Recommendation of Repeated Ammonia Tests for Intrahepatic Portal-Systemic Shunt Without Cirrhosis in Elderly Patients With Psychiatric Symptoms

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ABSTRACT: We report an elderly male patient with hyperammonemia induced by intrahepatic portal-systemic shunt without cirrhosis (IPSSwoC). The occasional emergence of his erratic behaviors was misdiagnosed as a psychiatric disorder. Regardless of his uneven symptoms, IPSSwoC was suspected due to his hyperammonemia. The contrast computed tomography of the abdomen revealed a congenital type of IPSSwoC. As blood ammonia levels are inconstant, repeated blood tests are recommended when this disease is suspected in elderly patients with psychiatric symptoms.

KEYWORDS: Portal-systemic shunt without cirrhosis, hyperammonemia, psychiatric symptoms

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Introduction

Portal-systemic encephalopathy (PSE) is frequently recognized by hyperammonemia in patients with portal-systemic shunt (PSS) due to chronic hepatitis and cirrhosis. It is very rarely seen in patients with congenital intrahepatic PSS without cirrhosis (IPSSwoC).[1] Many elderly patients with psychiatric symptoms frequently visit outpatient clinics of general medicine, but the diagnosis of IPSSwoC is often difficult to obtain because symptoms of PSE and hyperammonemia levels are inconstant.

Case

A 74-year-old man with behavior abnormalities (indoor urination and poriomania) was referred to our hospital for further examination. When the symptoms suddenly occurred before 1.5 months, head magnetic resonance imaging in some neighbor clinic ruled out brain lesions. A psychiatric disorder was suspected and quetiapine was prescribed, but his condition did not improve. After 2 weeks, an electroencephalogram was examined and showed general continuous slow wave patterns, and his blood test revealed hyperammonemia (218 μg/dL) in the previous clinic. Hepatic encephalopathy (HE) was suspected, but his psychiatric symptoms diminished spontaneously without any specific treatment by the time of his first visit to us. His consciousness was normal on examinations. His data showed just slight hyperammonemia (Table 1). He did not exhibit any neurological abnormal findings and any assertive symptoms associated with chronic hepatitis or cirrhosis, including flapping tremor, but his family quite a few times witnessed his behavior abnormalities. He had severe constipation and regularly used laxatives. At his second visit, he looked normal, but his venous ammonia level (135 μg/dL) was high again. Contrast computed tomography of the abdomen revealed a large right portal-middle hepatic venous shunt (Figure 1, striped arrows) and a left portal-left hepatic venous shunt (Figure 1, dotted arrows). He was diagnosed with IPSSwoC, type Ia on the Watanabe classification.[1] Considering his age and complications from the curative operation, conventional medical therapy was indicated. We advised him to take laxative and water for avoiding constipation and dehydration to prevent hyperammonemia. During 1.5 years of follow-up, he was well without any psychiatric symptoms.

Discussion

Congenital IPSSwoC is very rare and easily misdiagnosed as psychiatric disorders because both symptoms resemble each other. This case was type B of HE according to International Society for Hepatic Encephalopathy and Nitrogen Metabolism (ISHEN) practice guidelines.[2] We did not examine blood citrulline in the present case, but type D of HE (urea-cycle disorders) could be ruled out because of elder age and clinical

Table 1. Laboratory data at the first visit.

WBC	5000	/μL	(4000–9000)	**ALP**	**417**	U/L	(115–359)	Na	143	mEq/L	(136–145)
RBC	462	×10⁴/μL	(4.27–5.70)	γ-GTP	13	U/L	(10–47)	K	3.9	mEq/L	(3.5–5.1)
Hb	14.4	g/dL	(14.0–18.0)	TP	6.7	g/dL	(6.7–8.1)	Cl	108	mEq/L	(98–107)
Ht	41.6	%	(40.0–52.0)	Alb	52.2	%	(54.6–66.1)	Ca	8.8	mg/dL	(8.6–10.1)
PLT	16.4	×10⁴/μL	(15.0–35.0)	α1	3.8	%	(2.70–4.30)	**Ammonia**	**79**	μg/dL	(12.0–66.0)
CRP	<0.1	mg/dL	(<0.3)	α2	8.8	%	(6.20–10.50)	PT	1.07	INR	999.0–1.15)
T-Bil	**2.7**	mg/dL	(0.2–1.0)	β1	6.7	%	(5.00–7.50)	T3	1.25	ng/mL	(0.70–1.76)
D-Bil	0.3	mg/dL	(0.0–0.2)	β2	5.9	%	(3.50–6.60)	T4	10.5	μg/dL	(4.8–10.5)
AST	27	U/L	(8–38)	γ	22.6	%	(12.3–22.8)	TSH	2.65	μIU/mL	(0.50–5.00)
ALT	19	U/L	(4–43)	BUN	9	mg/dL	(8–20)	HBsAg	(–)		
LDH	200	U/L	(119–229)	CRE	0.60	mg/dL	(0.44–1.15)	HBsAb	(–)		
ChE	**201**	U/L	(217–491)	CPK	93	U/L	(62–287)	HCV Ab	0.4		(0.00–0.90)

Note: Bold values are abnormal values. Ammonia 79 is significant and important, but T-Bil 2.7, ChE 201, ALP 417 are just slightly abnormal.
Abbreviations: α1, α1-globulin fraction; α2, α2-globulin fraction; β1, β1-globulin fraction; β2, β2-globulin fraction; γ, γ-globulin fraction; γ-GTP, γ-glutamyltranspeptidase; Alb, albumin fraction; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, asparatate aminotransferase; BUN, blood urea nitrogen; ChE, cholinesterase; CPK, creatine phosphorus kinase; CRE, creatinine; CRP, C-reactive protein; D-Bil, direct bilirubin; Hb, hemoglobin; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; Ht, hematocrit; LDH, lactate dehydrogenase; PLT, platelet; PT, prothrombin time; RBC, red blood cell; T3, triiodothyronine; T4, thyroxin; T-Bil, total bilirubin; TP, total protein; TSH, thyroid-stimulating hormone; WBC, white blood cell.

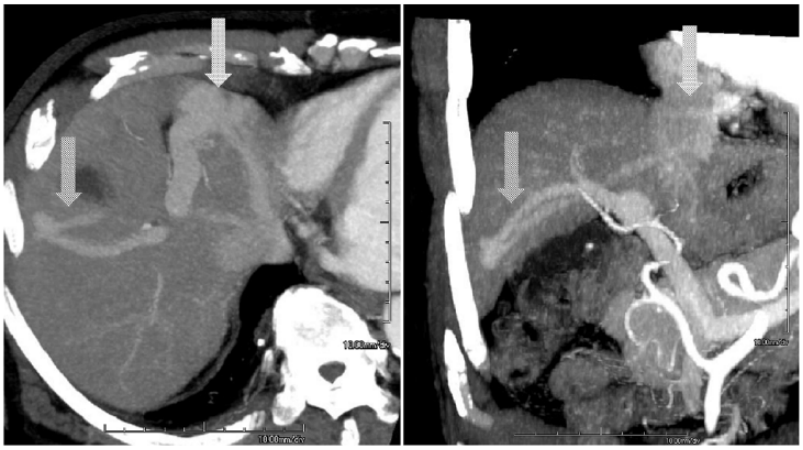

Figure 1. Contrast computed tomography of the abdomen. Striped arrows: a large right portal-middle hepatic venous shunt. Dotted arrows: a left portal-left hepatic venous shunt.

finding.[3] Precipitating factors of HE (eg, excess protein, infection, diuretics, hyponatremia, acidosis, gastrointestinal bleeding, trauma, sedatives) worsen the relevant components (hyperammonemia, hyponatremia, inflammatory cytokines, benzodiazepines) and oxidative stress–derived brain damages.[4] Hyperammonemia is an important diagnostic clue to diagnose acute liver dysfunction; however, blood ammonia level does not always correlate with degrees of PSE in chronic liver disease.[5] Encephalopathy from IPSSwoC intermittently occurs in the elderly, probably because of the irregular susceptibility of the brain to ammonia by aging.[6,7] To understand the correlation between blood ammonia levels and the PSE, we extracted Japanese congenital or idiopathic PSS without cirrhosis cases from the National Center for Biotechnology Information literature search sites[3,8–20] and estimated grades of PSE based on the symptoms described in them according to the guideline[21] (Table 2). There was a moderate correlation between blood ammonia levels and the estimated grades of PSE of PSS without cirrhosis (Figure 2, $r^2 = 0.495$).

We should note that repeated ammonia blood tests are important for the diagnosis of IPSSwoC in elderly patients when they present psychiatric symptoms because blood ammonia level could be changeable according to daily activity and because of the factors of hyperammonemia. Limitation is that the grade of PSE was estimated only through the information described in each paper. It is necessary to accumulate and evaluate IPSSwoC data prospectively. And it is important to investigate how many blood ammonia tests are needed to not overlook IPSSwoC.

Table 2. Fourteen cases of Japanese PSE by PSS without cirrhosis.

AGE	SEX	BLOOD AMMONIA[a], μG/DL	ASTERIXIS	ESTIMATED GRADE OF PSE[21]	REF. NO.
67	Female	84	+	1	12
60	Male	100	+	1	14
60	Female	131	+	2	11
66	Female	141	+	2	16
66	Male	170	–	1	20
75	Male	184[a]	–	4	15
73	Female	187	–	1	9
69	Female	210	–	2	3
72	Female	211	+	4	18
49	Female	217	+	3	13
74	Male	218	–	2	This study
69	Female	228	+	3	10
63	Male	273	N/A	2	19
80	Female	300[a]	+	3	8
37	Female	317	–	4	17

Abbreviations: N/A, not applicable; PSE, portal-systemic encephalopathy; PSS, portal-systemic shunt.
[a]These 2 values reported in the papers were confirmed unit errors by personal communications.

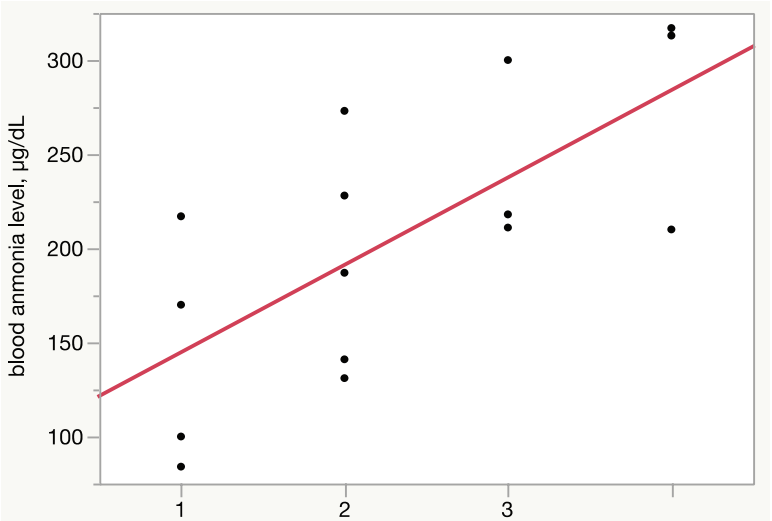

Figure 2. The correlation chart between blood ammonia levels and estimated grades of portal-systemic encephalopathy of portal-systemic shunt without cirrhosis.

Author Contributions

The corresponding author is MA. TS, MT, YK, JT and TI treated this case in Tohoku University hospital. NO followed up the patient. KS analyzed the images. MA, TS, NS, RA, TN, HK and ST searched and analyzed every Japanese report of PSS.

REFERENCES

1. Watanabe A. Portal-systemic encephalopathy in non-cirrhotic patients: classification of clinical types, diagnosis and treatment. *J Gastroenterol Hepatol*. 2000;15:969-979.
2. Guerit JM, Amantini A, Fischer C, et al. Neurophysiological investigations of hepatic encephalopathy: ISHEN practice guidelines. *Liver Int*. 2009;29:789-796.
3. Cichoż-Lach H, Michalak A. Current pathogenetic aspects of hepatic encephalopathy and noncirrhotic hyperammonemic encephalopathy. *World J Gastroenterol*. 2013;19:26-34.
4. Häussinger D, Schliess F. Pathogenetic mechanisms of hepatic encephalopathy. *Gut*. 2008;57:1156-1165.
5. Ge P, Runyon B. Serum ammonia level for the evaluation of hepatic encephalopathy. *JAMA*. 2014;312:643-644.
6. Kiriyama M, Takashima S, Sahara H, et al. Case report: portal-systemic encephalopathy due to a congenital extrahepatic portosystemic shunt. *J Gastroenterol Hepatol*. 1996;11:626-629.
7. Raskin NH, Price JB, Fishman RA. Portal-systemic encephalopathy due to congenital intrahepatic shunts. *N Engl J Med*. 1964;270:225-229.

8. Takahashi S, Yoshida E, Sakanishi Y, Tohyama N, Ayhan A, Ogawa H. Congenital multiple intrahepatic portosystemic shunt: an autopsy case. *Int J Clin Exp Pathol*. 2014;7:425-431.
9. Furue Y, Hidaka H, Fujii K, Matsunaga K, Koizumi W. Intraperitoneal bleeding after balloon-occluded retrograde transvenous obliteration: a case report. *J Med Case Rep*. 2015;9:62-64.
10. Asakura T, Ito N, Sohma T, Mori N. Portosystemic encephalopathy without liver cirrhosis masquerading as depression. *Intern Med*. 2015;54:1619-1622.
11. Kawano A, Shigematsu H, Maruyama T, Nomura H, Shimoda S. A case of diffuse hepatic arteriovenous fistulae with hepatic encephalopathy, postprandial abdominal pain and biliary injury. *Nihon Shokakibyo Gakkai Zasshi*. 2009;106:1039-1048.
12. Taguchi Y, Takashima S, Hirade S, Inoue H. Disappearance of globus pallidus hyperintensity in a patient with portal-systemic encephalopathy after occlusion of the shunt vessel. *Rinsho Shinkeigaku*. 1999;39:565-569.
13. Yuki N, Yoshioka A, Yamaya Y, Saiki M, Hirose G. A case of portal-systemic shunt encephalopathy due to congenital portal vein hypoplasia presenting with abnormal cerebral white matter lesions on the MRI. *Rinsho Shinkeigaku*. 2002;42:544-547.
14. Saito M, Seo Y, Yano Y, et al. Successful treatment using coil embolization of a symptomatic intrahepatic portosystemic venous shunt developing through a patent ductus venosus in a noncirrhotic adult. *Intern Med*. 2013;52:555-559.
15. Okamoto N, Fukazawa S, Shimamoto M, Yamamoto R, Fukazawa Y. Remission of membranoproliferative glomerulonephritis associated with a noncirrhotic portosystemic shunt after percutaneous transhepatic portal vein embolization. *NDT Plus*. 2009;2:228-232.
16. Hiraoka A, Kurose K, Hamada M, et al. Hepatic encephalopathy due to intrahepatic portosystemic venous shunt successfully treated by interventional radiology. *Intern Med*. 2005;44:212-216.
17. Otake M, Kobayashi Y, Hashimoto D, et al. An inferior mesenteric-caval shunt via the internal iliac vein with portosystemic encephalopathy. *Intern Med*. 2001;40:887-890.
18. Nishimoto Y, Hoshino H, Sato S, et al. Extrahepatic portosystemic venous shunt without portal hypertension. *Intern Med*. 1997;36:886-889.
19. Teshima H, Hayashida N, Akashi H, Aoyagi S. Surgical treatment of a descending aortic aneurysm in a patient with noncirrhotic portal hypertension and a portal systemic shunt. *Circ J*. 2002;66:1176-1177.
20. Mori H, Hayashi K, Fukuda T, et al. Intrahepatic portosystemic venous shunt: occurrence in patients with and without liver cirrhosis. *AJR Am J Roentgenol*. 1987;149:711-714.
21. Blei AT, Córdoba J. Hepatic encephalopathy. *Am J Gastroenterol*. 2001;96:1968-1976.