Introduction

Inadequate glycemic control has been associated with depression, anxiety disorder, and cognitive impairment in patients with long-standing diabetes and both psychological and neurobiological mechanisms are involved in the development of such symptoms.[1] So far, there is no report of dissociative syndrome associated with hyperglycemia in patient with diabetes. Here we are reporting a case of repeated dissociative fugue associated with hyperglycemia, in an elderly with type II diabetes. Possible neurobiological mechanism has been discussed.

Case Report

A 73-year-old married illiterate male of urban background, was referred from the Department of Medicine for psychiatric evaluation and management for repeatedly traveling away from home without any apparent reason. During the episode, he would interact normally with others, did not reveal his identity, and had self-care intact. Except for the failure to recognize familiar people and behaving like a stranger, no abnormalities in his behavior were observed during traveling. The episode would last for many hours; thereafter he would realize to have traveled far away from home. He could not ascertain the reason and details of travel, though he could tell all details preceding the episode. Due to safety concern related to episode, the family members stopped allowing him to go alone out of home.

Physical examination revealed thin build, blood pressure 126/86 mmHg pulse 80/min. Systemic examination, including fundoscopy did not reveal any abnormality. Detailed physical and neurological examination were within normal range. Random blood sugar was 364 mg/dl, and hemoglobin A1c (HbA1c) was 5%. Other investigations such as total and differential blood count, serum electrolytes, blood urea, serum creatinine, liver function test, lipid profile, urine drug screening, and computed tomography scan and electroencephalogram (EEG) (standard and sleep deprived) were within normal range. Patient underwent detailed psychiatric evaluation. Detailed mental status examination and psychological evaluation of memory, executive function and intellectual function did not reveal any abnormality except for inability to give detailed account of those traveling episodes. There was no history suggestive of epilepsy, other physical illness, severe traumatic life event or abuse, memory loss apart from that for the episodes, transient global amnesia, dementia, delirium use of medication other than anti-diabetic agents, malingering, factitious disorder, substance abuse or any other psychiatric disorder at the time of presentation or in the past.

On further clarification on antecedent, the family members and patient reported that such episode occurred only when rice dosa (carbohydrate-rich food) was served in breakfast and...
patient missed the dose of anti-diabetic medication. After each episode, he was brought to the physician and random blood sugar level would be between 300 and 375 mg/dl and other reports (TC, DC, Hb, HbA1c, serum electrolyte, urine drug screening, and EEG) were within normal range. He was detected to have type II diabetes 3 years back and started on tablet metformin 500 mg before breakfast and except on the day of a dissociative episode, his blood sugar level were found to be in normal range. Initial 2 years of his illness, the compliance was good, but later he would miss the dose of anti-diabetic. As per the International Classification of Mental and Behavioral Disorders, 10th version,[2] a diagnosis of organic dissociative disorder was made (all episodes occurred during the peak of hyperglycemic state that has temporal relation in terms of onset of dissociative fugue symptoms and no alternative causation of the mental disorder were present). Since episodes were following the missing dose, counseling was done for possibility of occurrence of such episode if patient missed the anti-diabetic medication, nature of illness, the need for compliance and control of diabetes and possible consequences of uncontrolled diabetes. The family members were also explained about safety issues that may arise during episodes, the possibility of occurrence of such episode if patient missed the anti-diabetic medication and were advised to supervise the intake of anti-diabetic medication. Patient compliance improved and no further episodes were reported.

Discussion

This case report highlights that how a dissociative fugue of hyperglycemic state in patients with diabetes may be missed in routine consultation with physician, until it is grossly apparent in patient’s behavior. In elderly, such incidences are often considered as a symptom of dementia. Though dissociation is reported with diseases of central nervous system and other systemic disorders, with the best of our knowledge, this is first case report of hyperglycemia associated dissociation in patient with diabetes.[3][4] Traditionally, the dissociation is considered as an escape from overwhelming distress with partial or complete loss of control on voluntary actions or alienation of oneself or external world. Transient dissociation is common as a part of other psychiatric disorders such as acute stress disorder, posttraumatic stress disorder, depersonalization and derealization, panic disorder, psychotic disorder, sleep disorder, substance use disorder, and personality disorder.[5] In this case, elderly patient with the absence of other psychiatric disorders/other physical illness with consumption of carbohydrate rich diet and missing dose of anti-diabetic medication preceding each episode of dissociative fugue helps to conform the association with hyperglycemia. However, one should be very careful in considering such association, as abuse, traumatic life experience, and atypical presentation of psychiatric disorder in elderly is not rare that may present with such symptoms and hamper compliance of medication prescribed for common physical comorbidity including diabetes.[6] Though diabetes is known to impair attention, speed of information processing, motor skills, working memory, the mechanism involved in the occurrence of dissociative fugue is unknown [Figure 1].[7]

Figure 1: Possible mechanism of acute hyperglycemic associated fugue

Report of dissociation associated with used of ketamine and cannabis (N-methyl-D-aspartate [NMDA] antagonist effect) gave rise to a NMDA hypothesis of dissociation. Diabetes can induce NMDA receptor subunit composition resulting in cognitive impairment, and NMDA-receptor antagonists have shown to improve cognition in overactivation.[7] On the other hand, activation of NMDA receptors in the dorsal vagal complex lowers glucose production, and is involved in glucose-stimulated insulin secretion from beta cells.[8] Role of gamma-aminobutyric acid (GABA) and 5-HT2 is unclear. The activation of GABA (A) receptors decrease insulin secretion and GABA (B) receptor antagonist increase insulin release in pancreatic islets in type II diabetes.[9] GABA synthesis is impaired in hyperglycemic state.[9] GABA-A antagonism and 5-HT2a/2c agonism can induce dissociative-like symptoms.[10] 5-HT2a receptors are implicated in the molecular mechanisms of anti-diabetic medication.[11] Hyperactivation of the hypothalamic-pituitary-adrenal (HPA) axis is also reported in diabetes. Thus, in isolation or in combination with above pathophysiology, hyperglycemic state may result in dissociative symptoms. Other findings observed in patient with dissociation are reduced perfusion in inferior prefrontal and anterior temporal regions in the right hemisphere and abnormal functioning of the HPA axis, serotonin (5-HT2a, 5-HT2c), GABA, and opioid receptors.[12][13]

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