Case Report

Complete Remission in Newly Diagnosed Type 1 Diabetes Mellitus Patient

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Abstract

Type 1 diabetes mellitus is a chronic disease affects pancreatic beta cells. Usually it has a life long duration, however, in few cases, it can be transient. We reported a 20 year old male patient who visited the diabetic clinic of Lok Nayak Hospital with classical symptoms of type 1 diabetes mellitus. He was diagnosed with type 1 diabetes on the basis of lab parameters. He was found to be positive for ICA512 and GAD antibodies. Measurement of C-peptide was also done by mixed meal tolerance test. Initially, Insulin was advised to control hyperglycemia. After 2 weeks, he was given 14 infusions of Teplizumab injection, one infusion per day and the same has been repeated after six months. As per clinical judgment, it was assumed that he was not on placebo arm and probably received Teplizumab as investigational product. Teplizumab injection drastically reduces the insulin doses and after some time, his insulin was completely waived off. Complete remission was seen in this patient after treatment with Teplizumab injection. During the 4 years follow-up, this remission is still ongoing in this patient. He had normal fasting and home blood glucose concentration with normal HbA1c without insulin therapy from last 4 years. To keep his blood sugar values under control, patient was also advised regular exercise and a diabetic diet.

Keywords: Type 1 diabetes mellitus, Complete remission, Teplizumab, Auto antibodies.

Background

Type 1 diabetes mellitus (T1DM) is an autoimmune disease characterized by the dysfunction and destruction of insulin-producing beta cells by auto reactive T cells. Sherry N et al. have done small studies and have suggested that short treatments with anti-CD3 monoclonal antibodies that are mutated to reduce Fc receptor binding preserve β-cell function and decrease insulin needs in patients with recent-onset type 1 diabetes. In one of the phase 3 trial, assessment of the safety and efficacy of one such antibody, Teplizumab was done.[1] Recently it was found that Anti-CD3 treatment which works on our immune system is one of the best suited way to treat Type 1 Diabetes. Anti-CD3 treatment for 6 to 14 days in a patient at early stage of diabetes has a remarkable prolonged effect.[2] Cases of Type 1 Diabetes Mellitus are on the increase and exogenous insulin therapy is the only intervention regularly initiated for type 1 diabetes patients. Though complete remission is a rare phenomenon in type 1 diabetic patients but it cannot be ruled out completely. Though tremendous strides have been made in prediction of Type 1 Diabetes Mellitus, prevention and intervention strategies have not experienced the same success.

Evidence indicates that type 1 diabetes, an autoimmune process is most commonly based on the presence of Diabetes Auto Antibodies. Antibodies are specialized proteins present in our body to fight against foreign substances. But, sometimes they attack our own body cells, then they are said to be auto antibodies. These auto antibodies play a significant role in the detection of disease. There are multiple immunological markers present which are used to categorized different types of diabetes in young population. But it was not found in any studies that all these three antibodies are present together in youth onset diabetes mellitus in India.[3] Although much progress has been made towards understanding

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the respective roles of effectors and regulatory T cells in this beta cell destruction, the development of auto antibodies to beta cell proteins is widely considered simply a by-product of the autoimmune destruction of the beta cells, rather than having an active role in the pathogenesis as suggested by C S Hempe.[4] Frequently, in patients with type 1 diabetes, auto antibodies attack and destroy insulin-producing beta cells in the pancreas. It has been proved by earlier studies that several antibodies are responsible for the development of diabetes which include glutamic acid decarboxylase 65 antibodies (GADA) and islet cell antibodies (ICA). Evidence indicated that comparatively higher levels of auto antibodies have been reported in type 1 diabetes. It was also found that 95% of children having type 1 diabetes have high levels of islet cell antibodies and auto antibodies of GADA. It was also found that these auto antibodies were present before the symptoms of diabetes or pre-diabetes begin. Therefore, this is considered as one of the important diagnostic tools for type 1 diabetes.[5] As per William E. Winter et al., ICA are detected in 70% to 80% of individuals with new-onset T1DM. ICA positivity declines after the diagnosis of T1DM. After 10 years, few individuals remain ICA positive (approximately 5%). The presence of islet autoantibodies in persons with diabetes confirms an autoimmune etiology. In non-diabetic individuals, islet autoantibodies are strong predictors of the later development of T1DM. Greater the number of islet autoantibodies detected, greater is that individual's risk for T1DM.[6]

C-peptide was initially thought to be just a by-product of insulin production but researches have now depicted that it is an important marker of pancreatic beta cell function. Studies have linked the low level of C-peptide to diabetes complications and evidence suggests that maintaining higher levels of C-peptide is especially beneficial for type 1 diabetic patients. It proves to be an important biomarker for the early diagnosis of type 1 diabetes. Greater the number of islet autoantibodies detected in a patient, greater is the risk for developing type 1 diabetes in that patient.[7]

Patient Consent: Obtained

Case Presentation

A 20 year old male patient was diagnosed with classical type 1 diabetes. He does not have a 1st degree relative (i.e., mother, father, sister or brother) with a history of diabetes type 1. He was presented with weight loss, sweating and polyurea. At the time of examination, his body weight was 57 kg, height 182 cm and BMI was 17.21 kg/m^2. His initial blood glucose fasting was found to be 220 mg/dl with HbA1c value 8.9%. He was symptomatic for polyurea and weight loss but without ketosis. At the time of screening, his lab report showed the presence of ICA512 and GAD antibodies. C-peptide measurement was also done which was found to be significantly very low in this patient. Mixed meal tolerance test (MMTT) was performed for the measurement of C-peptide. Boost was given to stimulate C-peptide chains in patient and samples were withdrawn at certain intervals. EBV DNA was not detected and he was found to be hepatitis E positive. His biochemistry and complete blood count test was found to be within normal range. Mantoux test was performed to rule out any active or latent tuberculosis.

Patient was initially advised 36 units of insulin/day subcutaneously. Insulin is a naturally occurring hormone secreted by the pancreas. Many people with type 1 diabetes are prescribed insulin because their bodies do not produce insulin. This patient participated in double blind study and probably he received investigational product Teplizumab; an FcR-nonbinding anti-CD3 monoclonal antibody that has been tested in Phase II - III clinical trials and was shown to preserve the C-peptide levels and reduce the need for exogenous insulin.[8] It was assumed that he was on Teplizumab arm because after the treatment his insulin doses drastically reduced. This Teplizumaz has the property to preserve the remaining beta cells, present in the pancreas from further destruction. Teplizumab treatment preserves insulin production and reduces the use of exogenous insulin in some patients with new-onset type 1 diabetes. Two cycles of Teplizumab injections were given to patient at six months interval. In each cycle, Teplizumab infusion was given to patient for 14 days and the same has been repeated after six months. The most common adverse events observed during the treatment period were rash and hypoglycemia. Patient was given diary card to capture any such hypoglycemic episodes and adverse events that he may experience during the course of Teplizumab treatment. In addition, patient was closely followed for diabetic diet and exercise.

Result

His blood glucose values show a tremendous decline in sugar levels so it was assumed that he was not on placebo arm and he received investigational product Teplizumab. He experienced several hypoglycemic

episodes during the treatment period. He was trained properly to overcome these hypoglycemic episodes. After few weeks of treatment, his insulin doses drastically reduced which further went down and at one stage complete remission was observed.

Conclusion

Teplizumab infusions lead to greater reductions in insulin requirement. Patient's beta cells as expected were preserved from further destruction. Probably Teplizumab in combination with strict diet and regular exercise caused prolonged remission in this type 1 diabetic patient. Patient's blood sugar is within normal limit without any exogenous insulin requirement from last four years.

Discussion

Early diagnosis of type 1 diabetes is the key factor which not only reduces destruction of beta cells but at the same time also provides a blanket to protect our body from internal damages caused by auto antibodies and elevated blood sugar levels. As diabetes is a silent disease, many times it happens that patient is not aware of the symptoms. Early detection, proper treatment and diabetes awareness are the key factors to manage this silent killer.

At the initial level, efforts should be made to increase the rate of diagnosis of type 1 diabetes at much initial level or at pre-diabetes stage. Through genetic counselor, physician and diabetic counselor this can be done effectively as they are the ones who interact with patients. Efforts should also be made to find out the reason of developing diabetes through questionnaires, family history, dietary habits and life style of the person.[9] Diagnostic criteria should be used to differentiate between one types of diabetes from other. Clinical judgment should be taken accordingly. In addition, patient should be given diabetic education. First line of therapy should be used judiciously to treat type 1 diabetes. Early diagnosis of type 1 diabetes is an important tool but one cannot deny the role of diabetic diet and exercise in the management of diabetes.

It has been proved by several studies that Teplizumab has the property to protect pancreatic beta cells and it reduces the dose of exogenous insulin in type 1 diabetic patients. Same has been reported in this case study. Till date very few cases of complete remission in type 1 diabetes have been reported. Although complete remission in type 1 diabetic patient is a rare case, but it cannot be ruled out completely.

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Conflict of Interest: None

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