Splenectomy Followed by Hepatectomy for Hepatocellular Carcinoma with Hypersplenism and Portal Hypertension Caused by Macroglobulinemia

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Abstract. *Aim: To describe a patient with hepatocellular carcinoma (HCC), accompanied by hypersplenism and portal hypertension caused by macroglobulinemia, who underwent splenectomy followed by hepatectomy. Case Report: A 74-year-old man was admitted to our Hospital. He had previously developed primary macroglobulinemia, which had been completely cured by chemotherapy. At admission, he had a low platelet count (52×10^3/μl), and his liver function was impaired. Imaging showed a 5-cm-sized tumor, an esophageal varix, and splenomegaly, but not liver cirrhosis. The patient underwent splenectomy for hypersplenism and portal hypertension; the weight of his spleen was 2,400 g. After splenectomy, his platelet count increased to 259×10^3/μl and his liver function was improved. He safely underwent hepatectomy for HCC . The patient was discharged 14 days later without morbidity. Conclusion: These findings suggest that hepatectomy following splenectomy for hypersplenism and portal hypertension caused by macroglobulinemia, may effectively cure HCC in patients with liver dysfunction and thrombocytopenia.*

Hypersplenism is often accompanied by liver cirrhosis (1, 2), with splenectomy to improve liver function and thrombocytopenia (1-3). Myeloproliferative neoplasms are also accompanied by portal hypertension and hypersplenism, with splenectomy also reported to improve thrombocytopenia in these patients (3-5). This report describes a patient with hepatocellular carcinoma (HCC) accompanied by thrombocytopenia and portal hypertension secondary to hypersplenism associated with macroglobulinemia. Initial splenectomy effectively improved thrombocytopenia and portal hypertension, as well as liver dysfunction, enabling hepatectomy for HCC to be performed safely.

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Case Report

A 74 year-old man was admitted to our Hospital with a liver tumor. Previously, he had developed primary macroglobulinemia, which had been completely cured with chemotherapy. Computer tomography at admission showed a 5-cm tumor in segment 5 (Figure 1A) and splenomegaly (Figure 1B). Gastrointestinal endoscopy showed esophageal varices. Laboratory findings showed pancytopenia (hemoglobin 8.3 g/dl, platelet count 5.2×10^4/μl, white blood cell count 2,330/μl) and liver dysfunction (albumin 2.9 g/dl, prothrombin time 53%). The total bilirubin level was normal (0.5 mg/dl). The patient had not developed ascites or hepatic encephalopathy, and his indocyanine green dye retention rate at 15 min was normal (3.9%). He was classified as having Child-Pugh grade B cirrhosis. Serology showed that he was negative for hepatitis B and C. Virtual touch tissue quantification based on acoustic radiation force impulse, which has been reported to accurate and reliable for the assessment of liver fibrosis (6), showed no fibrosis (1.55 m/s). He was diagnosed with HCC accompanied by liver dysfunction, hypersplenism and portal hypertension that did not result from liver cirrhosis. We planned to perform hepatectomy for HCC after splenectomy to improve thrombocytopenia and portal hypertension caused by splenomegaly.

Hand-assisted laparoscopic splenectomy was performed. The spleen weighed 2,400 g. Platelet count (25.9×10^4/μl), hemoglobin concentration (9.1 g/dl) and white blood cell count (6,810/μl) were elevated after splenectomy. The patient also showed improvements in liver function tests (albumin 3.5 g/dl, prothrombin time 64%) The total bilirubin level remained normal (0.3 mg/dl).

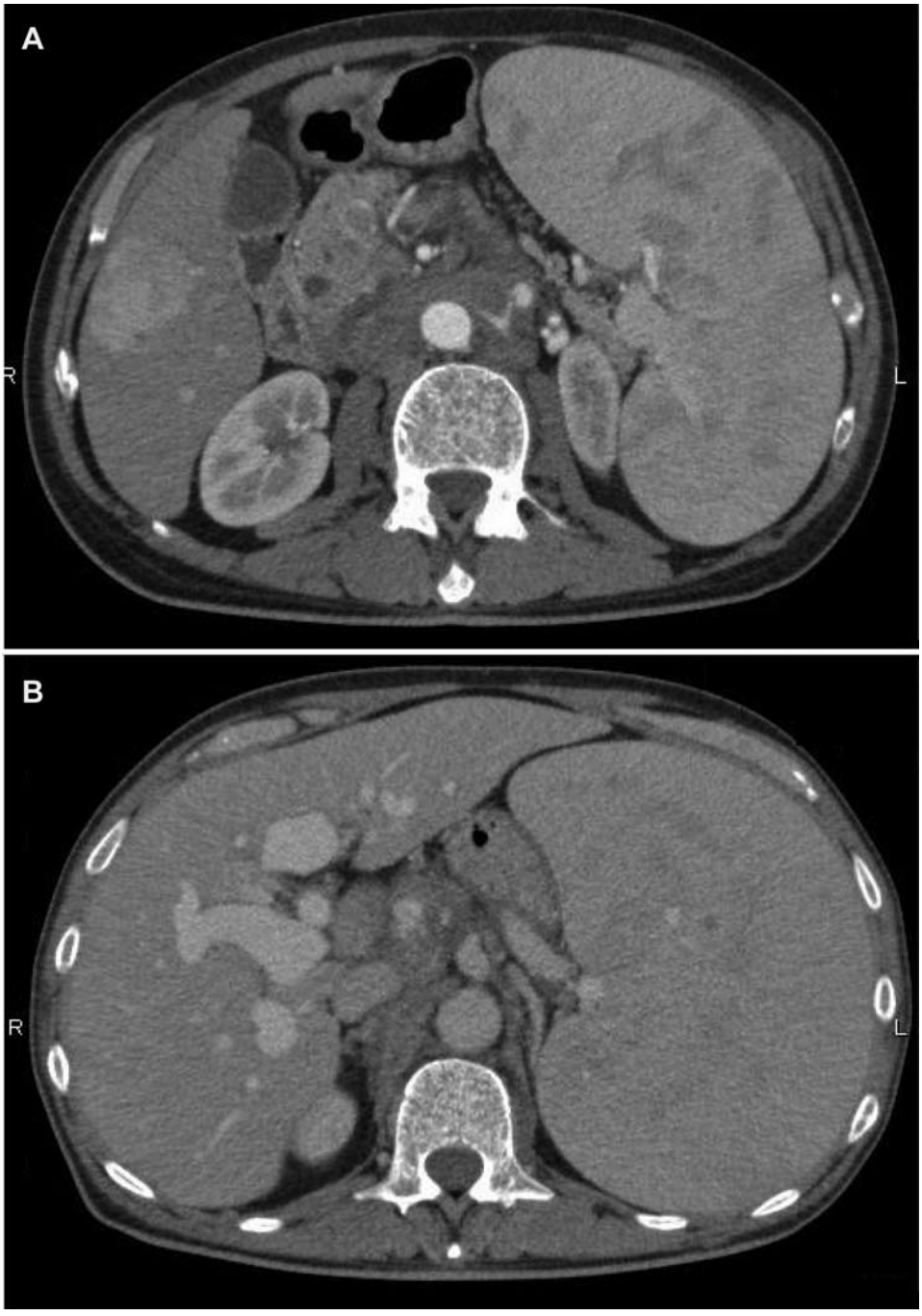

Figure 1. *Computed tomography showing a tumor measuring 5.0 cm in diameter located in segment 5 of the liver (A), and portal vein dilatation and splenomegaly (B).*

Laparoscopic hepatectomy for HCC was performed 28 days after splenectomy. Microscopic examination of the liver tissue showed that the tumor was composed of moderately differentiated HCC (Figure 2A), and there was no evidence of fibrosis in the non-cancerous liver tissue (Figure 2C). Infiltration of myeloid cells into the portal vein area was observed (Figure 2B). The spleen showed proliferation of atypical lymphoid cells, with features common to those in conditions such as lymphoplasmacytic lymphoma, indicating macroglobulinemia (Figure 2D).

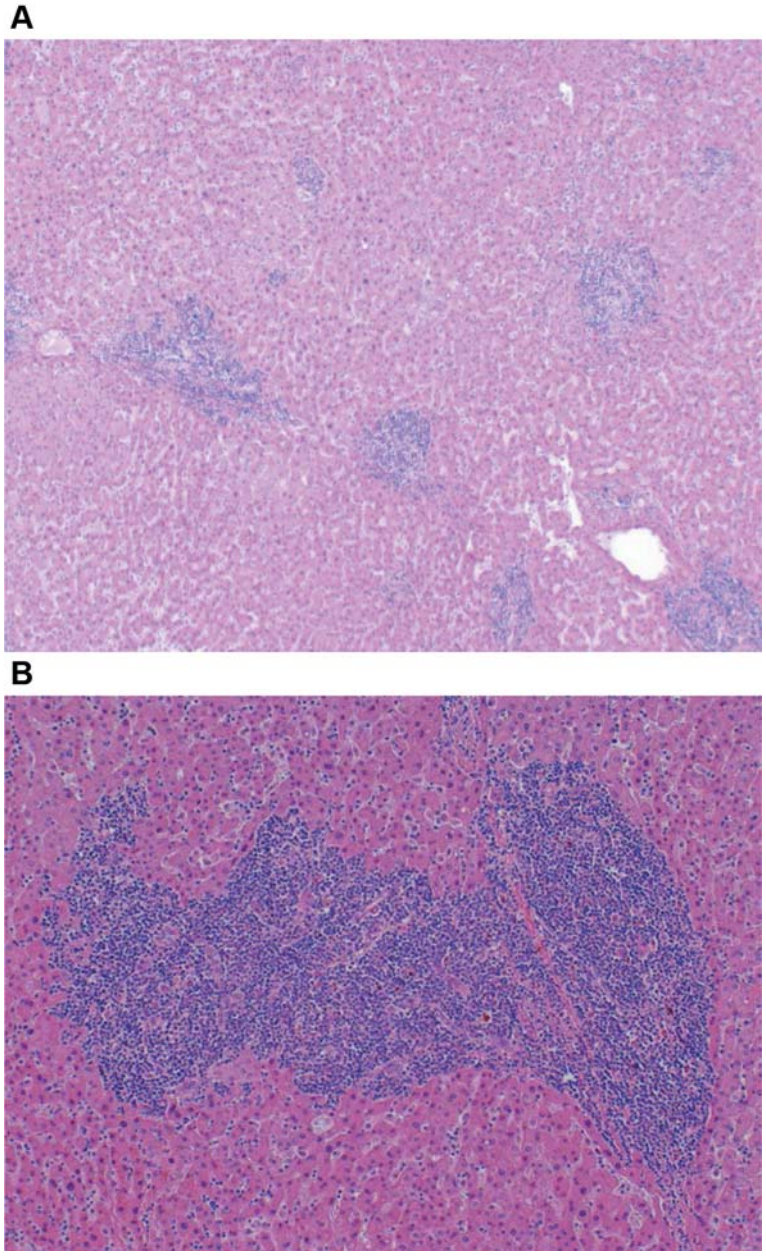

Figure 2. *Continued*

Discussion

Most patients with HCC have concomitant chronic liver diseases, such as liver cirrhosis (2, 7). Some patients with liver cirrhosis develop secondary hypersplenism (1). A low platelet count due to secondary hypersplenism is generally considered a contraindication for hepatectomy (1, 2, 8). Splenectomy usually results in an increase in platelet number, making hepatectomy safer by reducing potential bleeding risks (2, 3, 8, 9). Initial splenectomy in this patient improved the thrombocytopenia caused by hypersplenism, enhancing the safety of the hepatectomy. Partial hepatectomy after initial splenectomy may be effective in patients with HCC and hypersplenism. The most common cause of hypersplenism and portal hypertension is liver cirrhosis. Splenectomy in patients with hypersplenism and liver cirrhosis may reduce portal flow and portal pressure, improving liver cirrhosis (1, 10, 11). Despite the liver dysfunction and portal hypertension observed in this patient, pathological and imaging findings showed no evidence of

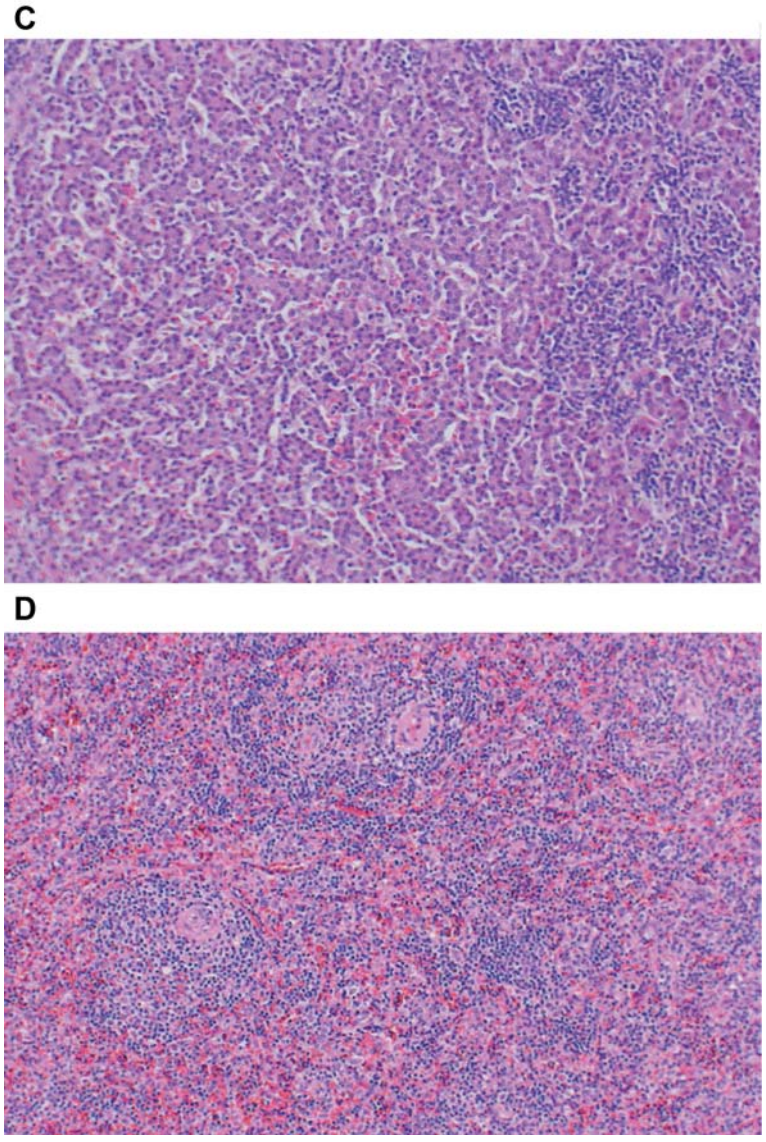

Figure 2. *Microscopic findings of the resected liver specimen showing absence of fibrosis from non-cancerous liver tissue (A)(×40), and infiltration of the portal vein area by myeloid cells (B)(×100). The tumor was composed of moderately differentiated hepatocellular carcinoma (C)(×100), whereas the spleen showed proliferation of small to medium-sized atypical lymphoid cells (D)(×100).*

liver fibrosis. Portal hypertension may also be caused by myeloid metaplasia (4). Portal hypertension in patients with myeloproliferative neoplasms may result from massive blood flow due to splenomegaly or sinusoid occlusion, and portal thrombosis in these patients may be due to infiltration of myeloid cells (4, 12). Pathological findings in this patient showed myeloid cell infiltration into the portal area. However, because splenectomy reduced portal hypertension, improving liver dysfunction, the latter may have been due to excess portal venous flow due to splenomegaly rather than to sinusoid occlusion due to infiltration of myeloid cells. Splenectomy may also be effective in improving liver dysfunction, including liver cirrhosis, due to portal hypertension accompanying myeloproliferative neoplasms.

No definite conclusions can be made on whether simultaneous or staged hepatectomy and splenectomy is a better strategy in patients with HCC and hypersplenism. Although synchronous hepatectomy and splenectomy has been reported to be safe (13), another report showed that out of 28 patients who underwent synchronous splenectomy and hepatectomy, 13 (46.4%) had postoperative complications and 5 (17.9%) died in hospital because of liver failure (14). Thus, the lack of an interval between splenectomy and hepatectomy must be balanced against the likelihood of

bleeding and portal vein thrombosis, which can lead to liver failure and death. Another study reported that the interval between splenectomy and hepatectomy should be more than 2 weeks to allow platelets to increase significantly (2). In our patient, hepatectomy was performed 4 weeks after splenectomy, after thrombocytopenia and liver dysfunction had improved. Technical advances in laparoscopic surgery and recognition of risk factors and effective treatment for portal venous thrombosis have resulted in safer and less invasive methods of performing splenectomy, especially laparoscopic splenectomy (15-18). Further investigations about the timing of splenectomy and hepatectomy for patients with HCC and hypersplenism are required.

In summary, this report describes a patient with HCC and hypersplenism secondary to macroglobulinemia who successfully underwent liver resection after splenectomy. The postoperative course of this patient was uneventful. Staged splenectomy and hepatectomy for patients with HCC and hypersplenism accompanied by myeloproliferative neoplasms may effectively improve thrombocytopenia and portal hypertension in these patients.

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