Journal of the Neurological Sciences 321 (2012) 58–64

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Portosystemic shunts: An underdiagnosed but treatable cause of neurological and psychiatric disorders

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ARTICLE INFO

Article history:
Received 20 January 2012
Received in revised form 20 July 2012
Accepted 20 July 2012
Available online 17 August 2012

Keywords:
Encephalopathy
Organic psychosis
Ammonia
Portosystemic shunts
MRI
MRS

ABSTRACT

Portosystemic shunts (PSS) remain an unrecognized cause of neurological or psychiatric disorders. Here we report 5 patients with neuropsychiatric presentations of PSS. Main presentations encompassed progressive Parkinsonism, organic psychosis, recurrent coma, recurrent delusion, cognitive decline and posterior cortical atrophy. None of our patients had a known history of liver disease and laboratory analyses of liver function were normal or only slightly perturbed. Only 16 similar cases of PSS revealed by neurological or psychiatric symptoms were found in the English literature. Clinical presentations were similar to our patients but asterixis, cerebellar symptoms and spastic paraparesis were noticed in some cases. EEG could be normal or could show non specific slow waves or even, rarely, triphasic slow waves. The most frequent and specific diagnostic features included hyperammonemia, abnormal brain magnetic resonance spectroscopy and visualization of the shunts by ultrasonography or abdominal imaging techniques. Therefore, in otherwise unexplained neuropsychiatric disturbances, ammonia should be routinely measured and, if elevated, a dedicated gastroenterologist or an expert radiologist should be consulted for potential PSS examination. Treatment of the shunts or of the hyperammonemia resulted in marked neurological or psychiatric improvement in all cases.

1. Introduction

Portosystemic encephalopathy (PSE) encompasses a wide range of motor and neuropsychological disorders that may develop in patients with portosystemic shunts (PSS) [1]. This condition has been essentially reported in patients with portal hypertension secondary to liver injury such as hepatic cirrhosis often linked to liver damage due to alcohol or viral hepatitis. Very few cases of PSE revealing PSS without a prior history of liver disease have been previously reported in the literature since its first description in 1964 [2] and it is difficult to delineate an accurate clinical picture from these isolated case reports. Here, we report 5 patients with various neurological and psychiatric symptoms revealing PSS. Clinical presentations included Parkinsonism, organic psychosis, coma, delusion or progressive posterior dementia. Only 16 previous cases were found in the English literature.

2. Methods

2.1. Inclusion criteria

Patients presenting with neurological or psychiatric symptoms revealing a PSS were included in this study. Patients had to meet the following criteria: (1) neurological or psychiatric disorders unexplained by another cause, (2) no known history of liver cirrhosis or of any progressive chronic or acute liver disease prior to neuropsychiatric symptoms, (3) normal or slightly disturbed liver function tests including prothrombin rate above 70%, albumine above 30 g/L, normal total and conjugated bilirubinemia, (4) liver enzymes i.e. γ-glutamyltransferase (GGT), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (AP) below 2.5-fold the normal values,

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http://dx.doi.org/10.1016/j.jns.2012.07.050

and (5) evidence for significant PSS on abdominal imaging by ultrasound or CT.

Results are expressed as mean ± SEM. Spearman correlation test was used for correlation analyses.

2.2. Patients

2.2.1. Report of cases (Tables 1 and 2)

2.2.1.1. Case # 1. This 55-year-old man presented with a 1 year-history of bradykinesia, dysarthria, bilateral rest and action tremor. He noticed episodes of hypovigilance after meals. Physical examination showed bilateral Parkinsonism and a tetrapyramidal syndrome. Blood tests revealed hypermanganesemia at 24.4 nmol/L (5<N<18), hyperammonemia at 78 μmol/L (N<48) and a slight increased of AST at 38 IU/L (20<N<32) whereas values of ALT, GGT and AP were normal. A positive serology to hepatitis C was discovered at this time. Because of these biological abnormalities, an abdominal ultrasonography was performed and showed large permeable portacaval shunts with a very tortuous shunt between the splenic and the left renal veins as well as a gastro-epiploic shunt. A splenomegaly of 11.2 centimeters (cm) was also observed without ascites. Computed tomography (CT) confirmed indirect signs of portal hypertension with a voluminous splenic vein of 2 cm in diameter and derivative spleno-renal pathway measuring 19 millimeters (mm) in diameter. Brain cerebral MRI showed atrophy and hyperintensities of the tail of both putamen on T2-weighted sequences (not shown). Brain magnetic resonance spectroscopy (MRS) evidenced a high level of a composite of glutamate and glutamine peaks (Glx) with low myo-inositol (mI). A dopamine transporter imaging with ^{123}I-FP-CIT SPECT did not show any significant reduction in striatal uptake suggesting absence of nigrostriatal degeneration. This homeless patient was lost to follow-up.

2.2.1.2. Case # 2. This 29-year-old man presented an 8 year-history of relapsing psychosis with profuse visual hallucinations. Simultaneously, he developed fluctuating cognitive dysfunction. Blood tests showed near normal liver blood tests but, during following years of follow-up, hyperammonemia (50–70 μmol/L) was noticed several times during psychotic relapses leading to further liver investigations. Because of hyperammonemia, an abdominal ultrasonography (US) was performed and showed hepatic dysmorphy, hepatomegaly, portal hypertension with a large umbilical vein of 7 mm in diameter, a splenomegaly evaluated at 14 cm and spontaneous spleno-renal shunts. Free and wedged hepatic pressures were respectively calculated at 2 and 40 mm Hg corresponding to an important increased of the portacaval gradient (38 mm Hg). Transparietal and laparoscopic liver biopsies showed hepato-portal fibrosis. Brain MRI was normal but brain MRS showed an increased Glx with reduction of choline (Cho) and absence of mI (Fig. 1A). Split liver transplantation was performed at the age of 27 allowing only partial reduction of psychiatric symptoms. Abdominal Doppler showed persistence of some PSS. After obturation of remaining PSS with coils through portography, ammonemia returned definitely within the normal range while psychotic symptoms totally disappeared. This was accompanied by sustained normalization of psychometric tests and of MRS (Fig. 1B).

2.2.1.3. Case # 3. This 38-year-old woman was admitted for a one year-history of recurrent delirium and unexplained coma. Her past medical history disclosed a pancreatic tumor with hyperparathyroiditis corresponding to multiple endocrine neoplasia type 1. Pancreatic tumor had been removed surgically 12 years before her admission, and ovarian and liver metastases were treated successfully by radio-surgery. Since this period, the cancer was considered to be in remission. During her hospitalization, she exhibited a comatose episode. At this time, diffuse aspect of metabolic encephalopathy on EEG led to a metabolic workup, disclosing hyperammonemia at 240 μmol/L. Liver function was only slightly perturbed with increased GGT and ALT. An abdominal CT revealed a tumoral compression of the superior mesenteric vein with an enlargement of ovarian veins and development of collateral PSS. Brain MRS disclosed high Glx and low mI. Her clinical condition improved with lactulose and a low protein diet while MRS normalized. However, the patient died few months later from cancer progression.

2.2.1.4. Case # 4. This 63-year-old man presented with an unexplained delirium lasting for 15 days accompanied by auditory and visual hallucinations. His medical history revealed removal of the pancreatic tail because of a cyst at the age of 30 as well as chronic alcohol intoxication stopped 4 years ago. EEG showed non-specific slow waves suggestive of metabolic encephalopathy. Hyperammonemia (109 μmol/L) was found together with MRS abnormalities including high Glx, reduction of Cho and absence of mI. Abdominal US-Doppler revealed a decreased portal flow evaluated at 200 mL/min equivalent to a speed of 4 cm/s. A gastro-epiploic shunt was observed and was attributed to the pancreatic surgery. Splenomegaly, an indirect sign of portal hypertension, was measured at 14 cm. Confusion was resolved after one week with lactulose and a low protein diet but some attention disorders remained. Control brain MRS 10 months later showed an improvement of Glx and mI abnormalities (not shown).

2.2.1.5. Case # 5. This 46-year-old woman presented with a six year-history of cognitive decline characterized by psychomotor slowing, memory loss, attention deficit, progressive dyscalculia, alexia and inferior altitudinal visual field defect. Standard blood and CSF analyses were normal. EEG showed slow waves. Cerebral perfusion scintigraphy with technetium 99 showed low fixation in the parietal and occipital cortex bilaterally suggesting posterior cortical atrophy i.e. a degenerative dementing illness involving posterior cerebral lobes. Six years after symptoms onset, a new brain MRI showed slight hyperintensities of both globus pallidus on T1-weighted sequences suggesting hepatocerebral degeneration (Fig. 1C). A metabolic workup was then performed disclosing hyperammonemia (129 μmol/L). An abdominal CT showed a situs inversus, a polysplenia, and a portal cavernoma without identified splenic vein and with an open mesenterico-caval anastomosis of 11.5 mm in diameter. The PSS had been surgically performed 15 years ago in the context of a gastrointestinal hemorrhage caused by a portal cavernoma. A low protein diet with lactulose was introduced, leading to marked subjective improvement after several days. Acalculia improved within several months and most cognitive disorders entirely recovered within 6 months. Only mild attention deficits persisted together with inferior visual field defect probably caused by occipital lobe degeneration.

2.3. Literature review

A literature review was performed using the pubmed data base and the authors' own bibliography. The same inclusion criteria were used (see above).

3. Results

3.1. Neuropsychiatric signs revealing PSS (Table 1)

From 1964 to Dec 2011, we found only 16 cases of PSS revealed by neurological or psychiatric symptoms in the English literature [2–12]. Overall, by pooling these 16 cases with our 5 cases, there were 8 males and 13 females. Age at onset of neurological or psychiatric signs ranged from 21 to 90 years (mean 55.8 ± 4.2). Neurological or psychiatric signs encompassed recurrent delusion (11/21), cognitive decline (10/21), recurrent episodes of coma (7/21), behavioral disorders (5/21), Parkinsonism (5/21), gait ataxia (5/21), asterixis (4/21), and spastic paraparesis (2/21). In addition, our patient # 5 had a very