Case Report

Title: Marked cognitive and ADL improvement by shunt embolization in an very old man with portosystemic encephalopathy mimicking Alzheimer’s disease. A case report

Soichiro Kondo¹, Kazufumi Takada¹, Taro Kojima¹, Kosuke Tanaka¹, Mitsutaka Yakabe¹, Eisuke Shibata², Yumi Umeda-Kamayama¹, Hidemasa Takao², Sumito Ogawa¹, and Masahiro Akishita¹

¹ Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
² Department of Radiology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

Corresponding author:
Taro Kojima, M.D., Ph.D.
Department of Geriatric Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan
E-mail: tkojima-tky@g.ecc.u-tokyo.ac.jp
Phone: +81-3-5800-8652
Fax: +81-5800-6530
Abstract
A 91-year-old man with chronic cognitive impairment underwent shunt embolization for portosystemic encephalopathy (PSE). He experienced intermittent episodes of impaired consciousness and decreased cognitive function and activities of daily living (ADL), for which Alzheimer’s disease was suspected. On admission, he was in a coma and PSE was diagnosed based on his high ammonia level and the computed tomography (CT) findings. After shunt embolization, the patient fully recovered from the impaired consciousness and experienced no recurrence. The patient’s Revised Hasegawa Dementia Scale (HDS-R) and Mini-Mental State Examination (MMSE) scores improved significantly from 12 and 17 to 30 and 29 points, respectively. The Barthel index score also improved from 55/100 to 85/100, suggesting a marked improvement in ADL. PSE progresses slowly in very old patients and may mimic the clinical course of Alzheimer's disease but without liver enzyme abnormalities. Therefore, it should be distinguished in every dementia case.

Key words
Hepatic encephalopathy, Shunt embolization, Older, Dementia
Introduction

Portosystemic encephalopathy (PSE) is a noncirrhotic form of hepatic encephalopathy (HE) caused by a portosystemic shunt even in the absence of pre-existing liver disease\(^1\). In general, PSE progression is associated with worsening cirrhosis. However, the clinical course of PSE in older patients has not been well documented. Thus, the efficacy of shunt embolization for older patients should be objectively evaluated using cognitive function tests and the activities of daily living (ADL) scale. While previous reports have described cases in which shunt embolization improved cognitive function and ADLs, none have reported this in patients >90 years of age or on the systematic evaluation using the Comprehensive Geriatric Assessment (CGA). Herein, we report a case of shunt embolization in an older adult with hepatic encephalopathy caused by an intrahepatic shunt and not by liver disease that resulted in marked improvement in cognitive function and ADL.

Case report

We experienced a case of a 91-year-old man whose cognitive function improved after shunt embolization for PSE. He had gradually talked less and less over a period of 1 year and two months and had experienced intermittent episodes of impaired consciousness for over 1 year before admission. His cognitive function and ADL declined, and he was unable to move. He was admitted to the University of Tokyo Hospital for pyelonephritis 1 year before his most recent hospitalization. Psychological assessment at that time showed disorientation and delayed recall, which led to a diagnosis of Alzheimer's disease.

One day, he was found lying on the floor and sent to the University of Tokyo Hospital. On arrival at the hospital, he was found to be in a coma (Japan Coma Scale III-100). His blood pressure was 161/83 mmHg, pulse was 68/min, respiratory rate was 23/min, oxygen saturation was 99% on a nasal cannula at 2 L/min, and body temperature was 36.8 °C. Physical
examination revealed normal pupil diameter and pupillary light reflexes. No involuntary movements or gross paralysis of the extremities were observed.

The patient had a history of hypertension, atrial fibrillation, chronic heart failure, left parietal lobe stroke, benign prostatic hyperplasia, and pyelonephritis and was taking an anticoagulant, a loop diuretic, and a histamine receptor antagonist. He had a history of smoking 40 cigarettes per day for 20 years. He drank alcohol occasionally but had no history of heavy drinking. Blood tests revealed an ammonia level of 232 μg/dL (normal range: 12–66 μg/dL), a white blood cell count of 6800 cells/μL, a C-reactive protein concentration of 0.40 mg/dL, a glucose level of 121 mg/dL, a sodium level of 147 mmol/L, a potassium level of 4.3 mmol/L, a corrected calcium level of 9.4 mg/dL, an estimated glomerular filtration rate (eGFR) of 43.2 mL/min/1.73 m², and a total bilirubin level of 1.0 mg/dL. The patient’s liver function was normal, and hepatitis virus was not detected. The patient had no history of liver disease. Computed tomography (CT) of the head revealed no apparent acute infarction or hemorrhage. Electroencephalography revealed no obvious abnormalities related to the loss of consciousness. To clarify the cause of the increased ammonia level, abdominal contrast-enhanced CT was performed that revealed a high-density area (the same density as that of the portal vein) in S6 of the liver, suggesting a portosystemic shunt (Figure 1A). Abdominal echography confirmed that the intrahepatic P6 line and right hepatic vein formed a portosystemic shunt. These results suggested that the coma was caused by hyperammonemia due to intrahepatic portosystemic shunts.

Following administration of extracellular fluid, the patient's consciousness improved the day after admission; therefore, conservative treatment was performed first. Oral administration of lactulose and branched-chain amino acid preparations was tested; however, no improvement in hyperammonemia was observed. Thus, portosystemic shunt embolization was considered.

Shunt embolization was performed on the 22nd day after admission. The catheter was advanced from the right femoral vein into the inferior right hepatic vein (IRHV). Portosystemic
shunts were confirmed by retrograde contrast imaging under balloon occlusion. Portal vein angiography showed that two P6 vessels supplied the bloodstream for the portosystemic shunt, and both vessels were successfully embolized with coils. No intraoperative complications, including bleeding, infection, pain, access site complications\(^1\)\(^5\), and straying of the coil into the systemic circulation, occurred. Postoperatively, the patient’s blood ammonia concentration improved and remained within the normal range (Figure 2).

The abdominal CT images obtained before and after embolization are shown in Figure 1. A portosystemic shunt leading from portal vein P6 to the IRHV was observed before embolization (Figure 3A). After the procedure, the position of the embolic coil was good and the shunt blood flow disappeared, confirming successful embolization (Figure 3B).

Cognitive function tests were performed 1 year before admission, before and after the procedure, and as an outpatient (7 months after the procedure). One year before admission, the patient scored 18 on the Revised Hasegawa Dementia Scale (HDS-R) and 23 on the Mini-Mental State Examination (MMSE), with disorientation and loss of points on the delayed recall. At this stage, the ADLs were preserved (Barthel index 70/100, Lawton IADL 5/8), and a diagnosis of Alzheimer's disease was not made. After admission, the HDS-R and MMSE scores were 12 and 17, respectively, lower than those 1 year prior. The patients’ scores for temporal disorientation, immediate and delayed recall, item recall, and verbal fluency worsened. At this point, the ADLs were significantly poorer than they had been 1 year earlier (Barthel Index 55/100). Based on the results of the cognitive function tests, complications of Alzheimer's disease were suspected. However, after shunt embolization, the HDS-R and MMSE scores improved significantly to 20 and 28 points, respectively. In an outpatient setting, the HDS-R and MMSE scores were 30 and 29 points, respectively, and the Barthel index also markedly improved to 85/100. No recurrence of impaired consciousness was observed during the 6 months after discharge.
Discussion

HE often occurs in the terminal stages of cirrhosis but can also occur due to shunt formation in patients without a history of liver disease. PSE accounts for approximately 10% of all cases, is relatively rare, and is characterized by (1) high blood ammonia levels without abnormal liver function, (2) repeated episodes of psychiatric symptoms, and (3) abnormal vascular shadowing in conjunction with the portal vein on contrast-enhanced CT. Because patients usually have no evidence of liver enzyme elevation or jaundice and the symptoms mimic those of dementia, this type of hepatic encephalopathy can be overlooked. A report in 2000 noted an average age of nine patients with the same disease type as that of the current patient as 56.9 years, suggesting that PSE develops in middle age or later. With the development of technologies such as CT and ultrasound and the increased recognition of PSE, a recent case report described a higher average age, ranging from 65 to 82 years. Therefore, the age range of patients with PSE could be older than that currently assumed.

While congenital malformations, complications after abdominal surgery, trauma, and liver biopsy can cause shunt formation, in many cases the cause of shunt formation is unknown. In the present case, there was no obvious acquired cause of intrahepatic shunt formation, and it was assumed that the condition was congenital. The patient would have been in a state of covert encephalopathy before the onset of cognitive decline and inappropriate behavior. He had experienced an episode of suspected cognitive decline and inappropriate behavior approximately 1 year and 2 months before admission, at which point the hepatic encephalopathy became overt. The onset of PSE is more common in older people, suggesting that congenital shunts may develop gradually due to blood vessel fragility and hemodynamic changes with aging. The function of the blood-brain barrier (BBB) also gradually declines in older patients, making it easier for toxic substances to reach the brain. Recent studies have shown that high
levels of ammonia in the brain accelerate damage to the BBB structure\textsuperscript{11}). Muscles are also a major metabolizing organ of ammonia, and the presence of sarcopenia increases the risk for HE\textsuperscript{12}\textsuperscript{,13}). Therefore, older age increases the likelihood of developing overt HE or manifesting psychiatric symptoms of HE.

In this case, the deficits in cognitive function tests resembled those of Alzheimer's disease, and the patient’s gradual cognitive decline led to the suspicion of complications of Alzheimer's disease at the time of admission. However, since the deficits disappeared after shunt embolization, the course of pure HE is believed to have mimicked that of Alzheimer's disease. Cognitive decline in HE is characterized by attention deficits, problems with working memory, and deficits in executive function\textsuperscript{14}). Some reports show that hyperammonemia impairs long-term potentiation (LTP), a synaptic model of learning, in the hippocampus, a brain region involved in memory acquisition\textsuperscript{15}\textsuperscript{,16}). Therefore, the clinical course of cognitive decline in HE is similar to that of Alzheimer's disease. Some patients suspected of having Alzheimer's disease may also have HE; thus, the measurement of blood ammonia levels should be considered when cognitive decline is exacerbated even in the absence of a history of liver disease.

Shunt embolization helps prevent the recurrence of attacks of disturbance of consciousness and improves consciousness level and physical function\textsuperscript{4}\textsuperscript{,5}\textsuperscript{,7}\textsuperscript{,17}). However, there have been no reports of successful shunt embolization in patients >90 years of age. This case was also unique in that the Barthel index was used to assess basic ADLs.

In conclusion, we report a case in which cognitive function and ADL improved after intrahepatic shunt embolization in a patient with HE caused by intrahepatic portosystemic shunt without liver disease. It is important to properly diagnose and treat PSE in very old patients.

**Disclosure statement**

The authors declare no competing interests.
**Figure legends**

Figure 1.

Contrast-enhanced computed tomography (CT) before and after embolization. A. Pre-embolization. The arrow indicates a potential portosystemic shunt leading from portal vein P6 to the inferior right hepatic vein (IRHV). B. Post-embolization. The arrow indicates a thrombus from the coil embolization site to the IRHV, suggesting successful embolization.

Figure 2.

Blood ammonia levels during hospitalization. Extracellular fluid was administered on days 1–4, lactulose and branched-chain amino acid preparations were administered on days 14–25, and shunt embolization was performed on day 22.

Figure 3.

Intraoperative findings of shunt embolization. A. Pre-embolization. Portal angiography showing that the two lines of P6 were the blood supply pathways for the portosystemic shunt. B. Post-embolization. Following the administration of contrast agent in the inferior right hepatic vein (IRHV) near the coil embolization, no blood flow is observed on the portal vein side, confirming that the shunt blood flow had disappeared.