

A Case Of Hypoglycaemia

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Introduction

Non-insulinoma pancreatogenous hypoglycaemia syndrome is a rare cause of spontaneous hypoglycaemia in adults. There are few case reports and most of these involve a history of bariatric surgery and are characterized by post-prandial hypoglycaemia^{1,2}. Poor understanding of the pathogenesis of this condition precludes a clear diagnostic approach and limits treatment options¹. Here we present a case of hypoglycaemia with no previous bariatric surgery and our treatment strategy.

Patient Description

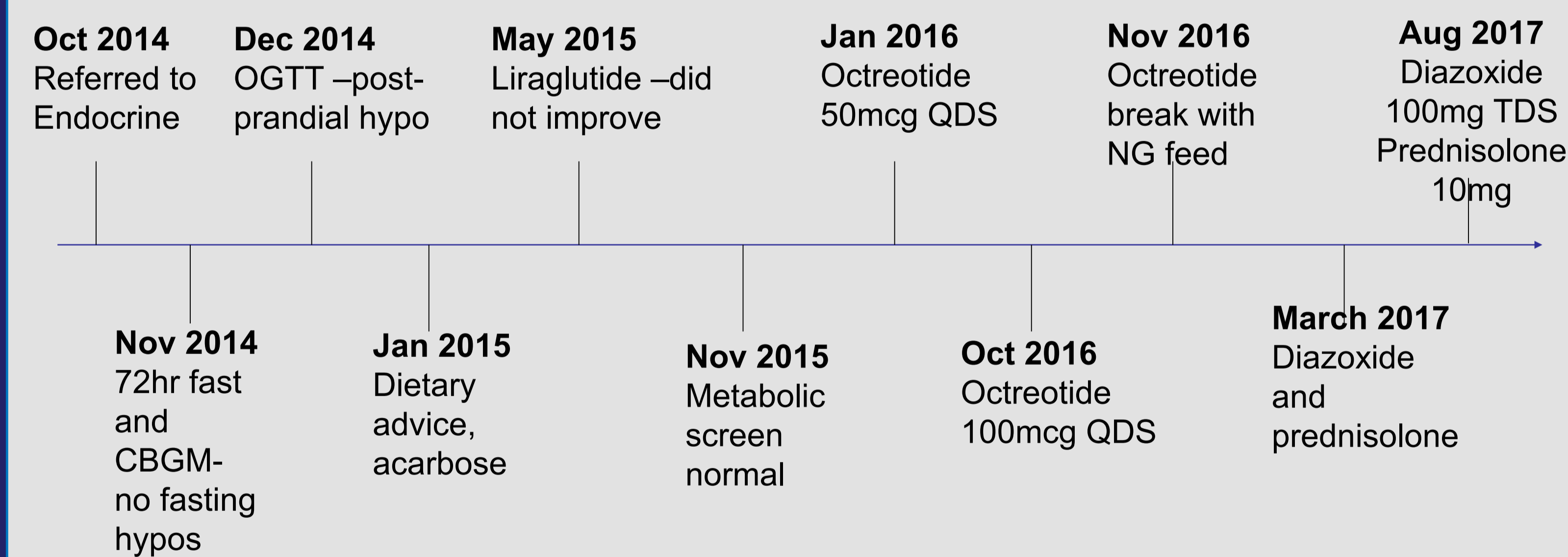
The patient is a 62 year old gentleman who presented with episodic hypoglycaemia extending over a period of 22 years. His past medical history and medications at present include:

- Marfan's syndrome,
- Mechanical AVR and aortic root replacement 2010,
- PPM with ICD.
- Paroxysmal atrial fibrillation
- Gout
- Asthma
- Depression
- Metoprolol 25mg tds
- Flecainide 100mg bd
- Warfarin
- Venlafaxine 300mg od
- Seretide Inhaler
- Ventolin Inhaler
- Omeprazole 20mg od

This gentleman initially presented to Cardiology Clinic in 2001 with episodes of syncope, palpitations, sweating and blackout. Over the subsequent years he had a permanent pacemaker inserted for complete heart block; an ICD inserted for episodes of ventricular tachycardia; and was started on metoprolol and flecainide for atrial fibrillation. Despite some symptomatic improvement, he continued to have similar episodes.

He eventually presented to the emergency department with symptoms as above and was found to be profoundly hypoglycaemic (Whipple's triad present) with a capillary blood glucose of 1.3 mmol/L and was referred to endocrinology.

Investigation and Treatment



72hr fasts and continuous blood glucose monitoring initially failed to reveal any fasting hypoglycaemia. A 5 hr OGTT did reveal however a nadir glucose of 2.4mmol/L at 2.5 hrs following a 75g glucose load. Basic biochemistry, hormone profiles (LH, FSH, testosterone, TFTs, ACTH, SST, cortisol, GH, IGF-1, urinary metanephrines), and sulphonylurea screen were normal.

Initial management was with advice on eating foods with a low glycaemic index and with the use of acarbose. This reduced the frequency of the episodes but they still continued to occur regularly.

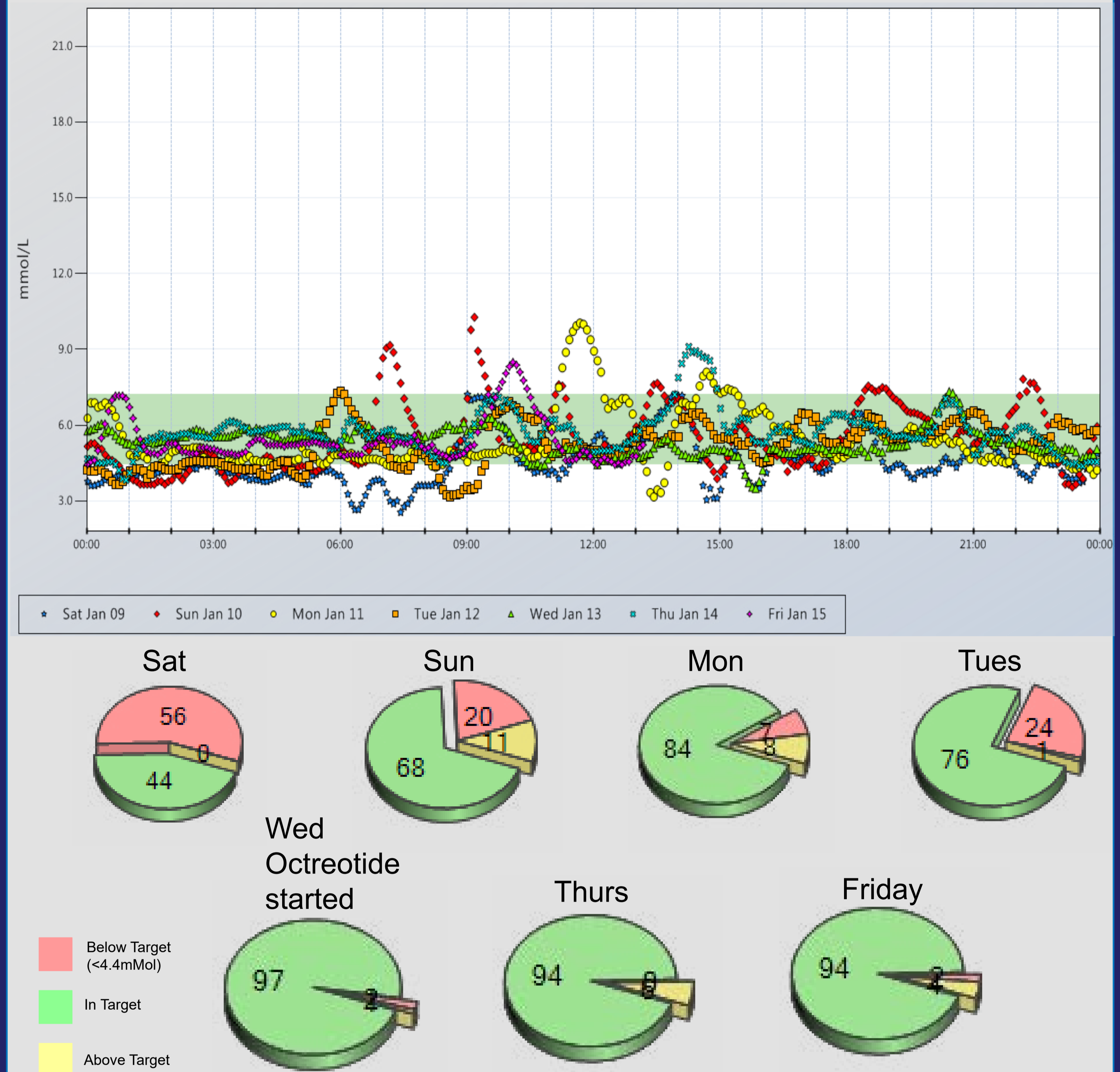
A metabolic screen at this time including Beta-hydroxybutyrate, free fatty acids, organic acids, amino acids and genetic screening for common mutations was also negative.

Further 72 hours fast and continuous blood glucose monitoring also revealed an element of fasting hypoglycaemia. At a blood glucose of 3.0 mmol/L c-peptide was measured at 1336pmol/L (<1030pmol/L), and insulin 21 pmol/L(<174pmol/L) (although the sample was haemolysed which may result in falsely lower insulin levels). Pancreatic imaging did not reveal any abnormality.

The patient was initially trialled on liraglutide 0.6mg OD but despite a dose increase, this failed to significantly impact on severity or frequency of hypoglycaemic episodes.

The patient was next commenced on octreotide 50mcg QDS. This produced a dramatic improvement as shown in the graphs, but unfortunately the patient developed tachyphylaxis and this beneficial effect diminished with time.

Continuous Blood Glucose Monitoring before/after Octreotide



Current Treatment

Despite an increase in dose of octreotide and treatment breaks, tachyphylaxis remained an issue with the use of octreotide. The patient was therefore started on prednisolone and diazoxide in place of octreotide. Whilst effective, diazoxide did have the side effect of hypotension, but attempts are currently ongoing to accommodate for diazoxide by a reduction in metoprolol and flecainide. The current regime is diazoxide 100mg TDS and prednisolone 10mg OD.

Discussion

This patient's investigations are suggestive of non-insulinoma pancreatogenous hypoglycaemia (NIPH). Differentials include insulinoma and insulin auto-antibody syndrome. The pathogenesis of NIPH is unclear but proposed mechanisms include GLP-1 induced beta cell hyperplasia^{1,4}. Genetic associations with genes affecting insulin secretion have also been reported⁵.

Similarly, there is conflicting evidence as to the best treatment for NIPH. Both Diazoxide and Octreotide have been used with variable success in the case reports^{1-3,6}. This case report lends support to the use of octreotide albeit with the disadvantage of tachyphylaxis. This case report also supports the use of prednisolone and diazoxide but again with the limitations of various adverse effects.

This case report also highlights a possible association between hypoglycaemia and cardiac arrhythmia as has previously been suggested in type 2 diabetes⁷. It is interesting to speculate whether his atrial fibrillation, complete heart block and ventricular tachycardia were all in fact induced by hypoglycaemia. Clearly further work is needed to investigate this association.

References

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