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Pellagrous encephalopathy and alcohol withdrawal delirium: A case report

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ABSTRACT

Chronic alcohol consumption is a common etiology, for pellagra is frequently under-diagnosed and thus not adequately treated. A 30-year-old gentleman presented with a history of consumption of alcohol in a dependence pattern for the previous 10 years with altered sensorium and hallucinatory behavior for 3 days. He exhibited skin lesions over sun-exposed regions of both the upper and lower extremities. He was diagnosed to have complicated alcohol withdrawal syndrome and alcoholic pellagra. He was treated with oral diazepam and multivitamins containing thiamine and niacin. The patient's behavioral problems and skin lesion improved gradually. Pellagrous encephalopathy was most likely a contributing cause of behavioral abnormalities and altered sensorium in our case and it could be recognized due to the presence of the typical rash. Pellagrous encephalopathy may manifest even without skin lesion. Niacin supplementation along with standard thiamine therapy is recommended in all cases of altered sensorium in heavy alcohol users.

Keywords: Alcohol withdrawal syndrome, delirium tremens, alcohol dependence, pellagrous encephalopathy, pellagra

1. INTRODUCTION

Pellagra has been linked to a deficiency of niacin (commonly known as nicotinic acid or vitamin B3) as well as its precursor, tryptophan. Pellagra's clinical presentation is commonly referred to as the "classic 4 D's," which denotes: Diarrhoea, dermatitis, dementia and death which is a potential outcome (Hegyi et al., 2004). Pellagra was typically detected in populations that subsisted mostly on maize and only occasionally consumed meat. Endemic pellagra was linked to poverty and malnutrition. Pellagra is now a disease of the past in developed nations due to the widespread availability of food fortified with niacin (Li et al., 2016). However, 'secondary pellagra' is still prevalent (Serdaru et al., 1988). Conditions that impede with tryptophan and niacin absorption or metabolism include anorexia nervosa, chronic alcoholism, persistent diarrhoea, ileitis, colitis, cirrhosis, carcinoid syndrome, Hartnup disease and HIV (Thornton and Drummond, 2014). Poor dietary input, niacin deficiency due to alcohol metabolism, malabsorption due to the

toxic action of alcohol on the stomach and cirrhosis are related to alcohol-induced pellagra. Insufficiency of the vitamin niacin in the brain can lead to severe neurological and psychiatric manifestations of the condition, including encephalopathy and psychosis. However, in individuals with alcohol use disorder or alcohol dependence syndrome, these symptoms are often misunderstood or not attributed to the pellagra. We present a patient with alcohol dependence syndrome who presented with neuropsychiatric symptoms and dermatological findings aided in the diagnosis of likely pellagra encephalopathy.

2. CASE SUMMARY

A 30-year-old unmarried painter, educated until middle school, with a family history of alcohol dependence syndrome in a first-degree relative, a medical history of pulmonary tuberculosis 4 years prior, a history of alcohol use for 15 years and dependence for 10 years, presented with complaints of agitation, aggression, fearfulness, suspiciousness and auditory hallucination for 3 days and 1 episode of generalized tonic-clonic seizure. The patient started consuming alcohol at the age of 15 years. The frequency and quantity of alcohol consumption increased gradually with development of tolerance, loss of control over alcohol use behavior, salience and withdrawal symptoms on abstinence and persistent use despite knowledge of physical harm over the last 10 years. The patient's most recent pattern of usage was about 15 units of Indian made foreign liquor, every day, with an eye opener drink to avoid withdrawal symptoms of tremors and sweating. In the last 3 years, occasional abstinence from alcohol for about 24-48 hours would precipitate alcohol related withdrawal seizures. He had received in-patient management for management of alcohol withdrawal symptoms and deaddiction on multiple occasions in the past. He had maintained abstinence for a maximum period of about 6 months. Relapses were usually associated with an initial lapse due to dysphoric craving.

In this background of alcohol use, the patient developed agitation, aggression, fearfulness, became suspicious of people and started hearing voices that others could not hear for the past 3 days. He reported that people he had borrowed money from, were coming to harm him or kill him. He was also reported to talk and gesture to himself by his family members. Following the onset of these symptoms, he stopped consuming alcohol for about 48 hours, after which he developed tonic clonic movements of the upper and lower limbs associated with up rolling of eyes, drooling of saliva and loss of consciousness. The episode lasted for about 3 minutes and the patient regained consciousness after 5 minutes. The patient restarted consuming alcohol after the seizure. His last drink was 4 hours before his presentation to us. The patient was provided in-patient care for management of his symptoms. On general physical examination, he had grade 3 clubbing, tachycardia, diaphoresis and his BMI was 18.3. Mild tremors were noted on bilateral outstretched hands. He exhibited hyperpigmented, well demarcated, scaly, itchy and flaky skin lesions over sun-exposed regions of both the upper and lower extremities suggestive of typical dermatological skin lesions seen in Pellagra. The skin was thick, crusty and cracked. On neurological examination, no ataxia, tremor or ophthalmoplegia was noted. On mental status examination, he was conscious, agitated and disoriented. His psychomotor activity was increased. The patient appeared hypervigilant and was constantly scanning the environment. The patient's affect was fearful. Persecutory delusions and 2nd person auditory hallucinations with threatening content were elicited. Blood investigations revealed low haemoglobin (11.1g/dl) and mildly elevated liver enzymes (AST=140 IU/dl, ALT=53 IU/dl, ALP=90 IU/dl). A differential diagnosis of alcohol withdrawal delirium, Pellagrous encephalopathy and Wernicke's encephalopathy were considered. He was started on Diazepam 20mg to manage possible complicated alcohol withdrawal and prevent alcohol withdrawal seizures. Multivitamin infusions consisting of 1500 mg of thiamine, niacinamide and pyridoxine each, 75 mg of riboflavin, 750 mg of pantothenol and 15 mg of cyanocobalamin was administered in three divided doses, in a day, as intravenous infusion diluted in 100 mL normal saline over 45 min for a period of 7 days. Parenteral multivitamins were well tolerated by the patient, who did not experience any allergic symptoms. Multivitamin treatment was switched to an oral formulation of vitamin B complex containing 10mg Thiamine and 45mg nicotinamide after 7 days of parenteral nicotinamide and thiamine at 1500 mg/day each. Diazepam was gradually tapered and stopped. The patient's agitation, psychotic symptoms and disorientation gradually improved over a week. Figure 1 illustrates the pellagrous lesion in our patient on the day of presentation and the subsequent resolution after 3 days and 7 days of niacin supplementation. Motivational enhancement therapy was administered. He was started on Baclofen 40mg as an anti-craving agent. He was also taught craving management techniques. Patient and family were psych educated about his diagnosis and the need for regular follow ups. On follow up after 2 weeks, the patient was abstinent from alcohol and there was further improvement in skin lesions as illustrated (Figure 1).

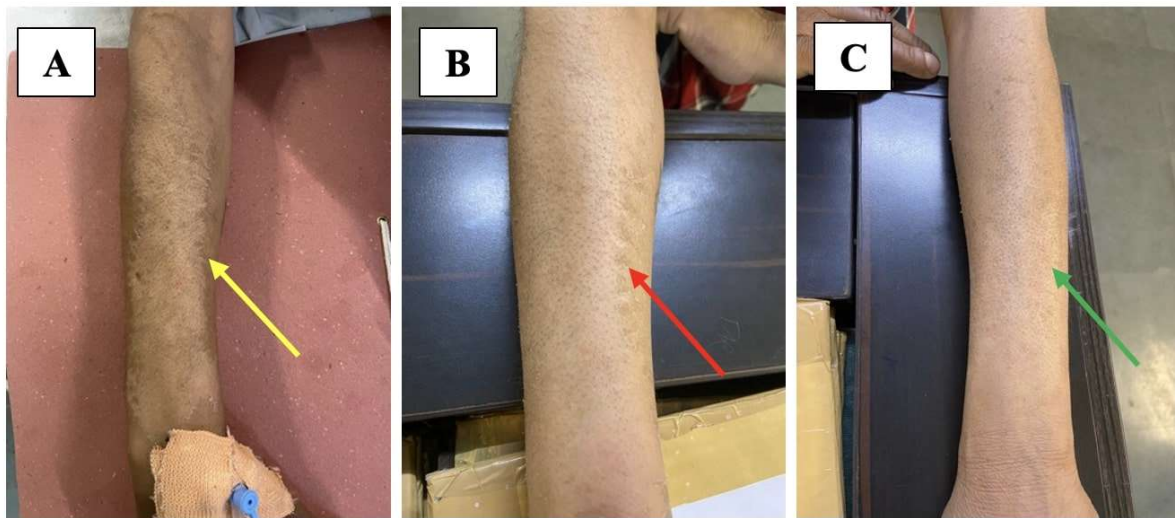


Figure 1 Pellagrous lesion A) On day of presentation; B) After 3 days of niacin supplementation; C) After 7 days of niacin supplementation

3. DISCUSSION

The prevalence of pellagra in the Indian population has not been extensively studied. However, comparable to developed nations, pellagra is expected to be uncommon (Gupta et al., 2014). Alcoholism has been linked to pellagra in a number of studies (López et al., 2014). Patients who have a history of persistent alcohol use are more likely to have inadequate oral nutrient intake since alcohol itself becomes a primary source of dietary calories. In addition, malabsorption can be brought on by injury to the villi of the duodenum as well as dysfunction in the pancreas. Alcohol can also hinder the body's ability to convert tryptophan into niacin. Our patient belonged to a community that consumed meat, with rice and wheat as their staple diet. Our patient's history of abusing alcohol for 15 years, 10 of which were spent in a pattern of dependence, was most likely the major contributing factor to the pellagra. Study suggests that the average number of years that patients with pellagra have been drinking alcohol regularly is twenty and that they consume an average of twenty units of alcohol per day (Narasimha et al., 2019). Our patient was noted to be consuming 15 units of alcohol every day.

Pellagra is characterised by a cluster of symptoms known as the traditional three "Ds" (dementia, dermatitis and diarrhoea). These symptoms are linked to the digestive tract, neurological system and skin, respectively. Pellagra can cause a variety of neurological symptoms, including cognitive impairment, apathy, seizure and psychosis. Niacin insufficiency in the brain decreases synthesis of serotonin and is responsible for neuropsychiatric symptoms. Similar to delirium secondary to other causes, presentation of pellagrous encephalopathy is variable and fluctuating.

The neuropsychiatric and gastrointestinal symptoms of pellagra are similar to the common problems that are experienced with chronic alcoholic use. Psychosis, delirium and seizures are frequently related to a complicated alcohol withdrawal syndrome, hepatic encephalopathy or Wernicke's encephalopathy in chronic alcoholics. As a result of the low prevalence of pellagra in the general population, the differential diagnosis of pellagra encephalopathy might not be considered for a particular clinical presentation. This is because doctors might not be familiar with the typical pellagrous skin lesion. Pellagra symptoms are similar to those of complex alcohol withdrawal and Wernicke's encephalopathy, making it difficult to tell the difference between the three conditions. In addition, Wernicke's encephalopathy and pellagrous encephalopathy might occur simultaneously in some patients. It has been reported that 1% of ADS inpatients visiting an Indian alcohol treatment centre have clinically diagnosed pellagra (based on skin lesions and response to niacin). Pellagra was also found to frequently occur in tandem with other severe neuropsychiatric symptoms such delirium tremens, convulsions and peripheral neuropathy. Our patient presented with neuropsychiatric symptoms of aggression, agitation, hallucinations, persecutory delusions, fluctuating orientation and seizure in the background of alcohol use. His last alcohol use was four hours before presentation. We were unable to delineate the symptoms of pellagra encephalopathy from alcohol withdrawal or a possible Wernicke's encephalopathy. The presence of typical dermatological lesion on the sun exposed areas of upper and lower extremities aided in considering a diagnosis of pellagra encephalopathy.

However, it is important to note that not all patients diagnosed with pellagra exhibit all three of the classic symptoms of the condition. According to the findings of a study that was carried out at a tertiary centre in India, only 10% of the patients of alcoholic pellagra exhibited all three symptoms. However, another study found that just 22% of pellagra patients were reported to have all

three symptoms. Consequently, doctors who solely base their diagnosis on the typical triad of symptoms may under diagnosis pellagra. Niacin deficiency can be hard to spot because there isn't a single, reliable biochemical test for it. Diagnosis of pellagra may be aided by measuring serum concentrations of niacin, tryptophan, NAD, NADP and 24-hour urine collections for N0-methylnicotinamide and 5-hydroxyindoleacetic acid. However, it can be time consuming and difficult to obtain these laboratory tests at most hospitals. Patient's history, physical examination and response to niacinamide supplementation may be the only practical and feasible way of confirming the suspicion of pellagra. Therefore, undetected encephalopathy in patients with heavy alcohol use should always be treated with multivitamin therapy that also includes niacinamide. Our patient received parenteral multivitamin therapy consisting of 1500 milligrams each of thiamine and niacinamide daily for 7 days. The occurrence of one vitamin deficiency should encourage the clinician to assess for additional vitamin deficiencies. Together, Wernicke's encephalopathy and pellagra can be challenging to diagnose. There is no way to identify for sure whether a patient's symptoms are due to Wernicke's encephalopathy, pellagrous encephalopathy or complicated alcohol withdrawal, as was the situation with our patient, although he exhibited the pellagrous skin lesion. Given that our patient consumed his last drink four days before his presentation and had signs (tachycardia, diaphoresis, hand tremors) suggestive of possible alcohol withdrawal on examination, he was detoxified with Diazepam 20mg. Over the course of a week, our patient showed gradual reduction in agitation, psychotic symptoms and disorientation. Patients with pellagra encephalopathy who were treated with the appropriate supplementations had delirium for a mean duration of 6 days.

Some cases of pellagra have been documented to worsen after treatment with thiamine and pyridoxine but without niacin. Untreated pellagra will worsen over the course of four to five years, resulting in death. Massive malnutrition due to recurrent diarrhoea and worsening neurologic symptoms has been suggested as the most common cause of death in such patients. It was shown that 27% of alcoholic patients who passed away in the hospital had neuropathology characteristics that were suggestive of pellagra. It is thus, recommended that all patients with chronic alcohol use presenting with neuropsychiatric symptoms should be administered with multivitamins that includes niacinamide. Initiating oral multivitamins comprising of preventive dose (20–30 mg/d) of nicotinamide on a regular basis in patients with chronic alcohol use can also be routinely done.

4. CONCLUSION

This case highlights considering differential diagnosis other than alcohol withdrawal delirium and Wernicke's encephalopathy for a patient with chronic alcohol use presenting with neuropsychiatric symptoms. Pellagrous encephalopathy was most likely a contributing cause for the behavioural abnormalities and altered sensorium in our case and it could be recognized due to the presence of the typical rash. Looking for characteristic features of pellagra and prompt treatment with multivitamins that includes niacin is of practical importance. However, pellagrous encephalopathy is known to manifest even in the absence of rash or diarrhoea. Therefore, niacin supplementation in conjunction with standard thiamine therapy is recommended in all cases of altered sensorium in heavy alcohol users.

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Authors' contributions

Each named author has substantially contributed to the underlying case and drafting this manuscript.

Informed consent

Written and oral informed consent was obtained from the patient.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

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