Hypoglycaemia, persistent delirium, and dementia

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ABSTRACT
A 70-year-old diabetic woman presented with prolonged episodes of delirium following hospitalisations for hypo- or hyper-glycaemia. Her persistent delirium mimicked dementia and probably precipitated the development of dementia. Hypoglycaemia is a risk factor for dementia, thus stringent glycaemic control is not advisable in frail diabetic older adults.

CASE REPORT
In September 2007, a 70-year-old woman with diabetes mellitus managed with insulin was first admitted for hypoglycaemia secondary to altered appetite with continuation of existing insulin regimen (based on a haemoglobin A1c level of 8.1%). During hospitalisation, the patient appeared more sluggish than usual; her mini mental state examination (MMSE) score was 13/30 (illiterate), which was used as a reference for future comparison. Standard dementia work-up to identify secondary causes was negative. Computed tomography of the brain revealed left cerebral infarcts and minimal small vessel disease (Figure 1). In older patients, cerebral vascular insults are common and can precipitate underlying Alzheimer’s disease.¹

Three weeks after discharge from hospital, the patient remained sluggish and was diagnosed with Alzheimer’s disease and prescribed cholinesterase inhibitor (CEI). Brain damage was probably secondary to prolonged hypoglycaemia or neuroglucopenia. Four months later, the patient’s condition had improved. Her MMSE markedly rose to 23/30; she could independently select her clothing and manage bathing and toileting. Nonetheless, CEI was continued. In January 2010, the diagnosis was reviewed and CEI was stopped, as Alzheimer’s disease was unlikely: the patient could go travelling alone and inject insulin at the correct dose unaided. No deterioration was observed subsequently.

In October 2010, she was hospitalised again for hypoglycaemia. Her MMSE was 17/30. She was kept under observation and her MMSE reverted to 23/30 after 3 months (Figure 2). She had 2 further admissions for glucose fluctuation. Her son complained that his mother had a poor memory, started to wet her pants, and forgot her insulin injections. Memory loss is the cardinal symptom of Alzheimer’s disease. Her incontinence was too early for Alzheimer’s disease and more likely related to polyuria, urinary infection, or neurogenic bladder secondary to diabetic neuropathy. The patient took meals irregularly because of her poor memory and time disorientation. She could no longer manage her personal hygiene. Her condition fulfilled the criteria for a diagnosis of Alzheimer’s disease or mixed dementia, despite an MMSE score of 23/30. She was re-commenced on CEI.

The patient had more admissions because of glucose fluctuation, likely related to irregular meals and inter-current infection. In September 2012, her MMSE score was 19/30. In November 2012, she had a fall and was sent to a nursing home. Her MMSE score was 15/30. She had further admissions and attended a geriatric day hospital, but was prematurely discharged because of failure to participate in rehabilitation. In retrospect, she probably had an ongoing hypoactive delirium. Her MMSE score was...
Figure 1. Computed tomography of the brain showing left cerebral infarcts and minimal small vessel disease.

Figure 2. Relationship between mini mental state examination (MMSE) scores, prescription of cholinesterase inhibitor (CEI), and hospital admission (a).
9/30 on discharge of the day hospital. Five months later, her MMSE score reverted back to 15/30. She managed to walk with a frame. She could identify the place, the person, and her age. Her haemoglobin A1c was 8.8%, which was an optimal level given her recurrent hypoglycaemia and frailty.

**DISCUSSION**

In our patient, the 4 risk factors for the development of dementia were (1) diabetes, (2) recurrent hypoglycaemic episodes, (3) cerebral infarcts, and (4) recurrent prolonged delirium. Delirium can predict future risk of dementia, and can persist for months in a quarter of patients. If delirium persists, its distinction from dementia or milder syndromes of chronic cognitive impairment becomes blurred. It is not known if persistent delirium is neurobiologically and prognostically distinguishable from dementia. Persistent delirium is associated with hypoactive symptoms.

Although hypoglycaemia is usually transient and readily reversible, it increases the risk of dementia. In animal studies, insulin-induced hypoglycaemia damages neurons that are responsible for memory and learning. In humans, hypoglycaemia also precipitates platelet aggregation and fibrinogen formation in cerebral circulation and causes micro-infarctions. Insulin increases beta amyloid secretion and inhibits its degradation. As hypoglycaemia is caused by either excessive endogenous or exogenous insulin, the associated dementia risk may be related to hyperinsulinaemia via beta amyloid metabolism.

Thus, treatment for diabetes in older adults should be individualised and based on the guidelines for glycaemic control in type-2 diabetes mellitus. To protect the brain, stringent glycaemic control is not advisable in frail older patients. However, poor glycaemic control can also be deleterious to cognitive function.

**CONCLUSION**

Persistent delirium can mimic dementia and can precipitate the development of dementia. Hypoglycaemia is a risk factor for dementia; thus stringent glycaemic control is not advisable in frail diabetic older adults.

**REFERENCES**