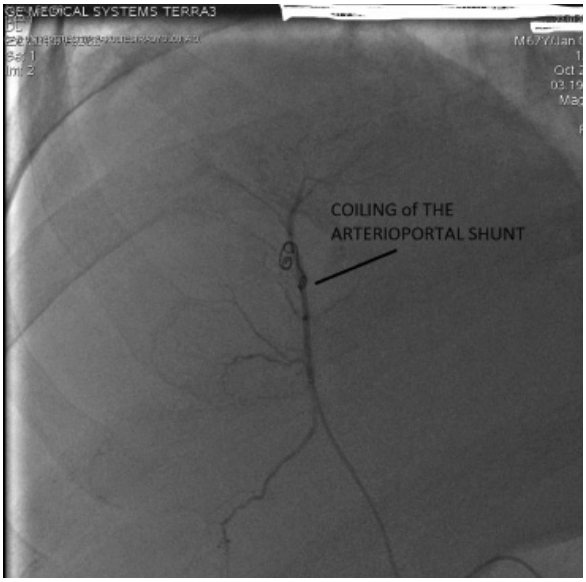

Figure 5. The coiling procedure in the computerised angiography

In the observational study of Okuda *et al*., the rates of intrahepatic arterioportal fistula formation were found to be 5.4% in liver biopsies, 3.8% in cholangiography and 26.2% in catheter decompression procedures of the biliary system.[13] The incidence of APF correlates with the size of the needle used in the procedure. Abdominal piercing lesions and malpractices during diagnostic procedures are among the most common iatrogenic causes of APF.[14] In our case, clinical manifestations occurred 4 months after the laparascopic procedure, suggesting a significant damage caused by the needle used during the procedure.

Treatment failures with interventional radiology procedures have been reported in APF cases associated with ascites. Dumortier *et al*. reported a patient with splenomegaly and ascites possibly related to an APF between the left branches of hepatic artery and portal vein.[15] Hepatofugal portal flow was detected in this case. The patient remained unresponsive to treatment. Despite two sessions of transcatheter endovascular embolization and the use of diuretics, the amount of abdominal free fluid continued to increase. Finally, a left hepatectomy with hepatic artery ligation was performed, the patient improved following this procedure and ascites regressed.

Callard et al. described glomerular lesions in 9 out of 10 patients with cirrhosis.[16] De Smet *et al*. reported a case of MPGN, 20 years after the creation of a portosystemic shunt, in a patient with idiopathic incomplete septal cirrhosis.[17] Soma *et al*. reported patients who developed hematuria and proteinuria, 7 to 13 years after portosystemic shunt surgery separating portal blood flow and systemic circulation.[18] Kidney biopsy revealed histological findings consistent with MPGN type 1. This study demonstrated that MPGN might develop secondary to porto-systemic shunts. In this case, acquired MPGN type 1 may result from the reduced clearance of immune complexes in the liver and their deposition in the glomeruli. In these cases, portal blood flow is directly shunted into systemic circulation through a porto-systemic shunt. In contrast with this case series, our patient developed MPGN after the formation of APF and iatrogenic MPGN rapidly developed 5 months after laparascopic surgery.

Arterioportal shunts develop as a result of the increased volume and our case showed the characteristics of post-sinusoidal portal hypertension rather than pre-sinusoidal portal hypertension. Depending on the location of the shunt, our patient developed congestive heart failure and this may explain the predominance of the clinical symptoms of post-sinusoidal portal hypertension. From this perspective, our case differs from other cases of portal hypertension and may contribute to the medical literature since the etiologic factors of the portal hypertension in our patient were multiorgan pathologies.

In conclusion, our case demonstrated that APF may result in progressive portal hypertension associated with ascites and heart failure. Low gradient APFs may be successfully treated with interventional radiology procedures. In addition, MPGN may occur secondary to WAVF and is a variant of shunt nephritis that may lead to unusual and diverse clinical manifestations. In conclusion, our case demonstrated that APF may result in progressive portal hypertension associated with ascites and heart failure. Low gradient APFs may be successfully treated with interventional radiology procedures. In addition, MPGN may occur secondary to AVF and is a variant of shunt nephritis that may lead to unusual and diverse clinical manifestations.

*The authors declare that there are no conflicts of interest.

C **CORRESPONDING AUTHOR:** Memduh Sahin Mersin City Hospital, Akdeniz-Mersin/Turkey memsahinsahin@hotmail.com

✔ **DELIVERING DATE:** 18 / 12 / 2014 • **ACCEPTED DATE:** 03 / 03 / 2016

REFERENCES

1. Tasar M, Gulec B, Bozlar U, et al. Intrahepatic arterioportal fistula and its treatment with detachable balloon and transcatheter embolization with coils and microspheres. Clin Imaging 2005; 29: 325-330.
2. Vauthey JNN, Tomczak RJ, Helmberger T, et al. The arterioportal fistula syndrome: clinicopathologic features, diagnosis, and therapy. Gastroenterology 1997; 113: 1390-1401.
3. Norton SP, Jacobson K, Moroz SP, et al. The congenital intrahepatic arterioportal fistula syndrome: elucidation and proposed classification. J Pediatr Gastroenterol Nutr 2006; 43: 248-255.
4. Gallego C, Miralles M, Mar´ın C et al. Congenital hepatic shunts. Radiographics 2004; 24: 755–772.
5. Kher V, Gulati S. Oxford textbook of clinical nephrology, Davidson AM (ed), Mesangiocapillary glomerulonephritis. Oxford University Press, Oxford 2005, 523-545.
6. Dash SC, Bhuyan UN, Dinda AK, et al. Increased incidence of glomerulonephritis wing spleno-renal shunt surgery in non-cirrhotic portal fibrosis. Kidney Int 1997; 52: 482–485
7. Soma J, Saito T, Sato H, Ootaka B, Abe K. Membranoproliferative glomerulonephritis induced by portosystemic shunt surgery for non-cirrhotic portal hypertension. Clin Nephrol 1997; 48: 274-281.
8. Karahima S, Hattori S, Nakazato H, et al. Membranoproliferative glomerulonephritis in congenital portosystemic shunt without liver cirrhosis. Clin Nephrol 2000; 53: 206-211.
9. Alkim C, Sahin TS, Oguz P, et al. A case report of congenital intrahepatic arterioportal fistula. Am J Gastroenterol 1999; 94: 523-525.
10. Donovan AJ, Reynolds TB, Mikkelson WP, et al. Systemic-portal arteriovenous fistulas: pathological and hemodynamic observations in two patients. Surgery 1969; 66: 474.
11. Rather LJ, Cohn R. Some effects upon the liver of complete arterialization of its blood supply. III. Acute vascular necrosis. Surgery 1953; 34: 207.
12. Schilling JA, McKee FW, Wilt W. Experimental hepatic-portal arteriovenous anastomoses. Surg Gynecol Obstet 1950; 90: 473.
13. Okuda K, Musha H, Nakajima Y, et al. Frequency of intrahepatic arteriovenous fistula as a sequela to percutaneous needle puncture of the liver. Gastroenterology 1978; 74: 1204-1207.
14. Lumsden AB, Allen RC, Sreeram S, Atta H, Salam A. Hepatic arterioportal fistula. Am Surg 1993; 59: 722-726.
15. Dumortier J, Pilleul F, Adham M, et al. Severe portal hypertension secondary to arterio-portal fistula: salvage surgical treatment. Liver Int 2007; 27: 865-868.
16. Callard P, Feldmann G, Prandi D, et al. Immune Complex Type Glomerulonephritis in Cirrhosis of the Liver. Am J Pathol 1975; 80: 329-340.
17. Smet AD, Kuypers D, Evenepoel P et al. 'Full house' positive immunohistochemical membranoproliferative glomerulonephritis in a patient with portosystemic shunt. Nephrol Dial Transplant 2001; 16: 2258-2262.
18. Soma J, Saito T, Sato H, Ootaka T, Abe K. Membranoproliferative glomerulonephritis induced by portosystemic shunt surgery for non-cirrhotic portal hypertension. Clin Nephrol 1997; 48: 274-281.