
HEPATIC ENCEPHALOPATHY MIMICKING STROKE

A Case Report¹

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ABSTRACT Atchison JW, Pellegrino M, Herbers P, Tipton B, Matkovic V: Hepatic encephalopathy mimicking stroke: a case report. *Am J Phys Med Rehabil* 1992; 71:114-118.

This case demonstrates focal neurologic deficit mimicking stroke with underlying hepatic encephalopathy. Unilateral weakness in patients with hepatic encephalopathy has not been previously described in the English language literature. A 46-yr-old white woman was admitted to an acute care hospital for left shoulder manipulation, underwent general anesthesia and appeared to have had a right cerebrovascular accident. At transfer to the rehabilitation hospital, in addition to the left hemiparesis, there were inconsistencies in the neurologic examination and signs of cognitive impairment and liver failure. The patient's response to an intensive, multidisciplinary inpatient rehabilitation program along with treatment of the liver dysfunction led to resolution of left-sided weakness and flapping tremor with independence in ambulation and activities of daily living. Relevant literature is reviewed. A thorough history and physical examination with liver function assessment should always be performed in patients with cerebrovascular accident and unusual recovery.

KEY WORDS: Encephalopathy, Ammonia, Stroke, Rehabilitation

Hepatic encephalopathy is a metabolic disorder of the nervous system in conjunction with hepatocellular disease or portal-systemic venous shunting. The disease is characterized by fluctuating neurologic signs, asterixis and electroencephalographic (EEG) abnormalities. Disturbances in consciousness can progress to disorientation and coma.¹

The fluctuating neurologic signs reported include rigidity, hyperreflexia, asymmetric deep tendon reflexes, extensor plantar signs, suck and grasp reflexes,² impaired motor coordination, sleep disturbances,³ seizure activity, diminished mental status and paraparesis.⁴ Asterixis or "flapping tremor," a nonrhythmic, asymmetric lapse in voluntary sustained posture of the head, neck and extremities, is commonly noted in the precoma stage. There are no previous English language reports of unilateral weakness or hemiparesis as the presenting picture of hepatic encephalopathy.

CASE REPORT

A 46-yr-old white woman was referred for left hemiparesis believed to be secondary to right cerebrovascular accident. She had been admitted to an acute care hospital as the result of a painful left shoulder with severe restriction of motion and underwent manipulation under anesthesia as well as Groshong catheter placement for long-term intravenous meperidine therapy. Her previous medical history included adult onset diabetes mellitus for 9 yr with some complaint of left lower limb sensory neuropathy, hepatitis of unknown etiology, a left Bell palsy, which had resolved, and esophageal varices for which she had recently undergone sclerosis treatment. Past surgeries included hysterectomy, splenectomy and cholecystectomy. She had no history of left-sided weakness and was entirely independent in ambulation and activities of daily living before admission.

After general anesthesia, the patient experienced an episode of loss of consciousness and on arousal was noted to have left-sided weakness and episodes of "shaking." EEG showed generalized slowing with questionable background epileptiform activity, and the patient was put on phenytoin. Initial computed tomography (CT) of the head without contrast and a repeated CT 7 days later with contrast were both normal, but T₂-weighted magnetic resonance imaging (MRI) of the brain showed a high intensity lesion of 5-6 cm in the right frontal lobe and multiple lesions in both parietal and occipital lobes. These

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findings were interpreted as being consistent with multiple infarcts or plaques.

On presentation for rehabilitation, the patient was lethargic with a flat affect, and pupils were equal but sluggish. Spider nevi were present throughout, and some right upper quadrant abdominal tenderness was noted with palpable liver. The neuromusculoskeletal examination revealed some mild left-sided facial weakness and ptosis, which were not noted on admission to acute hospital. All deep tendon reflexes were 2+ except the left biceps brachii, which was 3+. There was an equivocal Babinski on the left, but no Hoffmann's reflex, clonus or abnormal tone was present. Motor testing showed only trace contraction at the left shoulder. The rest of the left arm and the entire right side had greater than antigravity strength, but this response was inconsistent and could be demonstrated only with functional use, not on command. Passive range of motion of the left shoulder showed only 45° of flexion and 80° of abduction because of severe complaints of pain. The left lower limb showed extremely dysfunctional contractions with both agonist and antagonist muscle groups firing simultaneously, but very slowly. The sensory examination was normal except for some hyperesthesia of the left leg below the knee. Rapid alternating movements were normal except for slowing with the right hand. Gait was markedly abnormal with a narrow base, slow rhythm and continual falling to the left.

Treatment on admission included glucose checks every 6 h with sliding scale insulin coverage, phenytoin (100 mg twice/day), spironolactone (100 mg twice/day), trimethobenzamide (200 mg every 6 h as needed for nausea or vomiting) and meperidine HCl (25 mg intravenously every 2 h as needed for pain). The meperidine was changed to 50 mg intramuscularly three times per day, trimethobenzamide was discontinued, and 5000 units of heparin subcutaneously was initiated two times per day.

Initial testing showed some abnormal liver enzymes (Fig. 1) with an aspartate aminotransferase of 108 units/liter (normal, 0-60 units/liter) and alkaline phosphatase of 164 units/liter (normal, 0-100 units/liter), plus a markedly abnormal serum albumin of 2.1 g/dl (normal, 3.8-5.1 g/dl). Partial thromboplastin time was slightly elevated at 46 s (control, 23-35 s) as was prothrombin time at 12.7 s (control, 9.5-12.5 s). Target cells were noted in the peripheral smear. Repeat EEG showed diffuse slowing of background activity maximal in the right hemisphere with no epileptiform activity. Phenytoin level was therapeutic at 14.9 mg/liter (normal, 10-20 mg/liter).

The patient began physical and occupational therapy with emphasis on transfer training, balance activities and gait training, as well as progressive resistance exercises of all limbs, concentrating on strengthening, increasing the range of motion and decreasing the pain of the left shoulder. Even though

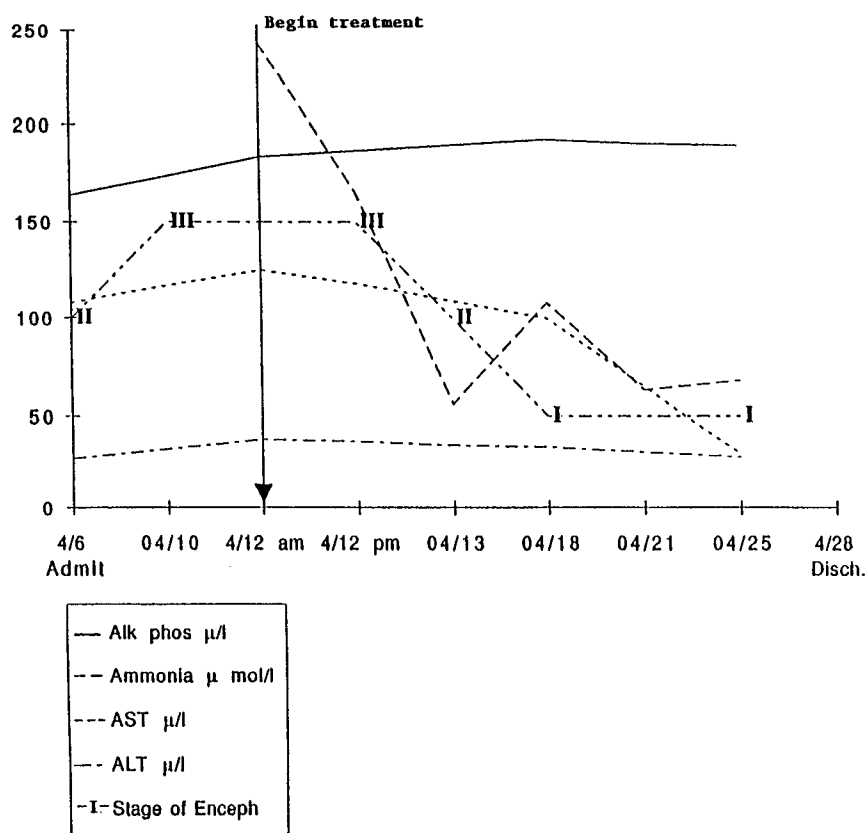


Figure 1. Comparison of serum liver enzymes with level of encephalopathy. Alk phos, alkaline phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

she was oriented on admission, a neuropsychologist was also asked to evaluate the patient because of the inconsistencies of her examination.

On the 1st day after admission, the patient suffered an unwitnessed fall while trying to transfer herself in the bathroom. A hematoma developed at the site of previous subcutaneous heparin injection and at the same time, her gums were bleeding without evidence of trauma to the area. Stat partial thromboplastin time was >180 s (control, 23–35 s). The heparin was discontinued, and protamine sulfate was administered because of her previous history of bleeding esophageal varices. Partial thromboplastin time decreased to 47 s by afternoon and 33 s by the next day.

By the 6th day of admission, the patient was incontinent of urine and stool, confused, oriented to name only, thought she was "at home" and was performing very inconsistently in therapies as the result of lethargy and fluctuating awareness. She once again fell while trying to transfer herself impulsively, and marked tremors (asterixis) were noted. Hepatic encephalopathy was suspected and her serum ammonia level was $243 \mu\text{mol/liter}$ (normal, 14–55 $\mu\text{mol/liter}$).

Treatment included 30 g of oral lactulose, a Fleet's enema, a no protein diet and intravenous hydration. The spironolactone was decreased, and phenytoin was replaced with carbamazepine for continued seizure prophylaxis. Following five doses of lactulose (a total of 120 g) over a 12-h period, extensive diarrhea occurred and a repeat ammonia level was $56 \mu\text{mol/liter}$. After 24 h, the patient was more alert and participating in therapies. A urinary tract infection was isolated and erythromycin was instituted. A low protein diet was restarted and the lactulose was decreased to 20 g twice per day.

Over the succeeding 5 days, the patient's range of motion of the left shoulder increased markedly to 120° of abduction and 160° of flexion; she required no pain medication. The asterixis, ptosis and left facial weakness resolved completely, and her endurance and concentration in therapy improved dramatically. She began to ambulate with supervision only, and became totally independent in transfers and activities of daily living on the unit. The ammonia level continued to fluctuate (Fig. 1); however, the neuropsychologist noted improved memory skills and less evidence of any perceptual difficulties or visual-spatial neglect. The results of a repeat MRI of the brain (Fig. 2) showed T_2 -weighted images with high signal changes in the cortical convexities and deep symmetric areas bilaterally. These changes were felt to be consistent with anoxia or hypoperfusion, or to be of metabolic origin, even though the large right frontal hyperintensity was still present (Fig. 2).

The patient experienced no further medical problems and the ammonia level stabilized in the high-normal range. After a family conference, she was discharged to home entirely independent in ambu-

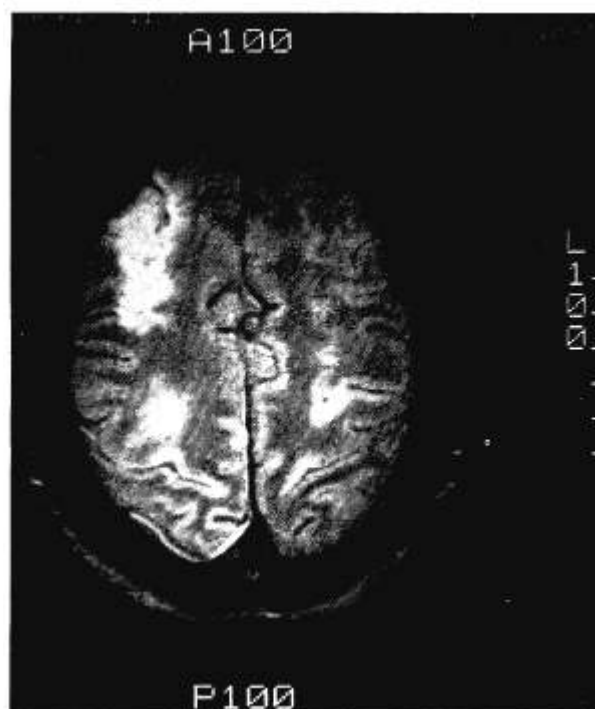


Figure 2. MRI scan showing abnormalities consistent with a metabolic origin.

lation and activities of daily living, with full, painless range of motion and strength of the left shoulder. She was alert and oriented with no verbal memory problems, although she demonstrated some "dependent behaviors" around her family. She was lost to formal follow-up, but was seen by chance at another hospital by one of the authors (M. P.) 3 months later. She had experienced recurrent medical problems, but had no evidence of left hemiparesis, shoulder pain or other neurologic abnormalities.

DISCUSSION

The diagnosis of hepatic encephalopathy is based on four criteria: (1) the presence of advanced hepatocellular disease, extensive portal-systemic collateral shunts, or both; (2) disturbances in awareness and mentation such as confusion, disorientation or coma; (3) changes in the peripheral neurologic examination, which often involve fluctuating findings in the sensory, motor and reflex examinations with an inconsistent pattern of pathologic reflexes; and (4) an EEG pattern of symmetrical, high voltage, slow waves, usually 2–5 per s (Table 1).¹

The pathogenesis of hepatic encephalopathy involves toxic substances absorbed from the intestine that the liver cannot metabolize and which thus accumulate in the brain. There are four commonly mentioned potential pathogens: (1) increased mercaptans in blood and cerebrospinal fluid; (2) the synthesis of false neurotransmitters, such as octo-

TABLE 1
Levels of encephalopathy

Stage	Motor/Reflexes	Asterixis	Mental Status	EEG
I	Slowed dyscoordination	+/-	Mild confusion, euphoria, depression, irritability	Normal
II	Ataxia, dysarthria, suck/grasp	+	Lethargic, drowsy, moderate confusion	Abnormal
III	Myoclonus, hyperreflexia	+	Somnolent but arousable; profound confusion/delirium	Abnormal
IV	Decerebrate	+	Coma, may be unresponsive	Abnormal

pamine; (3) increased plasma levels of short and medium chain fatty acids; and (4) hyperammonemia.³

Ammonia is thought to be the major toxic agent in this condition,⁵ although any condition that causes elevated brain or blood ammonia levels results in the formation of Alzheimer type II astrocytes.⁶ These astrocytes are the distinctive morphologic alteration in the brain of humans who have died as the result of hepatic encephalopathy,⁶ and the extent of change correlates well with the severity of the encephalopathy and the blood levels of ammonia.⁷ The formation of Alzheimer type II astrocytes preferentially effects the basal ganglia, the dentate nucleus of the cerebellum and the prefrontal and temporal regions of the cerebral cortex. This neurotoxic action is not well understood: earlier hypotheses included vasoparalysis, energy failure, neurotransmitter abnormalities or electrophysiologic derangements.⁶

A number of conditions can mimic hepatic encephalopathy, particularly in the alcoholic patient. Wernicke's encephalopathy, Korsakoff's psychosis, delirium tremens and acute intoxication are accompanied by confusion and can be confused with hepatic encephalopathy.¹ Previous reports have shown that subdural hematomas, meningitis, drug overdose and hypoglycemia can also have the same clinical presentation.¹

Although the distinctive abnormal laboratory finding in hepatic encephalopathy is an elevated serum ammonia,¹ Weissenborn et al.⁸ have shown that P300 auditory-evoked potentials are sensitive to early neuropsychologic changes because of hepatic encephalopathy. Serial neurologic examinations, CT or MRI of the brain, EEG and occasionally lumbar puncture are often necessary to exclude these other disease states.

In the case presented, the initial CT scans were normal, but the MRI scan seemed to indicate a right frontal infarct with many other areas of abnormality. After treatment for hepatic encephalopathy, a repeated MRI (Fig. 2) continued to show multiple areas of hyperintensity on the T₂-weighted images, which were thought to be the result of hypoperfusion or metabolic changes. These findings may be consistent

with earlier hypotheses regarding the mechanism of neurotoxicity in hepatic encephalopathy, which included vasoparalysis, neurotransmitter abnormalities and electrophysiologic derangements to specific areas of the brain.⁶ The clinical presentation of left hemiparesis, left facial weakness and other inconsistent neurologic findings correlates well with the areas of involvement on the MRI scan. Previous reports indicate that patients with subclinical stable lesions may develop focal neurologic signs when hepatic encephalopathy develops.⁴

The patient's rapid improvement after treatment is most likely the result of improved neurotransmitter function⁹ and increased perfusion to the areas involved. Newer neuroradiologic procedures such as positron emission tomography and single-photon emission computed tomography have the ability to measure these parameters, and might have been helpful in evaluating this patient.¹⁰

In the patient with stable inactive cirrhosis, there is usually a precipitating factor leading to hepatic encephalopathy. These factors may include gastrointestinal bleeding, increased dietary protein consumption, electrolyte disturbances because of excessive diuresis or vomiting, acute infection, heart failure and general anesthesia for surgery. In effect, anything that causes further deterioration of liver function can precipitate hepatic encephalopathy. As in this case, there may be more than one contributing factor: the patient had a known history of chronic hepatitis and bleeding esophageal varices, was on a diuretic, underwent general anesthesia and had a documented urinary tract infection. The simultaneous presence of these conditions most likely contributed to the onset of hepatic encephalopathy.

Treatment is centered on decreasing the serum ammonia level. Specific treatment should eliminate any blood from the bowel lumen, and then concentrate on decreasing ammonia production by excretion through defecation. Within 24 h neomycin or lactulose will reduce serum ammonia, and therefore an improvement in the stages of encephalopathy should be noted (Table 1).¹ Other supportive therapy should be instituted, including elimination of all dietary proteins, correction of fluid and electrolyte abnormalities, discontinuation of all medica-

tions metabolized by the liver, if possible, and treatment of any infection with antibiotics.

Our patient showed rapid improvement over the first 24 h (Fig. 1), but fluctuated for several days after the initial treatment. Once clinical improvement has been noted, some dietary protein should be reinstated to maintain positive nitrogen balance, especially when intensive physical and occupational therapy are being performed. Greenberger et al.¹¹ demonstrated that not only the quantity but the quality of the dietary protein may be important. Vegetable-derived protein has been shown to be superior to animal protein in the management of chronic encephalopathy.¹² Indeed, our patient had lower and more stable ammonia levels on a vegetable protein-only diet. This allowed her to stabilize medically and to demonstrate marked improvements in her functional status while being monitored by the multidisciplinary team.

CONCLUSION

This case shows the difficulty in diagnosing hepatic encephalopathy and the need for continued investigation in a patient with fluctuating neurologic status. The left-sided weakness and other neurologic signs changed continually, and our diagnosis was not confirmed until arterial serum ammonia was shown to be elevated.

This patient responded quickly to the administration of oral lactulose and protein restriction, and her acute and chronic neurologic abnormalities resolved. Not all patients with hepatic encephalopathy enjoy such a complete and rapid recovery after a decrease in the ammonia level. Neurologic and functional deficits may persist, and multidisciplinary rehabilitation may be indicated.

Therefore, in any patient with elevated liver enzymes and evidence of neurologic abnormality, a serum ammonia should be checked to rule out hepatic encephalopathy as the source of neurologic compromise. As always, maximal medical and functional improvements are dependent on the correct diagnosis, treatment and rehabilitation.

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