Multifocal stroke with proliferation of small cerebral arteries in hepatopulmonary syndrome

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Cirrhosis of the liver has been linked to several changes in risk of cerebrovascular disease and may increase the risk of hemorrhage while reducing the risk of ischemic stroke.^{1,2} The pathophysiology underlying these changes remains unclear, though intracranial hemorrhage and vascular malformations related to liver disease have been described.^{1,3} Cirrhosis may be complicated by hepatopulmonary syndrome (HPS), in which distal pulmonary arteries dilate, become tortuous, produce shunt physiology, and often produce arteriovenous (AV) malformations.⁴

Intracranial AV shunting most commonly occurs in a focal distribution with AV malformations and AV fistulas.⁵ AV malformations exist in a spectrum between focal and larger, diffuse malformations.⁵ We present a case of multifocal stroke associated with generalized dilation of distal cerebral arteries and AV shunting without evidence of AV malformation. This is a rare angiographic finding in stroke, and the comorbidity of cirrhosis with HPS suggests a common mechanism.

PRACTICAL IMPLICATIONS

Stroke in the setting of hepatopulmonary syndrome may be associated with diffuse cerebrovascular shunting rather than traditional stroke mechanisms.

Case report

A 68-year-old woman with a history remarkable for cirrhosis caused by nonalcoholic steatohepatitis and HPS diagnosed by intrapulmonary shunt on contrast transesophageal echocardiography presented with a 7-month history of stepwise cognitive decline. She initially presented to an outside hospital with acute confusion and a 7-mm intraparenchymal and intraventricular hemorrhage in the right thalamus was reported on CT. She returned partially to baseline but subsequently had several episodes of somnolence and confusion over the next 7 months with incomplete resolution between episodes. Within 2 weeks prior to presentation she had several more similar episodes with minimal interval recovery, this time also associated with persistent left arm weakness. Brain MRI was obtained at multiple time points over this span, initially demonstrating bilateral punctate foci of susceptibility artifact followed by diffusion restriction in the bilateral occipital lobes and corona radiata (figure), consistent with areas of cortical and subcortical acute infarct and hemorrhage. At transfer approximately 4 days later, the patient was alert but with delayed responses to questions and difficulty with complex commands. She had left arm and subtle left leg weakness, reduced sensation in the left arm, and an upgoing plantar reflex on the left. Laboratory values were notable for elevated international normalized ratio at 1.5, normal transaminases and bilirubin, and normal platelet count with negative antinuclear antibodies. Transthoracic echocardiogram demonstrated ejection fraction 66% without vegetation or thrombus, and no thrombosis was found on lower extremity Doppler. Further evaluation for inflammatory disorders and vasculitis was not performed.

MRI brain with magnetic resonance angiography on admission to our facility 4 days later showed interval appearance of new diffusion-restricting lesions in bilateral centrum semiovale and corona radiata with corresponding T2 hyperintensities, consistent with acute infarctions, and similar areas of susceptibility artifact (figure). Catheter angiography of the brain demonstrated

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Figure MRI brain and cerebral angiogram

MRI 6 months prior to presentation (A), susceptibility-weighted imaging, demonstrates multiple chronic microhemorrhages throughout bilateral cerebral hemispheres, most notable in parietal and occipital lobes, as well as a few areas of hyperintensity in similar regions, and T1-weighted images with gadolinium contrast (T1+C) show linear enhancing structures in bilateral occipital lobes. MRI 4 days prior to presentation (B), diffusion-weighted imaging (DWI), shows diffusion restriction in bilateral occipital lobes and left corona radiata with corresponding fluid-attenuated inversion recovery (FLAIR) hyperintensities consistent with small ischemic strokes. MRI at presentation (C), DWI, shows additional areas of acute infarct in bilateral occipital lobes, corona radiata, and centrum semiovale with corresponding FLAIR hyperintensities. T1+C shows increased vascularity in the occipital lobes as compared with anterior regions. In cerebral angiogram in the early arterial phase of a left vertebral injection (D, E), there is a proliferation of small arteries throughout the posterior circulation. In the midarterial phase (F, G), there is early opacification of cortical, cerebellar, and deep veins (arrowheads) indicative of arteriovenous shunting. In the arterial phase of a right carotid injection (H), there is early opacification of a deep vein (arrow) associated with a similar proliferation of small arteries.

generalized proliferation of small arteries with early venous opacification, demonstrating increased AV perfusion, consistent with diffuse AV shunting (figure). Areas affected on MRI corresponded to angiographic changes most prominently in the posterior circulation.

The patient remained stable for 1 week, at which time she was discharged to a rehabilitation facility. She continued to experience stepwise cognitive decline after discharge and was not stable for further investigations. Care was withdrawn and she died within 3 months.

Discussion

We report ischemic stroke and intracerebral hemorrhages associated with proliferation of small perforating arteries and diffuse AV shunting without AV malformation. While more focal intracranial shunting may be seen in AV malformations and fistulas, this diffuse intracerebral shunting throughout all vascular territories without evidence of malformation in this case may represent a stroke mechanism. In HPS, commonly seen findings on pulmonary angiography include distal arterial dilation with AV shunting, a finding that is remarkably similar to the cerebral angiogram in this patient.^{4,6} In HPS, hypoxia is a result of ventilation-perfusion mismatch due to AV shunting. Similarly, we propose that cerebral ischemia in this case may result from AV shunting in affected brain regions.⁷

This similarity observed in this case with comorbid cirrhosis and HPS suggests that the cerebrovascular changes in this patient share an underlying mechanism with HPS, possibly related to failure of hepatic clearance of angioproliferative factors from blood in both cases. While the relationship between this rare angiographic finding and cirrhosis with HPS remains difficult to validate with a single case, future cases will likely require histopathology to further investigate the mechanism of angioproliferation and to confirm a link between the development of shunting in cerebral and pulmonary tissue.

Author contributions

J.R. Younce authored and edited the manuscript, figures, and legend. D.T. Cross III contributed to production of the figure, authorship of the figure legend, and editing of the manuscript for intellectual content. M.S. Goyal contributed to production of the figure, authorship of the figure legend, and editing of the manuscript for intellectual content. J.-M. Lee edited the manuscript, figures, and legend for intellectual content.

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