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Coexistence Of Pellagra With Wernicke's Encephalopathy In An Alcoholic Patient: Case Report And Review Of Literature

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SUMMARY: We report a case of 30-year-old male chronic alcoholic presented with gait disturbance from last 1 year associated with cognitive impairment along with auditory and visual hallucinations. Intermittently had few episodes of seizures (GTCS). Despite continuous treatment he developed scaly itching skin rashes associated with photosensitivity and marked pain with heightened response to touch. He further worsened as he started hearing abnormal voices, suspiciousness and agitated behavior. Further the ataxia worsened and he also developed bilateral ophthalmoparesis. During hospital stay myoclonus was noticed which was startle in nature. Possibility of alcoholic pellagra encephalopathy (APE) along with Wernicke's encephalopathy (WE) was kept and treatment was reviewed and adequate nicotinamide with thiamine supplementation was given. Clinical condition improved drastically in 1 week with resolving startle myoclonus along with resolved ophthalmoparesis. Ataxia resolved in the next one month.

KEYWORDS: Pellagra, Wernicke's encephalopathy, Alcoholics, Multivitamin deficiency.

INTRODUCTION

Deficiency of multiple vitamins in an alcoholic and malnourished patient is like a situation in which to expect the unexpected. Vitamin and nutritional disorders associated with alcohol dependence are increasing in India. Wernicke encephalopathy and Beri Beri both resulting from vitamin B1 deficiency are common disorders (1).Wernicke encephalopathy is characterized by triad of global confusion, ataxia and ophthalmoplegia. While Beri Beri is characterized by polyneuropathy (dry beriberi) and high output failure (Wet Beri Beri). Wernickes encephalopathy is commonly observed in chronic alcoholic users. WE may present in nonalcoholic as well and its prevalence is around 2% in general population(2). WE is associated with other conditions which includes malignancy like Hodgkin lymphoma, bariatric surgery and celiac disease(3). Timely treatment leads to complete recovery. Korsakoffs psychosis is the other form of thiamine deficiency which is a result of irreversible complication of untreated wernickes encephalopathy. Thiamine plays a crucial role in maintaining the nervous, cardiovascular and locomotive system. Thiamine pyrophosphate (TPP), the biologically active form of thiamine, ia an essential coenzyme of many key enzymes in glucose metabolism including tricarboxylic acid cycle and pentose phosphate pathway. Thiamine deficiency leads to lactic acid accumulation through anerobic respiration, then brain cytotoxic edema and vasogenic edema. Thiamine is not synthesized in the body. It should be supplemented through diet. Daily requirement is 1 -2 mg related to carbohydrate intake.

Pellagra from niacin deficiency (vitamin B3 OR nicotinic acid) is relatively rare and under diagnosed condition(4). Niacin is contained in daily diet such as grains, cereals, meat, peanuts, eggs and fish. Acute pellagric encephalopathy is manifested by nervousness, insomnia, and hallucinations; and can confound with confusion, oppositional hypertonus, myoclonus and ataxia(5). Pellagra is known for its 4 D symptoms as diarrhea, dementia, dermatitis and death. The differential diagnosis between pellagra and non-specific erythema is important because of the reversibility of pellagra and prevent fatal condition, if left untreated. Pellagra is one of the important treatable causes of reversible dementia and psychosis. Pellagra should be one of the differential diagnoses in alcoholic or patients with malabsorption presenting to emergency department with altered sensorium. Rarity of pellagra in general population may lead physicians to exclude pellagra from their differential diagnosis. Recommended daily allowance in diet is approximately 5-20 mg/day of niacin equivalents depending upon age and sex. Niacin is required for the synthesis of NAD (nicotinamide adenine dinucleotide) and NADP (nicotinamide adenine dinucleotide phosphate)(6). Serotonin synthesis is impaired due to niacin deficiency leading to mood changes and cognitive impairment. And this serotonin impairment leads to mood changes and cognitive impairment. This can mimic delirium as neurological symptoms are variable and fluctuating. Dermatological manifestations of pellagra are in the form of sunburn

like dry and rough erythema over the sun exposed skin in a bilateral and symmetrical pattern especially on the dorsum of the hands, V area of the neck, and face and exposed areas of legs and feet. There is skin photosensitivity in pellagra as was there in our patient as well. Pathophysiology of skin sensitivity is as follows: decreased synthesis of tryptophan metabolite picolinic acid leads to zinc deficiency. This in turn can decrease histidine metabolite, urocanic acid, and possibly also increase levels of hem precursor 5- aminolaevulic acid and photoreactive porphyrins(7). NAD is responsible for repair of the ultraviolet radiation induced DNA damage in human skin. Niacin deficiency impairs this process. Niacin deficiency leads to diarrhea among gastrointestinal complaints. There is mucosal inflammation of the small intestine and colon and gastric mucosal atrophy in pellagric patients. Alcoholics are also prone to develop diarrhea for multiple other reasons including effects of ethanol on the intestines and steatorrhea from concomitant chronic pancreatitis. So, making a diagnosis of pellagra is difficult but it should be suspected when patients present with above mentioned complaints as specific treatment leads to improvement.

CASE PRESENTATION

Mr A 30-year-old man, primary graduate, heavy alcoholic for more than 15 years, presented with history of imbalance while walking from last 1 year which gradually worsened in last 6 months rendering him dependent on family members for daily routine activities. Also, in the last one year he had problems in maintaining attention with delayed response to any questions. Also he had 2 to 3 episodes of GTCS along with intermittent hallucinations with episodes of self talking in last 6 months. He was taking multi vitamins and thiamine (100 mg OD). Despite the treatment he developed multiple episodes of diarrhea that lasted for 1 month along with scaly itchy rashes. Rashes were extremely itchy and painful with heightened response to touch. Dermatology was consulted and his rash was described as dull dark erythema with overlying loose scale in photo distribution mainly in dorsal arms and legs; sparing the clothing bearing areas of chest and upper arms and legs. Nicotinamide supplementation was started (250 mg BD). Skin lesions responded drastically and recovered completely within 2 weeks. Not to the surprise patient presented within few days with complaints of diplopia with bilateral gaze restriction with auditory and visual hallucinations and episodes of self talking. During hospital stay noticed to have startle myoclonus. Noise and cutaneous stimulation stimulated their occurrence, but intention and action had no obvious effect.

On examination he was conscious oriented and was tachycardic with normal rest of vital signs. His speech was slow and incoherent. And he did have delusions and hallucinations. There was evidence of malnutrition in the form of thin built and sunken eyes with pallor and bald red tongue. Bilateral fine hand tremors were present on extended upper limbs. Neurological examination showed horizontal as well as vertical eye movement impairment. No abnormalities in cranial nerve findings except for impaired eye movements. Motor examination revealed 5/5 power with preserved reflexes. Cerebellar features were present in the form of finger nose incoordination and disdiadokinesia and gait was possible only with support with short steps with swaying to either side on walking. Cardiac, respiratory and abdominal examination was unremarkable.

INVESTIGATIONS

HEMOGLOBIN	7.9 gm/dL
WBC	8390/uL
PLATELET COUNT	3 LAKHS
MCV	88.5fL
MCHC	35.3g/dL
MCH	31.2 pg
ESR	70mm/hr
SODIUM	130 mmol/L
POTASSIUM	4.28 mmol/L
CHLORIDE	91.00
SERUM CREATININE	0.62mg/dL
TOTAL PROTEIN	7gm/dl
ALBUMIN	4.20gm/dL
GLOBULIN	2.80gm/dl
HbsAg	NEGATIVE
HCV	NEGATIVE
HIV	NEGATIVE

TOTAL CHOLESTEROL	149 mg/dl
TRIGLECERIDES	141.70 mg/dl
HDL CHOLESTEROL	32.30 mg/dl
VLDL CHOLESTEROL	28.34 mg/dl
LDL CHOLESTEROL	89.00 mg/dl
CSF ANALYSIS	
CELLS	LESS THAN 5 CELLS ALL LYMPHOCYTES

His hemoglobin was 7.9 gm/dl. Common metabolic encephalopathies (hepatic, disturbed water and electrolyte imbalance, hypoglycemia, hypercalcaemic, hypocalcaemic) were excluded by normal laboratory tests. CSF examination was normal and excludes meningitis and subarachnoid hemorrhage. MRI brain revealed diffuse cerebral with cerebellar atrophy.

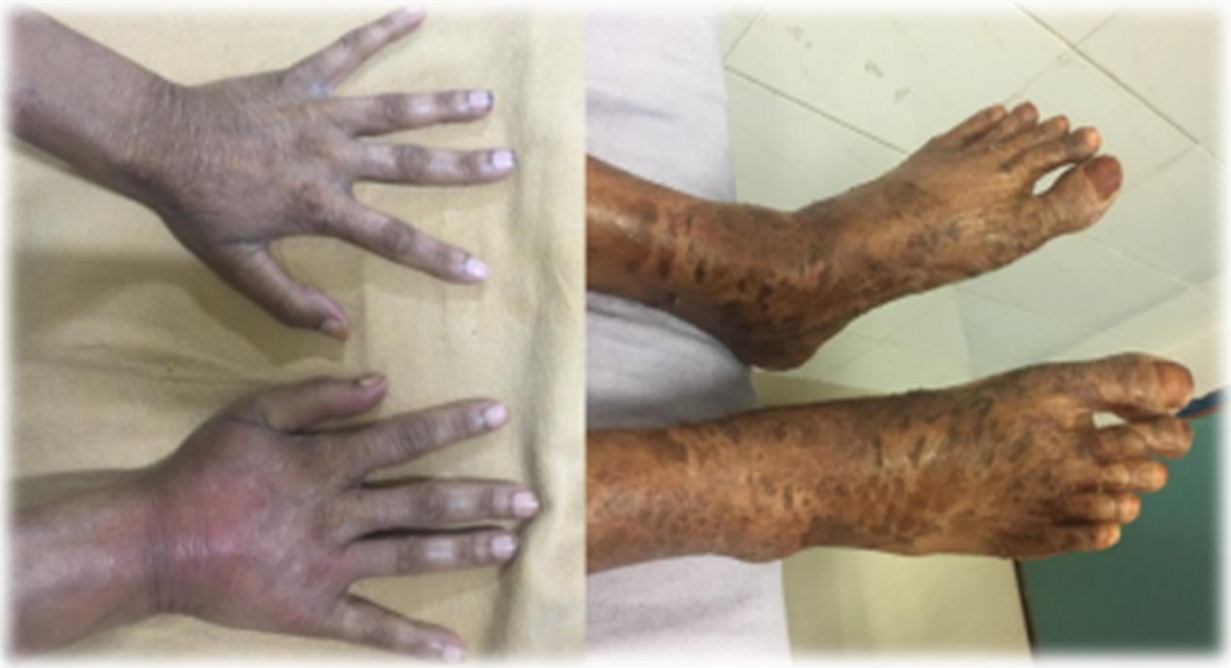

FIGURE1: Skin rashes over hands and legs in the exposed areas before treatment.

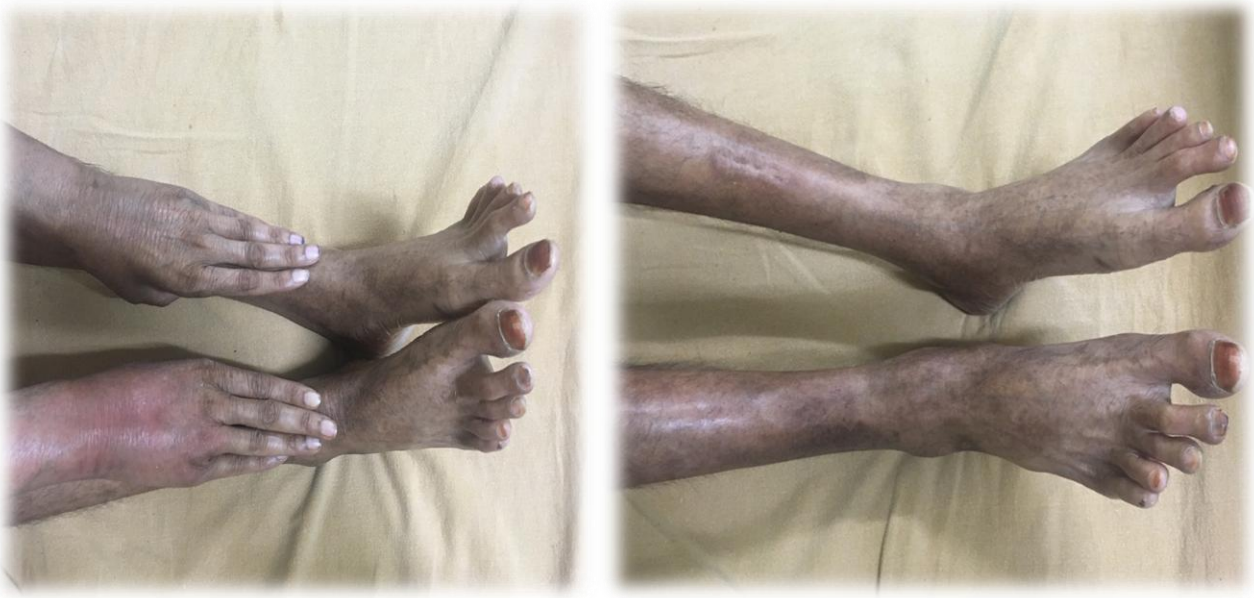

FIGURE 2: Skin rashes over hands and legs after treatment.

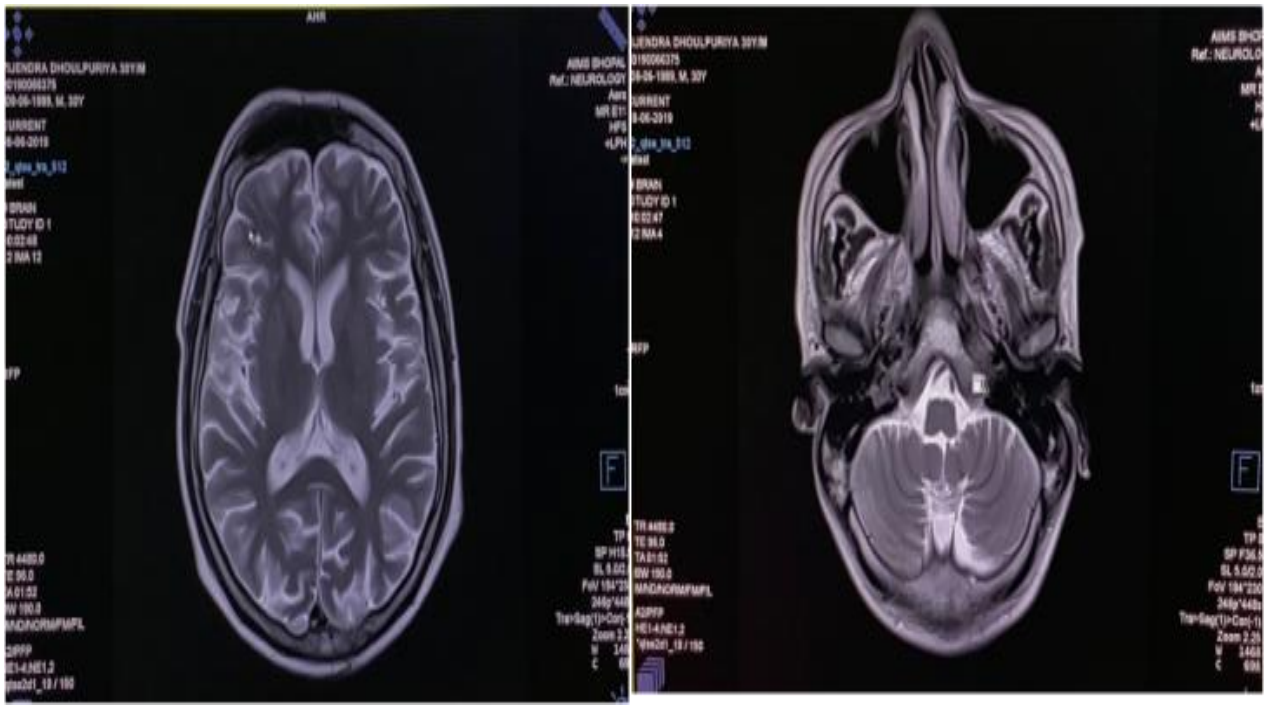

FIGURE 3: MRI brain was within normal limits.

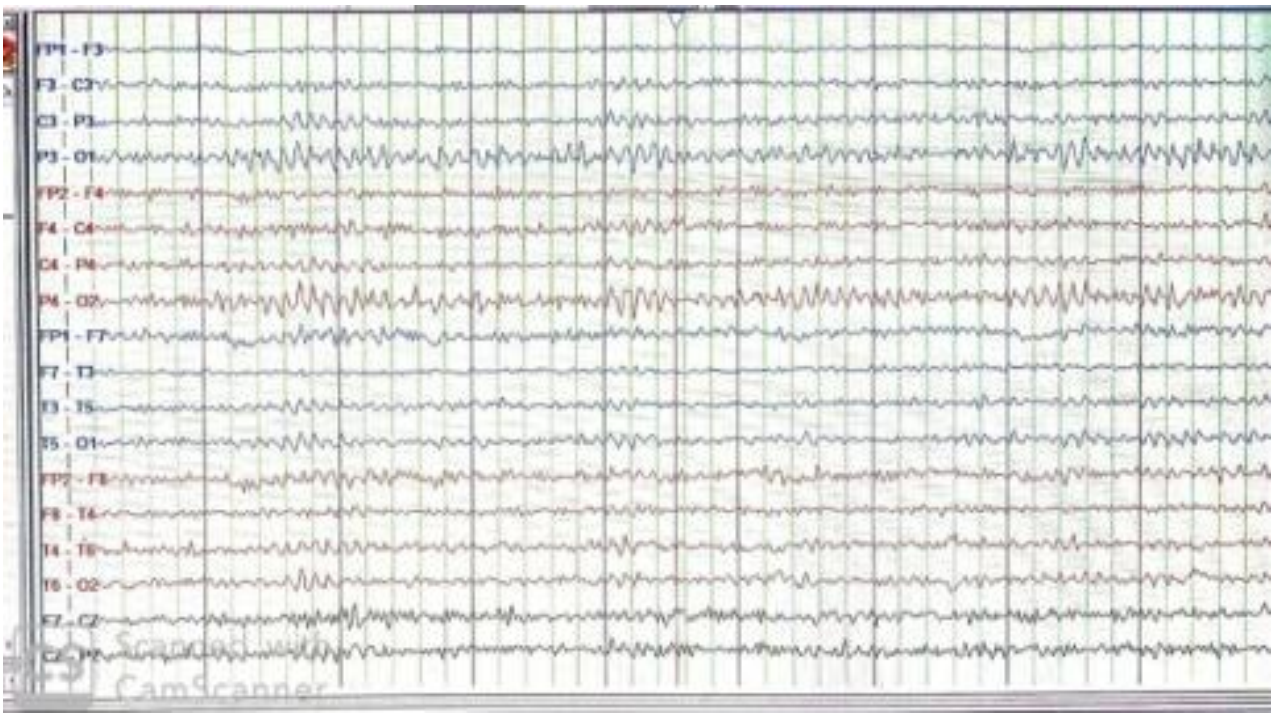

FIGURE 4: EEG showing normal waves from anterior to posterior leads.

TREATMENT

Nicotinamide 300 mg BD was given along with higher intravenous dose of thiamine as recommended for acute wernicke encephalopathy by the royal college of physicians. Thiamine was increased to 500 mg intravenously 3 times daily for 3 days followed by 250 mg iv for next 5 days followed by 100 mg orally TDS during hospital stay. In view of response to nicatinamide plus thiamine with pellagra skin lesion diagnosis of pellagrous encephalopathy with wernickes disease was considered.

OUTCOME AND FOLLOW UP

He showed dramatic improvement over next 3 to 4 days. Myoclonic jerks reduced in frequency and eventually disappeared. Ophthalmoplegia and his complaints of diplopia resolved. Ataxia improved in next 1 month.

DISCUSSION

Pellagra is nutritional disorder that occurs as a result of a severe cellular deficiency of niacin. The diagnosis of pellagra is clinical. Testing of serum and urine levels of niacin and its metabolites can be performed but these tests are not routinely recommended (8)(9); neither widely available nor reliable (10). The diagnosis is confirmed by rapid resolution of symptoms after starting niacin replacement. Replacement with nicotinamide is often recommended to avoid flushing commonly caused by niacin(4).

Pellagra is considered to be the cause of a vicious cycle of diarrhea and malabsorption of important nutrients. As in our case alcoholics usually suffer from multivitamin deficiency like thiamine which is commonly reported. Wernickes encephalopathy secondary to thiamine deficiency is a triad of confusion, ataxia and ophthalmoplegia. Our patient's symptoms resolved only after high doses of intravenous thiamine; so wernickes encephalopathy was obvious despite the patient showing myoclonic jerking which are more common in pellagric encephalopathy.

APE (acute pellagric encephalopathy) can present with other alcoholic encephalopathies like in combinations with Wernicke's disease (11). Serdaru et al (12)described APE associated in 13 cases with Marchiafava-Bignami disease and/or Wernicke-Korsakoff disease. Park et al (11) reported a case of APE with mental deterioration, myoclonic jerks and external ophthalmoplegia a feature of Wernicke's disease. Isolated cases of pellagra encephalopathy are been rarely reported. In chronic alcoholic patients' possibility of coexistence of multiple vitamin deficiency with pellagrous as well as wernickes encephalopathy should be considered. Niacin should be administered prior to thiamine with adequate intravenous dosages to prevent development of APE.

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