Heavy Metal Encephalopathy Masquerading as Hepatic Encephalopathy – A Case Report

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INTRODUCTION

In this case report we discuss a patient with neurological manifestations thought to be a case of hepatic encephalopathy. With no improvement in symptoms despite treatment, it created a diagnostic dilemma. Eventually, toxicological investigations were done which revealed that heavy metal poisoning could be the possible culprit.

Encephalopathy is characterised by impaired mental state as a result of a diffuse brain dysfunction or other psychiatric condition that induces unconsciousness, typically followed by diffuse electroencephalogram (EEG) anomalies. Both primary neurological and systemic disorders are root causes of encephalopathy. Encephalopathy results from several causes such as liver failure or liver cancer, metabolic abnormalities, anoxic encephalopathy, infections, exposure to harmful compounds such as lithium paint, synthetic contaminants (toxins), inflammations (systemic lupus erythematous, sarcoidosis), drug induced, demyelination (e.g., multiple sclerosis), degenerative process like Alzheimer disease, Parkinson disease and hereditary encephalopathies such as leukodystrophy of the white matter.[1]

Humans have used heavy metals since many years. While many harmful health effects of heavy metals have long been established, exposure to heavy metals continues to rise in some parts of the world, especially in underdeveloped countries. Emissions have decreased over the past 100 years in most developed countries. Heavy metals are prevalent and remain in the ecosystem, in general causing bio amplification. Living systems frequently associate with heavy metals in different proportions in the habitat. Heavy metal exposure induces lipid peroxidation, Deoxyribonucleic Acid (DNA) damage and protein modification by generation of oxygen free radicals. Exposure to these metals occurs in occupational areas by equipment, air, food and drinking water. Prolonged exposure to heavy metals may lead to neurotoxicity and brain damage. When symptoms of toxic encephalopathy emerge immediately following single acute exposure to high levels of toxic chemicals it is termed as acute toxic encephalopathy. Other than that if symptoms emerge insidiously over time in association with repeated or chronic exposure to low levels of neurotoxins it is called as chronic toxic encephalopathy.[2]

In some cases, diagnosis of toxic encephalopathy is complicated by the fact that toxic chemicals can also damage liver and kidneys. In these cases hepatic dysfunction must be successfully treated before diagnosis of toxic encephalopathy can be considered. It is a diagnosis of exclusion, so a full work up for other possible aetiologies such as hepatic, uremic and infectious should be done. In this case report we have discussed heavy metal encephalopathy masquerading as hepatic dysfunction.

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PRESENTATION OF CASE

A 50-year-old male patient who was a railways worker by occupation and a chronic alcoholic was found unconscious in his quarters. He was taken to the hospital where he was not responding to deep painful stimuli and had falling saturation. Patient was intubated in view of Glasgow Coma Scale (GCS) 3 and fall in saturation and taken on mechanical ventilator on volume control mode. He has no comorbidities such as diabetes, hypertension, tuberculosis, bronchial asthma thyroid disorders. He had tachycardia with a blood pressure of 110 / 70 mmHg. On systemic examination there was decreased air entry bilaterally, heart sounds were normal, central nervous system examination reveals normal tone with deep tendon reflexes were absent, power could not be assessed and plantar were mute. ECG revealed T wave inversion in lead II, III, augmented vector foot (AVF). Computed tomography (CT) of brain showed lacunar infarct in head of right caudate nucleus and right thalamus, diffuse brain atrophy, right ethmoid sinus osteoma.

Lab investigations revealed haemoglobin 12.9 g / dl, mean corpuscular volume (MCV) 94.4 fl, white blood cell (WBC) 5800 / cumm, platelets 1.51 lakhs, international normalized ratio (INR) 1.15, prothrombin time 14.4 secs, activated partial thromboplastin time (aPTT) 30.5 secs, urine albumin trace, sugar nil, 1 - 2 pus cells / hpf, urea 94 mg %, creatinine 2.7 mg %, sodium 142 mEq / L, potassium 5 mEq / l, alkaline phosphatase 102 IU, serum glutamic-pyruvic transaminase (SGPT) 497 IU, SGOT 1415 cent IU, 6.2 g percent overall protein, 3.3 g percent albumin, 2.9 g perglobulin, total bilirubin 2.5 mg %, conjugated 1.7 mg %, unconjugated 0.8 mg %, low-density lipoprotein (LDL) 32, very low-density lipoprotein (VLDL) 91, total cholesterol 225, triglycerides 454, HDL 102, serum amylase 183, serum lipase 106, serum ammonia 244, serum calcium 7.9, serum magnesium 2.6, serum phosphorous 4.4, creatine kinase-mb (CKMB) 70 and troponin I negative.

DISCUSSION OF MANAGEMENT

Patient was started initially on injectable antibiotics, osmotic diuretics, anticoagulants, antiplatelet agents, statins, thiamine supplements and other supportive medication. Deranged liver function test and raised serum ammonia were suggestive of hepatic dysfunction.

EEG was done which revealed no evidence of ectogenic discharges throughout hemisphere. Following this, patient was treated with bile acid sequestrants such as ursodeoxycholic acid, antibiotics such as rifaximin, laxatives, intravenous fluids administration, higher antibiotics and steroids (as a case of hepatic encephalopathy). With no improvement in symptoms the case was revised. Keeping his occupation in mind as railway employee, heavy metal intoxication was suspected. A blood panel was sent for toxicological investigations which revealed raised content of lead 250 (< 150), barium > 90 (< 30), uranium > 4.5 (< 1), strontium 58.17 (8 - 38), tin 7.2 (< 2), vanadium 0.84 (< 0.8), beryllium 0.03 (0.10 - 0.80), nickel 22.57 (< 15), manganese 76.95 (7.10 - 20) establishing the diagnosis as heavy metal encephalopathy. He was then treated with chelating agents. Unfortunately, due to delay in diagnosis and treatment his condition did not improve significantly.

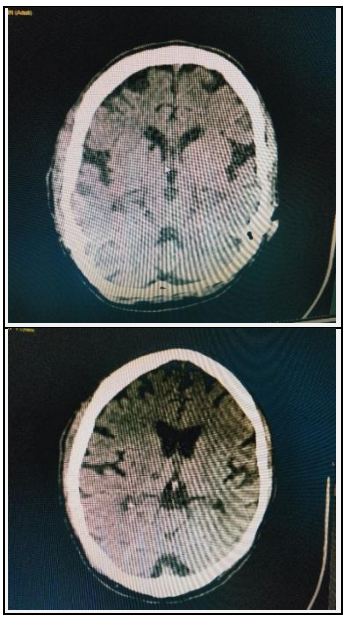

Figure 1.
CT Axial Section 1.5 mm Showing Ill-Defined Hypodense Lesion in Head of Right Caudate Nucleus and Right Thalamus

DISCUSSION

Encephalopathy is seen in several conditions which lead to cognitive dysfunction. Multiple factors lead to encephalopathy and manifest as hepatic or uremic encephalopathy. Hepatic encephalopathy is characterised by a neurological condition which results from insufficient liver function and / or portal systemic blood shunting. Hepatic encephalopathy can be classified broadly as manifested HE (in which bedside examinations and bedside tests help in detecting neurologic and neuropsychiatric abnormalities) or minimal HE (neurologic examination and mental status is normal along with psychometric testing abnormalities). In West Haven criteria, these criteria are based on severity –

- Grade 0 – Normal.
- Grade I - Mild deterioration: Sleep alteration, slight wreckage of analytical function, ill temper enhancement, metabolic tremor and muscular synchronisation stultification.
- Grade II - Moderate deterioration: Lethargy, grossly compromised intellectual function, disorientation to time, inappropriate or bizarre behaviour, dysarthric speech, diminished reflexes and ataxia.
- Grade III - Severe deterioration: Sleepiness, confusion, disorientation, paranoia or anger and clonus.
- Grade IV - Coma: Unconsciousness and dilated pupils.[3]

Hepatic encephalopathy manifest as confusion, changed awareness level and coma due to hepatic failure. Signs of HE such as flapping tremors (wrist extension leads to loss of posture and tremors in hand called asterixis) or abnormal movements, drowsy or baffled, eccentric behavior or severe personality changes, sluggish or slacked movement, Coma: unconscious and frigid. Hepatic encephalopathy diagnosis requires neurological, metabolic and psychiatric dysfunction to be excluded.[4] It occurs due to blood stream collection of toxic substances like ammonia (NH3) that are normally

detoxified in liver. Hepatic encephalopathy is classified into overt (neurological signs can elicit) and minimal hepatic encephalopathy (no neurological signs). Hepatic encephalopathy is subdivided as type A on account of acute liver failure (ALF), type B on account of portosystemic shunting and type C on account of cirrhosis.[5] Hepatic encephalopathy is reversible with treatment. Metabolic encephalopathy entails a deficiency of brain activity related to organ dysfunction mechanisms such as cardiovascular disease, liver disease and renal failure. Metabolic disturbances can produce hepatic encephalopathy by interacting with pathophysiological mechanisms with human exposure to toxic heavy metals is a universal threat. Concurrent heavy metal exposure is especially significant because of its long lasting impact on brain. The specific toxicological processes triggered by exposure to metal mixtures are still uncertain, however they share several similar forms of triggering cognitive, analytical and intellectual dysfunction and became irrational. The amalgamation of metals may set off collaborative effects due to their common binding inclination towards glutamate receptor, sodium potassium adenosine triphosphates pump, biological calcium, glutamate (neurotransmitter) which can lead to imbalance between the pro-oxidant elements like reactive oxygen species (ROS) and the antioxidants (reducing elements). In this process, reactive oxygen species preponderances over the antioxidant factors such as glutathione peroxidase (GPx), (GS), glutathione (GSH), metallothionein (MT-III), catalase, superoxide dismutase (SOD), brain-derived neurotrophic factor (BDNF), and CERB and ultimately steers to cognitive dysfunction.[6] The damage to the brain may be permanent or temporary depending on the cause. In this case, encephalopathy is caused due to intoxication of heavy metals as they precipitate and affect liver and masquerades as hepatic encephalopathy[7] and is treated accordingly. Later patient's condition did not improve clinically hence toxicological analyses availed the cause and was treated with chelating agents. By eliminating the exposure and considering the toxin and its dosage, individual's neurological symptoms may improve.[8] Still delay in diagnosis gives less benefit in this patient. In addition to taking a good history, there are also unique constellation of symptoms such as mild confusion, attention deficits, seizures and coma in acute condition, symptoms are insidious and signs unrecognized in chronic exposure which aid the physician in distinguishing one type of encephalopathy from another.[9] In this case patient's condition masquerades as hepatic encephalopathy till the end and winded up as heavy metal toxic encephalopathy.

CONCLUSIONS

Parallel work up is required for early diagnosis and management in a case of encephalopathy. In this case, heavy metal encephalopathy mimicked hepatic encephalopathy. Therefore an alternate approach is paramount if there is no improvement in the patient's condition with ongoing management.

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