Idiopathic recurrent stupor mimicking status epilepticus

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ABSTRACT

Stupor is defined as a deep sleep or behaviourally similar unresponsiveness from which the subject can be aroused only by vigorous repeated stimuli. Causes of stupor may be related to brain damage, toxic or metabolic encephalopathies. Idiopathic recurring stupor is a stupurous condition of unknown aetiology, unrelated to structural, toxic or metabolic disturbance. This condition responds to flumazenil, a benzodiazepine antagonist. We describe a 60-year-old man presenting with abnormal jerky movements of the body and who was wrongly treated as status epilepticus. He responded to flumazenil which confirmed the diagnosis.

Keywords: flumazenil, idiopathic recurrent stupor, stupor

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INTRODUCTION

Idiopathic recurring stupor (IRS) is a rare condition characterised by non-hereditary, episodic, transient unresponsiveness of unknown cause, lasting two hours to five days, with a frequency of three to seven attacks per year. Ictal electroencephalography (EEG) shows characteristic fast background activity. Flumazenil (a benzodiazepine antagonist) transiently awakens the patients with normalisation of EEG. Initially, all cases were described from Italy, but later on, cases from other places have also been reported. Maximum duration of recurring stupor is reported up to 16 years without diagnosis.[1,2] We present a 60-year-old man with a history of repeated transient unresponsiveness for the past three years, and who had an unusual clinical presentation.

CASE REPORT

A 60-year-old man, a lawyer by profession, was referred to us with a history of recurring episodes of unresponsiveness for the past three years. The attacks usually started with a loss of personal care in the morning after awakening as the first symptom, slowly progressing to jerky movements of right upper limbs and face, and finally leading to stupor within one to two days. The stuporous condition lasted 36–48 hours, followed by remission of symptoms and attainment of normal activities. Each time during such attacks, he was evaluated, and his biochemical and clinical examinations were normal. Inter-ictal EEG was normal. Clinical evaluation of this patient included investigations for complex partial seizure, non-convulsive status, cerebrovascular disease, *Herpes simplex* encephalitis and metabolic coma. His biochemical parameters including electrolytes, blood sugar, liver and renal functions, thyroid function test and blood ammonia levels, were within normal limits. Cerebrospinal fluid (CSF) examination revealed a minimal rise in proteins with no cells, normal sugar, negative smear/culture and antibody for *Herpes simplex* and *Cryptococcus*. Magnetic resonance imaging and inter-ictal EEG were also normal. He had a history of poor behavioural tolerance, and a habit of using analgesics or tranquillisers regularly without medical supervision. He also had history of insomnia and was a habitual user of oral alprazolam/diazepam.

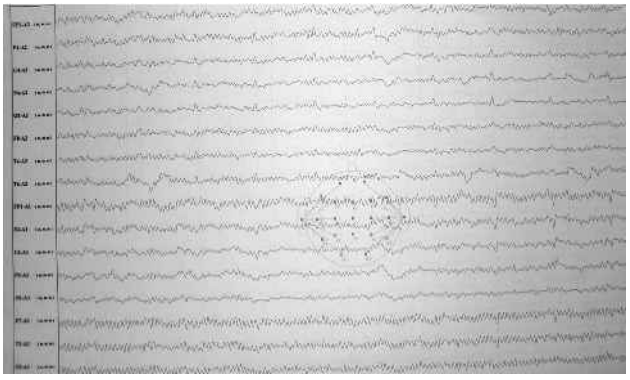

Fig. 1 Ictal EEG shows fast background electrical activity with absence of epileptic activity.

At the time of his first presentation, the patient was in the remission phase of the fourth episode of such stupor. He had spontaneous regression of symptoms within four days, and was discharged with the advice to come on recurrence of symptoms. He presented after three months to the emergency department with vigorous clonic movements of the head and limbs and unresponsiveness. The clonic movements were so severe that emergency treatment was done for status epilepticus with intravenous midazolam (0.3 mg/kg) and loading dose of phenytoin sodium (15

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mg/kg).When the patient showed no improvement in clonic jerks in the next one hour, we decided to paralyse the patient with artificial ventilation and midazolam infusion for controlling the activity. The next morning, neuromuscular paralytic agent along with midazolam and propofol infusion was stopped for detailed neurological assessment. The patient was found to have vigorous shaking of the upper half of the body with clonic jerks at the rate of one jerk per second, both proximally and distally. Due to these clonic movements, he incurred subluxation of the left shoulder joint. His eyes were open at that time with partial awareness. We started him on clonazepam and continued phenytoin sodium on the second day.

On the third day with continuous clonic movement, ictal video-EEG recording was done, and it surprisingly revealed no epileptic activity but only a fast background rhythm of 20 Hz (Fig. 1). At this juncture, the only possibility of IRS remained and an injection of flumazenil 1 mg was given as a test dose. The patient showed remarkable recovery in clonic jerking and in sensorium. The response was transient and lasted 20 minutes. Seeing this response, we immediately stopped all antiepileptics and sedatives. We could not get oral flumazenil for maintenance therapy, but after withdrawal of antiepileptics and withholding benzodiazepine, he had gradual recovery. He was gradually weaned off the ventilator, and the patient became fully conscious and responsive.

DISCUSSION

Presentation of a patient in a stupor is a common diagnostic problem for emergency departments everywhere. A relapsing remitting type of unresponsiveness is commonly associated with vascular, metabolic or toxic encephalopathies.[3] Endozepine stupor is only considered after excluding common aetiologies and a high index of suspicion. IRS as an entity for diagnosis is a recent phenomenon first reported by Tinuper et al in 1992.[4] Diagnosis rests on the characteristic ictal EEG findings of background 14 Hz activities, detection of benzodiazepine-like factor (endozepine 4) in CSF, and characteristic improvement in stupor after injection of flumazenil.

In our case, the patient presented with abnormal movements favouring a diagnosis of myoclonus or epileptic partialis continua. It was only the presence of fast rhythm discharges without epileptic activity on ictal EEG that helped in ruling out non-convulsive status as a cause of stupor. Since previous reports had not reported abnormal movements in their patients, the diagnosis was delayed and we wrongly administered benzodiazepines for controlling the jerks. This resulted in prolongation of the episodes. As the facility for endozepines assay was not available, it could not be used for detection. We had also considered the possibility of psychiatric illness, particularly the Manchausen syndrome, as the patient was a habitual user of anxiolytics and tranquillisers. Previous reports had not found any psychosis or other psychiatric illness in these cases. Seeing the patient's condition, with the need for prolonged ventilation, the possibility of Manchausen syndrome was not very likely. Ultimately, a quick response to flumazenil was a strong indicator towards IRS.

We could not provide a good explanation for these clonic and myoclonic jerks in our case, but these could be explained by exaggerated flapping tremors (negative myoclonus), like in other metabolic encephalopathies. This may be a rare and difficult presentation in IRS, as the treatment can result in a delayed and poor outcome. Ictal EEG was important to exclude status epilepticus. We concluded that clonic and myoclonic jerks might be rarely associated with IRS, which can be confused for seizures, but normal ictal EEG and prompt response to flumazenil injection are important clues for confirming the diagnosis.

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