

A 30-year-old lady with polyuria, polydipsia, weight loss and newly diagnosed diabetes mellitus

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A 30-year-old lady presented with polyuria, polydipsia, weight loss and newly diagnosed diabetes mellitus with a fasting plasma glucose of 16.5 mmol/L and HbA1c of 13.4%. She had a previous history of thyrotoxicosis at age 25, had received treatment with carbimazole for one year and had been in remission since then. Her previous menses were regular and she had delivered a 3.2 kg healthy baby 6 months ago. She had gestational diabetes during her pregnancy which was diet controlled satisfactorily. She did not have any family history of diabetes and was not taking any medications. Physical examination revealed that she was mildly underweight with a BMI of 17.5 kg/m². Her BMI before pregnancy was 19 kg/m². Her pulse was 84/min and there was mild tremor. There was a small goitre which was diffusely enlarged. There was no sign of diabetes-related complications. Her urine was negative for ketone and she was not clinically dehydrated.

Since 2007, metformin has been recommended by the ADA/EASD as the first-line treatment for Type 2 diabetes. However, it should be noted that while guidelines can usually be applied to “typical” patients, they may not be applicable if the clinical features are atypical. It should be clear that there are many atypical features which make this patient different from the usual cases of diabetes: 1) This is a very young lady, and the prevalence of diabetes is expected to be very low; 2) It is unusual for young Type 2 diabetes patients not to have any family history of diabetes; 3) She was underweight at the time of consultation and had been low/normal before the development of diabetes; 4) There is a background of auto-immune disease, namely history of thyrotoxicosis; and 5) The hyperglycaemia was rather acute at onset, as evidenced by the fact that she only required diet control during her pregnancy. All of these facts beg two important questions—is there any acute precipitating factor for her diabetes? Or is this a case of atypical diabetes, such as latent autoimmune diabetes in adults (LADA)?

In this clinical setting, two major diseases need to be seriously considered as precipitating factors for her hyperglycaemia—thyrotoxicosis and tuberculosis. Thyrotoxicosis has to be considered because of typical age and previous history of thyrotoxicosis. The rate of relapse of Graves' disease is in fact around 50%. Moreover, thyroid problems tend to recur during the post-partum period, especially for those with a previous history of thyroid diseases. Infection can also cause acute hyperglycaemia. In Hong Kong, the most common cause of chronic infection is tuberculosis. Further investigations for these two possibilities were arranged. CXR was normal. However, TSH was suppressed down to <0.001 mIU/L and free T4 was 30.6 pmol/L, suggesting a diagnosis of thyrotoxicosis.

With regard to the management of her glycaemic control, the best treatment for this lady is insulin treatment. There was a study conducted in China on the management

of 382 newly diagnosed Type 2 diabetes patients [1]. These patients had a mean HbA1c of 9.7% at the time of diagnosis and were randomized to three treatment modalities for a few weeks, aiming at ideal glycaemic control. These treatment modalities included multiple injection (MDI), insulin pump and oral hypoglycaemic agents (sulphonyurea and metformin). These patients were taken off drug treatment after maintaining ideal control for two weeks and were subsequently put on diet control alone. The patients were defined as reaching endpoint once their fasting plasma glucose rose beyond 7.0 mmol/L. At the end of 1 year, the proportion of patients who could be controlled with diet alone was much higher in the insulin pump and MDI group compared with the oral hypoglycaemic agent group (55.1% versus 44.9% versus 26.7% respectively). The results of this study suggested that treating newly diagnosed diabetics with insulin resulted in beta-cell protection or recovery for at least one year. However, it should be noted that these patients had a rather high HbA1c at baseline and the observation period was only up to 1 year. Therefore, it is unclear whether patients with less severe hyperglycaemia will benefit from insulin treatment. This may well account for the different observations in the UKPDS study, which included patients with a much milder degree of hyperglycaemia and suggested that early insulin treatment was not beneficial.

This lady was hence put on multiple injections using insulin glargine as basal insulin and insulin aspart to control post-prandial hyperglycaemia. She was also treated with carbimazole for her thyrotoxicosis. Her free T4 was normalized within 6 weeks of treatment and her insulin requirement was dramatically reduced from 40 u daily to 18 u daily. Her HbA1c was reduced to 6.7%. At this junction, we should seriously consider whether patients should be maintained on insulin therapy or changed to oral hypoglycaemic agents if the patient so wishes. Obviously, the choice of oral hypoglycaemic agent is important due

to their different profiles in long-term glycaemic control. With regard to this lady, the lean body built and young onset all pointed to the possibilities of LADA, with which the pathogenesis is autoimmune destruction of pancreatic beta cells. LADA differs from Type 1 diabetes in that the destructive process is slower and hence the patients do not present with diabetic ketoacidosis. It is often mistaken as Type 2 diabetes. The diagnosis can be confirmed by checking glutamic acid decarboxylase antibody, which turned out to be strongly positive in this case. A diagnosis of LADA was hence made. No treatment has been convincingly shown to prevent the natural course of the disease, although some small studies suggest that rosiglitazone may prevent the

natural deterioration of beta-cell function. On the contrary, sulphonyurea has been shown to be associated with less preservation of stimulated c-peptide compared with insulin. After a detailed discussion with the patient, she decided to continue with her insulin treatment and glycaemic control remains ideal upon subsequent follow up visits.

Reference

1. Weng J, Li Y, Xu W, et al. Effect of intensive insulin therapy on beta-cell function and glycaemic control in patients with newly diagnosed type 2 diabetes: a multicentre randomised parallel-group trial. *Lancet* 2008;371(9626):1753-60.

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QUESTIONS

1. Which of the following are not typical clinical features of LADA?
 - a. Strong family history of diabetes
 - b. Background of autoimmune diseases
 - c. Lean body build
 - d. Young age at time of diagnosis
2. According to the recent study in China, which of the following treatments was shown to have resulted in better pancreatic beta-cell function at one year in newly diagnosed Type 2 diabetes patients with HbA1c ~ 9.7%?
 - a. Sulphonyurea
 - b. Metformin
 - c. Insulin
 - d. Rosiglitazone
3. According to the UKPDS study, for patients with mild degree of hyperglycaemia, which of the following treatment can prevent the natural deterioration of glycaemic control over 10 years?
 - a. Metformin
 - b. Sulphonyurea
 - c. Insulin
 - d. None of the above
4. Which of the following are recommended as first-line treatment for Type 2 diabetes by the ADA/EASD?
 - a. Insulin
 - b. Metformin
 - c. Sulphonyurea
 - d. Glitazones

ANSWER FORM

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