Case Report

A CASE REPORT ON CASPR2 POSITIVE AUTOIMMUNE ENCEPHALITIS PRESENTING AS DELIRIUM IN AN ALCOHOL-DEPENDENT PATIENT: A DIAGNOSTIC DILEMMA

Arya Jith[1*], Kathleen Anne Mathew[1], Dinesh Narayanan[1], Sheen Maria Jacob[1]

[1] Department of Psychiatry, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham University, Kochi
*Corresponding Address: Department of Psychiatry, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham University.Kochi. Email:aryaji2008@gmail.com

ABSTRACT

Delirium, a major psychiatric emergency commonly encountered in alcohol withdrawal state, can have various aetiologies. Here we present a case of protracted delirium in an alcohol dependent patient, which on detailed neurological workup was diagnosed to be autoimmune encephalitis with CASPR2 (contactin-associated protein-like 2) antibodies. Subsequent treatment with immunotherapy and steroids lead to the resolution of symptoms.

Keywords: Delirium, autoimmune encephalitis, alcohol withdrawal, CASPR2

INTRODUCTION

Delirium in an alcohol dependent patient can have multifactorial aetiology. Alcohol withdrawal state, metabolic abnormalities like hypoglycaemia and electrolyte imbalance, infection, trauma causing intracerebral and subdural haemorrhages, Wernicke's encephalopathy and hepatic encephalopathy are the common etiologies. They are usually explored and addressed at the initial presentation of delirium.[1] However, protracted delirium poses a diagnostic challenge to clinicians and causes significant morbidity to the patient.[2] Autoimmune encephalitis is a clinical entity that can have complex neurological presentations, including delirium, seizures, and psychosis. Anti-CASPR2 antibody has been recently recognised as associated with autoimmune encephalitis, with less than 100 cases being reported so far.[3] Here, we present a case of protracted delirium in an alcohol dependent patient, which was diagnosed to be anti-CASPR2 positive autoimmune encephalitis, on initiating treatment for which resolution of symptoms was achieved.

CASE REPORT

68 year old single male, living alone, presented with features suggestive of alcohol dependence for 20 years with no past history of withdrawal seizures or delirium. Family members reported that they had noticed an increased intake of alcohol for the last six months and that the patient started having tremors even during periods of continuous alcohol intake. They also noticed unsteadiness of gait, which they attributed to a fall and was not evaluated. Two days before admission, the patient was found unresponsive on the road with faecal incontinence. Family members who reached the spot noticed that patient was confused and had difficulty walking. The patient was brought to the Gastromedicine outpatient department the next day.

According to the patient's report, the last intake of alcohol was three days before admission. The possibility of an episode of alcohol withdrawal seizures was

Access the article online:
https://kjponline.com/index.php/kjp/article/view/265
DOI: https://doi.org/10.30834/KJP.34.1.2021.265
Received: 10/04/2021. Accepted: 30/05/2021.
Web publication: 07/06/2021

QR Code

Please cite this article as: Jith A, Mathew KA, Narayanan D, Jacob SM. A case report on CASPR2 positive autoimmune encephalitis presenting as delirium in an alcohol-dependent patient: a diagnostic dilemma. Kerala Journal of Psychiatry 2021;34(1):54-56

considered initially, and he was admitted for evaluation. He was afebrile with a pulse rate of 98/min and blood pressure of 150/100 mm Hg. Complete blood counts, electrolytes, sugars, blood urea, and serum creatinine were normal. Serum bilirubin (1.5mg/dL), AST (95 IU/L) and ALT(50 IU/L) were mildly elevated. USG abdomen showed features of chronic liver disease. evening, the patient was noted to have worsening of sensorium with agitation, hallucinatory behaviour and disturbed sleep. The patient was provisionally diagnosed to have alcohol withdrawal delirium. Parenteral thiamine supplementation at a dose of 100 mg three times a day was initiated. On the Clinical Institute of Withdrawal Assessment of Alcohol Scale (CIWA-Ar), the patient was noted to have a score of 26 and was started on Lorazepam 12 mg in divided doses. Subsequent titration in the dose of Lorazepam was done based on CIWA-Ar scores. The patient was transferred to psychiatry as he was unmanageable in the Gastromedicine ward. The dose of thiamine was increased to 1500mg per day. A low dose of antipsychotic (quetiapine 25mg twice daily) was added to control agitation. Even after continuing the treatment for ten days, the patient persisted to have disorientation and ataxia; neurological findings of rigidity of upper limbs and bradykinesia were also noted. Mini-Mental State Examination (MMSE) score was noted to be 10. A neurology consultation was sought, and Magnetic Resonance Imaging (MRI) was advised. MRI showed no features suggestive of Wernicke's encephalopathy. The electroencephalogram (EEG) was within normal limits. As a result, a secondary workup was done. Serum autoimmune panel showed positivity for CASPR2 (contactin-associated protein-like 2) antibody, and all other antibodies were negative. Cerebrospinal fluid (CSF) autoimmune and paraneoplastic panel was normal. A whole-body PET CT was done to rule out any underlying malignancy, which was found normal. The patient was started on iv immunoglobulin therapy and a pulse dose of iv methylprednisolone for five days, followed by oral steroids. The patient showed symptomatic improvement over the next one week and was discharged. On follow-up, the patient had an MMSE score of 28 and was found to be maintaining the improvement. A limitation of this case report is that since the patient had no reliable informant, there are deficiencies in the history obtained. Informed consent was taken from the patient for the write-up of this report.

DISCUSSION

Protracted delirium in an alcohol dependent patient requires special attention to exploring etiologies, including uncommon causes. Autoimmune encephalitis can be a rare cause of protracted delirium. It has been broadly divided into two main categories, those associated with intracellular neuronal antibodies and those associated with cell membrane antibodies.[4] Voltage-gated potassium channel complex (VGKC) plays an important role in restoring the cell to its resting state following an action potential. Antibodies against VGKC, which are present on the neuronal membranes of both the central and peripheral nervous system, were initially thought to be associated with autoimmune syndromes like Morvan syndrome, neuromyotonia, and limbic encephalitis. However, subsequent research showed that antibodies were not directed to VGKC but associated proteins, including leucine-rich glioma inactivated 1(LGI1) and contactin-associated protein-like2(CASPR2). Patients with LGI1 antibodies present with limbic encephalitis, often associated with hyponatremia and faciobrachial dystonic seizures.[3] Patient with CASPR2 antibodies are predominantly older males and can present with a wide variety of peripheral or central nervous system symptoms. It can also be associated with malignancies, especially thymoma, seen in 20% of the patients.[5] Cognitive disturbances, cerebellar symptoms, seizures, insomnia, autonomic dysfunction, weight loss, peripheral neuropathy, peripheral nerve hyperexcitability, and neuropathic pain are among the frequently observed symptoms.[6],[7] Since many of these symptoms are also present in a patient with alcohol withdrawal delirium, it can be arduous for the clinician to reach this diagnosis, especially at the initial presentation. In our patient, predominantly central nervous system symptoms were present, associated with CASPR2 antibodies. However, LGI1 antibodies were found to be negative. Immunotherapy is the treatment of choice in encephalitis associated with either of these antibodies.[8]

CONCLUSION

Despite addressing commonly associated etiologies, the persistence of delirium in an alcohol withdrawal patient necessitates a detailed neurological workup to look for rare autoimmune and paraneoplastic etiologies as well.

Timely diagnosis and intervention can considerably reduce morbidity and possible mortality in this set of patients.

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