

## Case Study: Cognitive Impairment, Depression, and Severe Hypoglycemia

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The following case study illustrates the clinical role of mental health professionals who specialize in the treatment of people with diabetes. This case describes the diagnostic dilemma presented by a patient with diabetes and a history of severe hypoglycemia complicated by other medical, psychiatric, social, and functional problems.

Cognitive impairment (e.g., memory loss, increased distractibility, and confusion) can present a difficult diagnostic problem for clinicians because it can be symptomatic of many underlying and undetected clinical conditions. Careful diagnosis is crucial because some causes may be progressive and irreversible, whereas other causes may be reversible with medical or psychiatric treatment. Some of the more noteworthy causes are related to medication, alcohol, aging, depression, and, as in this case study, the possible consequences of recurrent severe hypoglycemia related to diabetes.<sup>1</sup> Diabetes, of course, may cause an increase in cognitive decline over the course of time because of vascular risk factors.<sup>2</sup> Some evidence suggests that acute hyperglycemia may have a negative impact on cognitive performance.<sup>3</sup>

Depression is the most common of the reversible causes of memory impairment, and people with diabetes are twice as likely to suffer from depression as those without diabetes.<sup>4</sup> Recent evidence suggests that diabetes may create alterations in regions of the brain that are associated with affect regulation and increase the risk for developing a depressive disorder.<sup>5</sup> Fortunately, problematic medications can be modified, and alcohol misuse or depression can be treated. Unfortunately, despite its relevance to the

course of diabetes, depression is recognized and treated in fewer than one-third of people with diabetes.<sup>4</sup>

The relationship between recurrent severe hypoglycemia and cognitive impairment remains unclear. Both prospective and longitudinal studies of cognitive function have been so plagued by methodological problems that it is difficult to unequivocally determine whether patients who experience repeated episodes of severe hypoglycemia are at risk for permanent brain injury or intellectual impairment. However, those with diabetes of long duration, especially with comorbid neuropathy, may be at higher risk for cognitive deficits resulting from hypoglycemia.<sup>6,7</sup> A meta-analysis of studies about cognitive performance in patients with type 1 diabetes found that lowered cognitive performance was associated with the presence of microvascular complications but not with the occurrence of severe hypoglycemia.<sup>8</sup> Recently, the Epidemiology of Diabetes Interventions and Complications study, a follow-up to the Diabetes Control and Complications Trial (DCCT) reported that multiple severe hypoglycemic episodes did not lead to increased risk for cognitive impairment in the subjects who had participated in the DCCT.<sup>9</sup>

### Case Presentation

Steve is a 67-year-old white widower and retired accountant. He was referred for psychosocial evaluation at the diabetes clinic after an emergency room (ER) visit to a local hospital. He arrived at the ER with confusion and a severe hypoglycemic episode after taking an overdose of insulin. He denied suicidal intent or alcohol abuse

and claimed to have mistakenly taken insulin lispro rather than his insulin glargine dose. The ER staff was suspicious about his claim because there had been eight similar ER visits for severe hypoglycemia within the last 2 years. He explained these previous events as a result of mixing up the types of insulin he injected.

After psychiatric assessment he was not judged to be a suicidal risk. He was discharged after his blood glucose levels stabilized, and he promised to pursue outpatient mental health treatment. His hemoglobin A<sub>1c</sub> (A1C) at the time was 7.9%—his lowest on record for several years. Generally, his blood glucose levels displayed wide swings. He explained that high blood glucose levels made him feel more apathetic about eating and depressed about his diabetes self-management.

### Personal history

As a child, Steve attained developmental milestones at expected times. His father was in the Army, and as a result, Steve had moved 32 times before he graduated from high school. He was an excellent student throughout high school but only managed mediocre grades in college because of family conflict. He dropped out of college in his junior year and moved to a South Pacific island for 1 year.

After returning to the United States, he earned an undergraduate degree in English and then a second degree in accounting. After graduation, he married and worked for 20 years as an accountant in a group practice. Later, Steve started his own accounting firm, but he had difficulty keeping organized and recalls being constantly late for business meetings and failing to complete projects on

time. In hindsight, Steve believes that he has struggled with depression on and off for > 30 years. He first recalls feeling depressed after his diagnosis with diabetes 36 years ago. He felt more depressed after he lost his 47-year-old sister to colon cancer in 1988, and then his 74-year-old father died from heart disease in 1991. But, he says his life “really fell apart” when his 54-year-old wife died from lung cancer in 1995. He contemplated suicide for 3 months but never acted. During this desperate period, he marginally functioned, lost many business clients, and was forced to close his company.

Overwhelmed by depression, he moved to the West Coast to live with his mother and worked at unskilled jobs. Diabetes complicated his emotional struggles, with blood glucose control fluctuating wildly and ranging from episodes of ketoacidosis that required hospitalization to severe hypoglycemic events that resulted in car crashes. Depression complicated his diabetes management, and after a hypoglycemia-related auto accident in which he ran over several pedestrians, he decided to stop working and was approved for social security because of psychiatric disability.

He came to the East Coast in 1998 to briefly visit his younger brother and decided to stay. Although he still lives near his brother, he says they have had only sporadic contact since a falling out after Steve “passed out” during a severe hypoglycemic episode. In 2000, Steve got engaged, but his fiancée left him to marry the father of her child. He says he felt devastated by the loss of yet another woman who had “become everything” to him. Since then, he has withdrawn socially and does not leave his apartment unless it is necessary. He has trouble managing his money, keeping his apartment neat and orderly, taking medications on time, and maintaining any structure in his day.

### Medical history

Steve punctually arrives at the correct hour but often on the wrong day for his medical appointments. He grapples with neuropathy, retinopathy, and unpredictable blood glucose levels. He monitors his blood glucose levels 8–12 times/day and tries to be careful about

what he eats. He also has sleep apnea, and his sleep patterns are highly erratic. He frequently does not fall asleep until 4:00 A.M. and then may only be able to sleep for 2 hours. Often, he will then nap for several hours in the afternoon. He began continuous positive airway pressure treatment for his sleep problems in 2003 but did not tolerate treatment. He has switched to bilevel positive airway pressure (biPAP) within the last 18 months but only tolerates it for up to 3 hours each night. Additional diagnoses include hyperlipidemia, hypertension, atrial fibrillation, Meniere’s disease, tinnitus, and arthritis. His medication list includes atorvastatin, lisinopril, hydrochlorothiazide, warfarin, meclizine, and folic acid. He does not smoke and only rarely drinks alcohol. Only his paternal grandmother had diabetes.

### Psychiatric history

Depression has plagued Steve since his diagnosis with diabetes. As noted earlier, his depression intensified after the deaths of his sister and father, but he did not descend into a suicidal mood until his wife died 10 years ago. Four years ago, he underwent electroconvulsive therapy (ECT), and although he continues to have occasional suicidal ideation, he has not made an attempt and has had no further psychiatric admissions. Both of his parents, his brother, and his sister suffered from depression. A maternal aunt suffered from dementia. His mother also struggled with alcohol abuse until her death from emphysema in 2004 at the age of 89. At the time of referral, he was taking fluoxetine, 40 mg, and venlafaxine, 37.5 mg, prescribed by a psychopharmacologist.

### Questions

1. Was Steve’s insulin overdose accidental or a suicide attempt?
2. What are the causes for his cognitive impairment?
3. How do his depression and cognitive problems affect his diabetes self-management?
4. What are the treatment recommendations?

### Discussion

When Steve started treatment, he was interested in learning how to

alleviate his depression and improve his diabetes care. He was pleasant, cooperative, thoughtful, and tactful, and his language was eloquent but often emotionless. He tended to give very detailed and pensive answers to questions.

Careful clinical evaluation found that his insulin overdose was best explained by lack of attention rather than suicidal intent, desire for secondary gain, or fear of hyperglycemia. His eight previous severe hypoglycemic episodes raised the question of why this intelligent man kept repeating the same mistakes. His history hinted at troubles with complex cognitive functions (e.g., ability to plan, sequence, prioritize, organize, and initiate) that extended back to his college days. He reported that in the past year he had experienced more memory problems, sometimes forgetting names and having word-finding difficulties despite a sophisticated vocabulary base. He had also noticed increased short-term memory problems and a decline in attention span during the same period of time.

Earlier in the year, an episode of extremity weakness and fatigue had led to neuroimaging studies that revealed no evidence of neurological injury or stroke. Certainly, depression, perhaps further complicated by ECT, aging, 3 decades of diabetes, and recurrent episodes of severe hypoglycemia, may have contributed to his cognitive decline. In fact, he reported feeling more depressed within the past 6 months. He was referred for neuropsychological testing to further understand his changes in cognitive function and target treatable symptoms.

Neuropsychological tests indicated that his baseline functioning was in the superior range. He exhibited strengths across most cognitive domains, including memory, language, reasoning, and complex cognitive functioning. In contrast, he demonstrated relative weakness in mental speed, mental flexibility, word retrieval, and fine motor control. There was evidence for a moderate to severe level of clinical depression. Compared with prior testing (3 years previously), he exhibited a decline in processing speed, mental flexibility, word retrieval, and fine

motor control. It was theorized that these changes were related to the cumulative effects of poor sleep, worsening depression, and multiple hypo- and hyperglycemic events. His care provider felt that unless his medical conditions were properly treated, his cognitive abilities would continue to fluctuate, and he would have even more difficulty circumventing these problems.

The care provider recommended that he try to regulate his sleep patterns, specifically avoiding long afternoon naps, and use his biPAP machine to help improve sleep. Better sleeping patterns should improve his attention span and overall cognitive functioning. The need for continuation of individual psychotherapy and psychiatric medications for depression was evident and eagerly accepted by Steve. Pursuing his therapy at a diabetes clinic easily opened the door for a referral to other members of the diabetes team (including an endocrinologist, dietitian, and nurse educator) to help regulate his erratic blood glucose levels. It also allowed for diabetes care to be truly collaborative.

It is widely accepted that depression can create more difficulties in maintaining treatment adherence and that the hardships of managing diabetes can lead to depression.<sup>4</sup> Steve lost his appetite when depressed and increased his risk of hypoglycemia. He was maintained on fast-acting insulin to provide more flexibility with meals and was prescribed an insulin pen to avoid mixing up different types of insulin.

Steve attended Blood Glucose Awareness Training sessions. This is a well-documented psychoeducational program that offers several empirically validated benefits for people with type 1 diabetes. Benefits include improved accuracy of blood glucose estimations, improved detection of hypoglycemia and hyperglycemia, improved judgments related to decisions about treatment when blood glucose is low, and a reduction in episodes of severe hypoglycemia.<sup>10</sup>

Despite being quite likeable, Steve reported feeling isolated and lonely. He said he often felt “disengaged” from others, emotionally detached, and affectively flattened. To provide structure to his day, increase his level

of cognitive and social stimulation, and learn from others about how to cope with diabetes and depression, he was referred to a hospital-based group for people suffering from depression and to one of the clinic’s diabetes support groups. For additional social connection, he was encouraged to pursue his interest in photography.

Steve followed through on all recommendations. He has not had a severe hypoglycemic episode during the past 7 months. His A1C has changed from 7.9% at the time of referral to 8.3%, most likely reflecting the avoidance of severe lows. In individual therapy, he continues to work on his tendency to be too passive and mercilessly self-critical, and in the groups he is gaining more awareness of his tendency to feel either emotionally detached or overwhelmed by others. He has also enrolled in photography classes.

### Clinical Pearls

- How can one tell if a patient is depressed? Suspicion may be raised by history or reports of relatives, but most often it is the clinical discussion that discovers the cognitive and affective symptoms of depression, such as fatigue, insomnia, weight loss, poor concentration, loss of interest or pleasure in daily activities, sadness, helplessness, and hopelessness. Asking simple questions, such as “During the past month, have you been bothered by feeling down, depressed, or hopeless?” and “During the past month, have you been bothered by little interest or pleasure in doing things?” can be as successful as formal surveys when screening for depression.<sup>11</sup>
- How can one tell if a patient is cognitively impaired? Suspicion may be raised by difficulties with orientation, attention, reasoning, and memory problems, such as difficulty learning new information or remembering old information. Other clues include difficulties with calculations, perceptual disturbance, or language disturbance, such as word finding or perseveration. Complex cognitive functions, such as planning, organizing, sequencing, and abstracting, may be impaired. In a clinical interview, it is often difficult to follow the logical sense of a cognitively impaired patient’s presentation.<sup>12</sup>
- How can one tell the difference between cognitive deficits caused by depression and those caused by brain injury? Depression can cause slowing of information processing, decreased attention and concentration, and learning problems. It can be difficult to know whether mild deficits in concentration or learning are caused by depression, mild traumatic brain injury, or both. Often, the most practical approach to such cases is to treat the depression first and then re-evaluate the patient for any residual neurocognitive deficits. Some areas of cognition are also not generally affected by depression, for example, language, problem solving, visual spatial analysis, complex cognitive functions, and visual or auditory perception.
- When should one refer someone for neuropsychological testing? The most common reasons are when:
  - ◆ A medical condition is suspected to have affected brain health (e.g., recurrent severe hypoglycemia or hyperglycemia)
  - ◆ Situational explanations for changes in emotions or cognitive functioning cannot be readily identified
  - ◆ Relatively sudden, unexpected, and unaccounted for changes appear in mental or cognitive performance that affect work or daily functioning.<sup>13</sup>
- Who is appropriate to refer to a support group? Patients who are willing to listen to others and talk about themselves are good candidates for a support group. Exclusionary criteria include refusal to abide by group guidelines and serious problems with interpersonal relatedness. Contrary to popular opinion, patients who do not do well in groups are not good group candidates. Caution also needs to be exercised when including patients who are highly impulsive, acutely suicidal, or psychotic.<sup>14</sup>

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