JGH Open An open access journal of gastroenterology and hepatology
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JGHF Journal of Gastroenterology and Hepatology Foundation
doi:10.1002/jgh3.12351

BRIEF REPORT

Shunt occlusion prior to lenvatinib administration prevents hepatic encephalopathy and hyperammonemia

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Key words
encephalopathy, lenvatinib, portosystemic shunt.

Accepted for publication 21 April 2020.

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Declaration of conflict of interest: None

A 60-year-old woman was diagnosed with alcoholic cirrhosis and underwent partial hepatectomy for hepatocellular carcinoma. She had multiple recurrences of hepatocellular carcinoma and underwent multiple locoregional and radiation therapies. A molecular-targeted agent (sorafenib) was administered for increased intrahepatic involvement and distant metastases. The hepatic reserve was Child-Pugh score A, but severe hepatic encephalopathy and hyperammonemia appeared 3 days after administration of 800 mg of sorafenib. Sorafenib dose was then reduced to 400 mg, and treatment for hepatic encephalopathy was initiated. However, hepatic encephalopathy did not improve, and administration of the molecular-targeted agent was discontinued. Thereafter, due to the increase in metastatic lesions (Fig. 1a), readministration of a molecular-targeted agent was considered. However, in this patient, there was a portosystemic (superior mesenteric vein–ovarian vein) shunt (Fig. 1c). Thrombosis or portal vein tumor thrombus was not observed in this patient; the test for congenital shunt was also negative, and it was considered to be a spontaneous portosystemic shunt associated with portal hypertension with cirrhosis. As hepatic encephalopathy occurred during the administration of sorafenib, readministration of a molecular-targeted agent was considered to be a high risk factor for hepatic encephalopathy. Therefore, we performed a shunt occlusion prior to the readministration of a targeted drug. The coil and *n*-butyl-2-cyanoacrylate were used to occlude the superior mesenteric vein–ovarian vein shunt (Fig. 1d). Two weeks after shunt occlusion, we administered lenvatinib at 8 mg. Grade 2 hand-foot syndrome and proteinuria appeared as adverse events of lenvatinib administration, requiring lenvatinib dose reduction and temporary withdrawal. However, lenvatinib administration could be continued without the onset of hyperammonemia or hepatic encephalopathy. Lenvatinib administration reduced metastatic lesions at 12 and 24 weeks (Fig. 1b).

Lenvatinib, a potent Vascular Endothelial Growth Factor (VEGF) inhibitor, enhances sinusoidal vascular resistance associated with the contraction of hepatic stellate cells in patients with developing hepatofugal portosystemic collaterals.[1] As a result, a mechanism likely to cause shunt-type hepatic encephalopathy due to an increase in hepatic portal venous blood flow is presumed.[1,2] In this case, shunt occlusion prior to lenvatinib administration prevented hyperammonemia and hepatic encephalopathy. Namba et al.[3] also reported that portosystemic shunt occlusion was effective for continuing lenvatinib administration. Shunt occlusion may be an effective treatment option for the administration of molecular-targeted agents in patients with portosystemic shunts.

References

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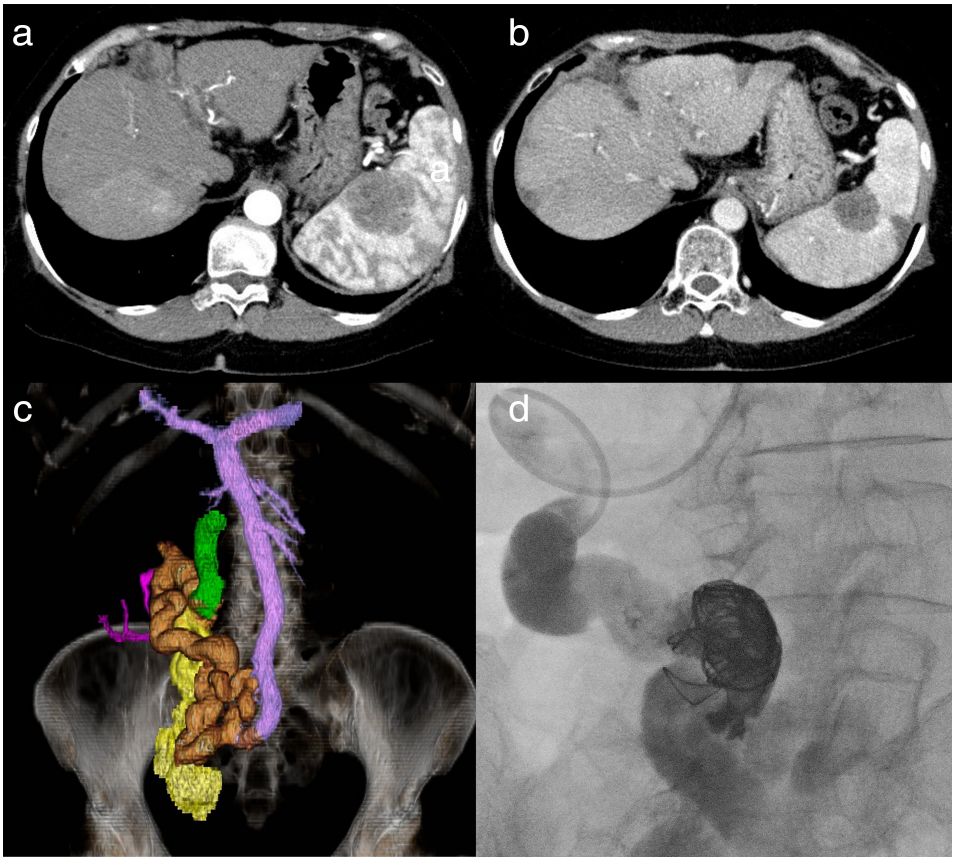

Figure 1 (a) Abdominal contrast-enhanced computed tomography (CT) before lenvatinib administration. Multiple metastases mainly metastasized around the spleen. (b) Abdominal contrast-enhanced CT 24 weeks after lenvatinib administration. Multiple metastases are smaller in size. (c) Reconstructed image of portosystemic shunt. Green indicates the ovarian vein, purple indicates the superior mesenteric vein, and orange indicates the shunt. (d) Angiographic image during shunt embolization.