

INTRODUCTION

Type B insulin resistance (TBRIS) is a rare autoimmune disorder which disrupts normal glucose homeostasis. It can manifest in a wide variety of ways ranging from extreme insulin resistance, spontaneous hypoglycemia and in some cases an initial manifestation of extreme insulin resistance followed by intractable hypoglycemia¹. There has been no well standardized treatment for this condition, although there has been some reported success with immunomodulatory therapy². We report a case of TBRIS occurring in a T1DM patient whom achieved euglycaemia and antibody clearance with an insulin pump. To our knowledge, this is the first reported case of remission in TBRIS with the usage of an insulin pump.

CASE PRESENTATION

We present a patient whom first presented to us at the age of 12. Her first presentation to us was of an acute admission for raised blood glucose levels (BM) and osmotic symptoms which had occurred insidiously over a 4 week duration. She had a raised BM reading of 20.8mmol/L on presentation and elevated ketones in her urine. Her Glutamic Acid Decarboxylase (GAD) antibodies was positive and her initial Hba1c was 62mmol/mmol.

She was diagnosed as Type 1 Diabetes Mellitus (T1DM) and was started on a twice daily mixed insulin, her insulin regime was thereafter intensified to a basal bolus regime with escalating dose titration as her diabetes remained poorly controlled as reflected by rising Hba1c levels (62 rising to 79mmol/mmol over a 4 year period).

5 years after her initial diagnosis, she was admitted to the ward with her first episode of hypoglycemia. Her insulin doses were adjusted and investigations consisting of a short synacthen test, coeliac screen, insulin levels and insulin antibodies were done. Her coeliac screen was negative, the short synacthen test yielded a normal adrenal response, however her insulin antibodies returned as positive together with a markedly raised insulin level of 34500pmol/L.

She continued to have recurrent hypoglycemic episodes and it was then decided that she was to be started on an insulin pump. She had no further hypoglycaemic episodes whilst on the pump and her glycaemic control improved. A repeated Insulin level and insulin antibodies were done after being on the insulin pump for 10 months and these revealed a markedly reduced insulin level but persistently positive insulin antibodies.

The patient thereafter requested to be changed back to subcutaneous insulin injections, at that time she had no further hypoglycemic episodes and her BM reading were stable. 2 weeks after transitioning to subcutaneous insulin injections her hypoglycemic symptoms recurred. A repeated insulin level and insulin antibody were done at that time and revealed that her insulin levels had again risen (>500pmol/L) and her insulin antibodies were positive.

Due to worsening hypoglycaemic episodes, she was restarted back on the insulin pump. Her hypoglycemic episodes resolved a few days after recommencement.

2 years after the second commencement of the insulin pump an insulin level and insulin antibody level were repeated and this returned at 17.8pmol/L (Insulin levels) with negative insulin antibodies.

DISCUSSION

Type B insulin resistance syndrome (TBRIS) is a rare autoimmune condition resulting from polyclonal autoantibodies that may activate or inhibit the insulin receptor³.

This syndrome is typically associated with other autoimmune conditions, the commonest being Systemic lupus Erythematosus (SLE) and it commonly presents with severe insulin resistant hyperglycemia, often requiring requiring high doses of insulin, it may also manifests as an intractable hypoglycemia or a hyper-hypoglycemic state although this is less common¹. The mechanism of hypoglycemia in TBRIS has been postulated to be from the ability of the antibodies to mimic insulin effects on target tissues⁴.

Association of this condition with Type 1 Diabetes Mellitus (T1DM) is extremely rare and has only been reported in 2 cases^{5,6}. It maybe under-looked in patients with diabetes as the abnormal glucose homeostasis maybe attributed to the progression or complication of treatment of diabetes itself.

There is currently no standardized treatment for TBRIS, treatment with immunosuppression and steroids have been trialed and have shown some degree of success in TBRIS associated severe hyperglycaemia². Treatment for TBRIS associated hypoglycemia on the other hand has thus far been limited and not widely reported. To further complicate this, TBRIS associated hypoglycemia has been shown to be a negative prognosis indicator¹.

In our patient, the insulin pump was the unexpected solution, not only did it help with amelioration of her hypoglycemic episodes and normalization of her glucose levels but it also seemed to have an effect on insulin antibody clearance. The exact mechanism of this is unknown and to our knowledge, has never been demonstrated before.

CONCLUSION

In conclusion, with this case, we would like to highlight the rare occurrence of TBRIS in T1DM as well as the temporal association shown by usage of an insulin pump together with the reduction of insulin levels and to some extent, insulin antibody clearance.

REFERENCES

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TIMELINE OF EVENTS

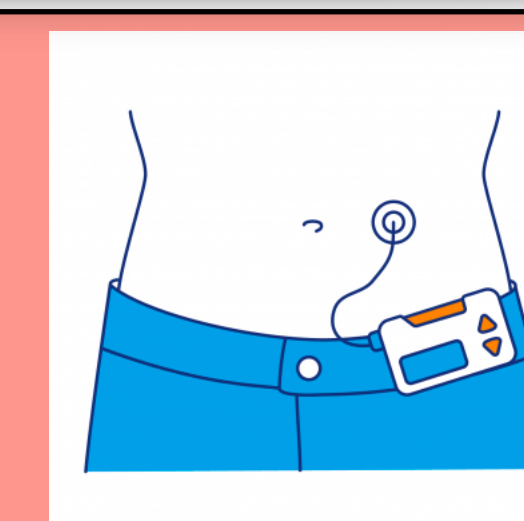
June 2006 (Age 12)
Initial presentation of hyperglycemia
GAD Ab positive
Hba1c: 62
Started on Mixtard 30 13 units AM and 9 units PM

June 2006- January 2010 (Age 12 to 16)
Hba1c rose to 79
Transitioned from Mixtard to basal bolus regime consisting of Novorapid and Levemir.

November 2011 (Age 17)
First admission for hypoglycemia
Short synacthen test :Cortisol baseline 318nmol/L rising to 1014nmol/L
Coeliac screen: Negative for coeliac disease
Insulin doses reduced during admission

3 further admissions for hypoglycemia in the months of November- December 2011
Had recurrent hypoglycemic episodes at home despite stopping insulin
Insulin antibodies: Positive

December 2011 (Age 17)
Commenced on insulin pump
Hypoglycemia episodes resolved



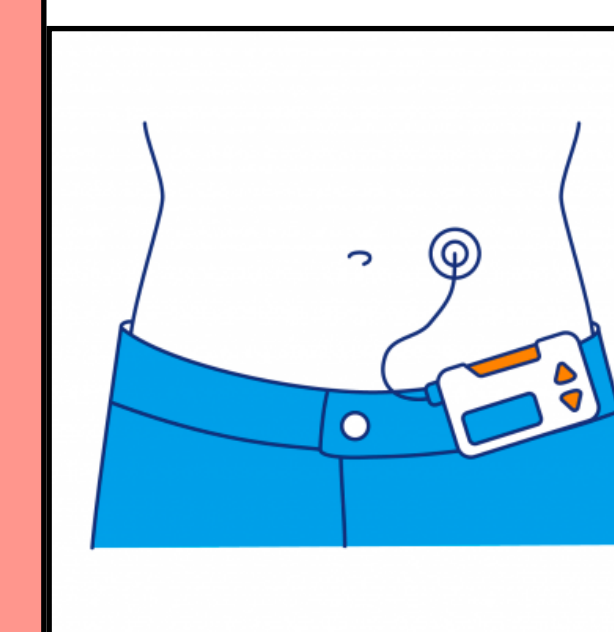
Hba1c reading in March 2012
4 months post commenced on insulin pump 73mmol/L

September- early October 2012 (Age 18)
On Insulin pump for 10 months
Hba1c: 66
No hypoglycaemic episodes whilst on insulin pump
Patient decided to switch back to basal bolus insulin regime in October 2012

Insulin levels 78pmol/L
Insulin antibodies: Positive

Late October 2012 (Age 18)
Hypoglycaemic episodes recurred, very frequent with multiple episodes on a daily basis despite insulin dose reduction
Insulin Antibodies: Positive
Insulin level > 500

January 2013
Recommenced on insulin pump due to recurrence of severe hypoglycemic episodes



March 2015 (Age 21)
On second commencement of insulin pump for 2 years and 3 months
Insulin levels: 154pmol/L
C-peptide < 94
Insulin antibodies: Negative
No hypoglycemic episodes
Hba1c 55