OBSERVATIONS

Type 1 Diabetes Caused by Interferon α-2α in Polycythemia Vera Therapy

One of the main problems with long-term interferon α-2α (IFNα-2α) therapy for chronic viral hepatitis and malignant tumors is the development of autoimmune abnormalities. Up until now, there have been few reports about type 1 diabetes caused by IFNα-2α therapy in patients with polycythemia vera (PV) (1).

A 59-year-old male patient without history of diabetes, whose fasting blood glucose (FBG) and A1C were 70.6 mg/dl and 4.8%, respectively, was diagnosed with PV in October 1999. He had been initially treated with Hydrea for 6 months, but the response had been unfavorable. Therefore, he switched to IFNα-2α (recombinant interferon α-2α; Shanghai Roche Pharmaceuticals, Shanghai, China) therapy, and the dose was 3 MU every other day. The patient achieved complete response after 9 months of IFNα-2α therapy. However, he presented with new symptoms of polydipsia, polyuria, and weight loss. Laboratory investigation revealed that he had severe hyperglycemia (FBG 390.6 mg/dl, A1C 12.7%) and definite insulin secretion deficiency (C-peptide: fasting 0.9 μg/l [1.1–3.2 μg/l], 2-h postprandial 1.3 μg/l). Thus, a diagnosis of type 1 diabetes was made, and the patient received intensive insulin therapy immediately. Six years after initial IFNα-2α therapy, he tested positive for insulin antibody, islet cell antibody, and GAD antibody. His blood glucose has been well controlled with intensive insulin therapy. At the last visit, in December 2008, 9 years after the PV onset, the patient survived and remained free of disease with permanent IFNα-2α therapy.

IFNα-2α has been shown to be effective in correcting thromobocythemia and controlling excess red cell mass in patients with PV. Long-term relapse-free survival has been reported with IFNα-2α therapy, and a number of patients have achieved partial responses after treatment. But the reported cumulative incidence of all autoimmune disorders, an important side effect of long-term IFNα-2α therapy, ranged from 1 to 3% (1,2).

The pathogenesis of endocrine autoimmunity in response to IFNα-2α therapy has not been well established. The prevalence of type 1 diabetes development in patients receiving IFNα-2α for chronic hepatitis C ranges from 0.08 to 0.7%, and the latency of diabetes onset after IFNα-2α therapy commencement ranges from 10 days to 4 years. In addition, a timely suspension of IFNα-2α therapy is rarely accompanied by regression of clinical diabetes. Previous studies showed early progression to insulin dependency in a few type 2 diabetic patients who tested positive for islet autoantibodies. It has been reported that the risk of type 1 diabetes development is higher in subjects with HLA haplotypes and/or with a family history of type 1 diabetes (3,4).

In conclusion, it is important for clinicians to be familiar with side effects of long-term IFNα-2α therapy. For genetically and immunologically predisposed individuals or patients with preexisting type 2 diabetes, islet autoantibodies and/or islet function deficiency should be closely monitored during IFNα-2α treatment. This strategy warrants a diagnosis of type 1 diabetes at an early stage to avoid the occurrence of life-threatening complications.

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