

Early-onset dementia in type 1 diabetes mellitus

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Abstract

This case displays the difficulty of managing type 1 diabetes with young-onset dementia, with co-existing medical challenges that have an effect on each other.

We outline current evidence on how hypoglycaemia could have potentially led to the patient's cognitive impairment, and demonstrate the difficulties that may be encountered in the management of recurrent hypoglycaemia in diabetic patients with dementia due to both declining cognition and associated psychiatric symptoms.

In the light of this we would call for additional research to aid in the management of this complex and increasing cohort of patients. Copyright © 2016 John Wiley & Sons.

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Key words

diabetes; dementia; Alzheimer's; hypoglycaemia; type 1

Introduction

It has been difficult to establish whether type 1 diabetes mellitus and Alzheimer's disease have a clear link in the underlying processes. Due to the rising prevalence of Alzheimer's disease and the extending life expectancy of type 1 diabetes, this combination of clinical problems has been increasingly observed.

The case described below demonstrates an individual person with both of these conditions, the interaction between the two, and the difficulties in management that may be encountered.

Case history

Mr D was diagnosed with diabetes at the age of 19 years. Between his diagnosis and the age of 48 years in 2009 he lived a healthy, active lifestyle but with a self-determined level of tight glucose control and associated history of recurrent hypoglycaemia. His HbA_{1c} ranged from 50–58mmol/mol previously; however, it went as low as 45mmol/mol in 2009. It was noted during clinic consultations that his capillary blood glucose reading could range from 4–7mmol/L with multiple hypoglycaemic episodes (<4mmol/L). Aside from diabetes, his only other medical problems were hypercholesterolaemia, treated with simvastatin, and a susceptibility to Raynaud's phenomenon.

A positive family history of Alzheimer's disease was noted, his father dying of such at the age of 78 years. Our patient frequently exercised and was very health conscious,

including taking part in and managing a karate school. Having been employed as a builder, he was obliged to stop work at around the age of 48 years due to recurrent difficulties with hypoglycaemia, and also because his Raynaud's disorder restricted his physical occupational capacity.

He confirmed that, prior to the diagnosis of dementia, he was aware of his hypoglycaemic episodes and that these were usually associated with strenuous exercise. On numerous occasions the diabetes team discussed with Mr D his tight control and recurrent hypoglycaemia. It was evident that he had fixed ways of giving his insulin and did not want to change much.

In 2009, he was diagnosed with depression; he was commenced on fluoxetine by his GP and was appearing to improve in mood on this treatment. At this point, his diabetes was managed with a basal-bolus regimen of once-daily glargine and lispro insulins as directed. He had elected to alter his own basal regimen and split his dose of glargine to once in the morning and once at bedtime.

Between 2009 and 2012 his glycaemic control became more unstable with an increasing frequency of severe hypoglycaemia, often requiring help from his mother and eventually necessitating his relocation to live with her. During this period, his HbA_{1c} ranged between 48–52mmol/mol. This was felt, for the most part, to be due to his persistence with a higher dose of glargine, despite encouragement

from all members of the diabetes multidisciplinary team to stop this. His rationale, when he was questioned regarding this, was that his blood glucose had been high, although objective evidence for this was limited.

In the light of his worsening memory and positive family history for Alzheimer's disease, he was referred in 2012 to old age psychiatry and to a consultant neurologist. Clinically, he was noted to have a degree of poor cognition and apraxia. An MRI scan showed global brain atrophy disproportionately affecting the hippocampus and temporal lobes, in keeping with a diagnosis of Alzheimer's disease. He was commenced on donepezil and, given the early age of onset and the familial component, referral to a tertiary centre was recommended.

On commencement of donepezil he incidentally seemed to have high blood glucose readings, with capillary glucose measurements ranging from 6–14mmol/L, and his HbA_{1c} went as high as 93mmol/mol. Despite this he soon returned to tight control, suffering again from frequent hypoglycaemia and on one occasion having a seizure that required paramedic intervention. Following on from this, we agreed a plan with his mother, who was the main carer, and adjustments were made to his insulin with the aim being to relax control of his diabetes in view of his challenging complex medical need. The aim was to optimise his diabetes control but without compromising him by causing recurrent hypoglycaemia.

After this, he still had very occasional hypoglycaemic episodes but these were less severe. His HbA_{1c} has been stable at around 70mmol/mol for the last two years. He regularly cycles to the gym but no-one is sure about the time he spends there nor what kind of activity he is doing.

Discussion

Mr D demonstrates an interesting case of two illnesses: type 1 diabetes with poorly-balanced glycaemic control and a new diagnosis of premature dementia, co-existing and of uncertain interaction.

A meta-analysis by Biessels *et al.* concluded there is evidence to

support an increased incidence of all forms of dementia in diabetic patients, but the relationship and the underlying pathophysiology are still controversial.¹ There is an ongoing debate that hypoglycaemia leads to cognitive impairment both acutely and in the long term. Acutely, the tendency is to affect predominantly working memory with some effect on mood.² On the other hand, the follow-up study of the patients who were involved in the Diabetes Control and Complications Trial for six and 18 years failed to provide any evidence that either tight glucose control or recurrent severe hypoglycaemia could lead to cognitive impairment in patients with type 1 diabetes.^{3,4}

Young-onset dementia (YOD) – dementia under 65 years of age – is a relatively rare disorder. It represents 5% of the 850 000 people with dementia in UK. Early Alzheimer's disease accounts for one-third of cases of YOD. Genes, such as PS1/PS2 (presenilin 1 and 2) and APP (amyloid precursor protein), are linked to early onset, and familial Alzheimer's disease.⁵

The diagnostic criteria of Alzheimer's dementia consists of gradual cognitive impairment and significant decline in daily activities, with supportive evidence of structural brain changes on CT/MRI scan such as symmetrical bilateral hippocampal atrophy, bilateral cerebral atrophy, and atrophy of preceuneus.⁶ Mr D's clinical presentation, family history and the diagnostic imaging findings would suggest the likely familial component of the Alzheimer's disease.

Equally, dementia has a proven effect on glycaemic control, with studies noting that patients with cognitive impairment have 83% higher rates of hypoglycaemia than those without.⁷ It seems evident that this can lead to a vicious cycle, whereby the diabetes patients who already have dementia are at high risk of developing frequent and potentially severe hypoglycaemia.⁸

In addition, other non-cognitive symptoms of Alzheimer's disease, such as depression and anxiety, are common and may play a role in promoting hypoglycaemia consequent to self-induced tight control and

Key points

- This case demonstrates the co-existence of type 1 diabetes and early-onset dementia, the interaction between the two and challenges to the management of both conditions
- It also highlights the difficulty encountered in managing hypoglycaemia in diabetic patients with dementia
- Early non-cognitive symptoms of dementia play a role in promoting hypoglycaemia in patients with diabetes mellitus

resistance to medical intervention.⁹ These characteristics have been observed in our patient, a sports enthusiast, a cyclist and one who strives to keep a tight control, but thereby experiencing recurrent hypoglycaemic events and an anxiety about the possible consequences of poor control.

In the light of this, we would call for additional evidence to be sought in order to provide a more comprehensive evidence base from which guidelines may be eventually produced for the management of this difficult cohort of patients.

References

1. Biessels GJ, *et al.* Risk of dementia in diabetes mellitus: a systematic review. *Lancet Neurol* 2006; 5(1):64–74.
2. Inkster B, Frier BM. The effects of acute hypoglycaemia on cognitive function in type 1 diabetes. *Br J Diabetes Vasc Dis* 2012;12(5):221–6.
3. Effects of intensive diabetes therapy on neuropsychological function in adults in the Diabetes Control and Complications Trial. *Ann Intern Med* 1996;124(4):379–88.
4. The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Research Group. Long-term effect of diabetes and its treatment on cognitive function. *N Engl J Med* 2007;356:1842–52.
5. Schott JM. Genetics of the dementias. *J Neurol Neurosurg Psychiatry* 2002;73(Suppl 2):II27–31.
6. Barkhof F, *et al.* Disorders mainly affecting white matter. In *Neuroimaging in Dementia*. Springer-Verlag Berlin Heidelberg, 2011; pp 177–242.
7. Feil D, *et al.* Increased risk of hypoglycemia in older patients with dementia and cognitive impairment: Is more intensive glycemic control at the expense of safety? [Abstract NR 20.] Presented at the American Association for Geriatric Psychiatry Annual Meeting, 2011.
8. Kilvert A, Fox C. The challenges of type 1 diabetes in older people. *Pract Diabetes* 2015;32(5):175–9.
9. Teri L, Gallagher-Thompson D. Cognitive-behavioural interventions for treatment of depression in Alzheimer's patients. *Gerontologist* 1991; 31(3):413–6.