Relapsing encephalopathy secondary to non-hepatic hyper-ammonemia

Sir,
A 76-year old man, with a past history of atrial fibrillation, hypertension, anterior and posterior circulation “transient ischaemic attacks” (TIA) over 3 years, subdural hematoma while on warfarin and peptic ulcer disease, presented with upper gastrointestinal bleed. There was no history of prolonged alcohol use and no signs of liver disease or portal hypertension. He was resuscitated with fluids and blood and underwent an emergency endoscopy. This revealed evidence of Billroth- II gastrectomy and a stomal ulcer with fresh blood and clot, that was injected. There were no varices to suggest porto-systemic shunting. Post endoscopy, he was unresponsive for 24 hours and subsequently improved to being drowsy with slurred speech. On the 3rd hospital day, he regained consciousness and returned to his pre-morbid state over one week. Investigations showed normal electrolytes, liver function tests and coagulation and mild renal impairment (creatinine 0.150 mmol/l). Haemoglobin concentration was 9.7 g/dl at presentation and improved to 11.6g/dl after transfusion. A computed tomography of the head was unremarkable except for evidence of previous surgery and generalised atrophy. A diagnosis of posterior circulation TIA was made. He returned to outpatient clinic in a month and was noted to be well.

One month later he presented with drowsiness and “tremor”. His wife reported “good” and “bad” days. He had asterixis but no focal neurological deficit. A complete work-up (including checking metabolic parameters, thyroid function tests, estimation of calcium, arterial blood gas (ABG) and serum ammonia) was performed. No new changes were noted on a repeat CT scan. By the next day, the patient improved and insisted on being discharged.

A month later he presented with confusion and encephalopathy. A diagnosis of relapsing encephalopathy secondary to hyperammonemia was made based on previous and current ammonia levels. His ABG showed respiratory alkalosis without hypoxemia. He was initiated on lactulose therapy and a protein-restricted diet. A work-up was undertaken to look for an underlying chronic liver disease. An ultrasound and CT scan of the abdomen showed normal liver architecture and no evidence of portal hypertension or porto-systemic shunting. Incidental small haemangiomas were noted in the
liver. Iron and copper studies, AMA, ANA and hepatitis serology were unremarkable.

Hyperammonemia commonly occurs in the setting of liver disease. Other non-hepatic causes include inherited disorders of the urea cycle, drugs notably valproate, urinary diversion, distal tubular acidosis, parenteral nutrition and hematological malignancies.[1,2] Urea cycle disorders present early in life and were considered unlikely in this patient and hence not tested for. No other cause could be identified. A provisional diagnosis of non-hepatic hyperammonemia was made.

It is likely that previous episodes in this patient were misdiagnosed as “TIA”. His clinical state as well as his constructional apraxia improved significantly (Figure 1) with lowering of ammonia levels and is in keeping with a recent study that showed correlation of serum ammonia levels with hepatic encephalopathy in patients with liver disease.[3] He has been on chronic lactulose therapy and protein-restricted diet over the last 2 years and has not had further overt manifestations of encephalopathy. No evidence of an underlying etiology has also become evident during the follow-up.

Non-hepatic hyperammonemia should be considered as aetiology for altered conscious state in patients who present with relapsing encephalopathy in the absence of evidence of liver disease.

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References