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.

XIAN-LING WANG, MD
YI-MING MU, MD
ZHAO-HUI LU, MD
JU-MING LU, MD
JING-TAO DOU, MD
CHANG-YU PAN, MD

From the Department of Endocrinology, Chinese PLA General Hospital, Beijing, China.
Corresponding author: Yi-Ming Mu, muyiming1962@sohu.com.
DOI: 10.2337/dc10-1266
© 2010 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http://creativecommons.org/licenses/by-nc-nd/3.0/ for details.

Acknowledgments— No potential conflicts of interest relevant to this article were reported.

References

1. Silver RT. Long-term effects of the treatment of polycythemia vera with recombinant interferon-alpha. Cancer 2006;107:451–458
2. Bai J, Shao Z, Jing L. [Clinical analysis of 185 patients with polycythemia vera.] Zhonghua Xue Ye Xue Za Zhi 2002;23:578–580 [in Chinese]
3. Soultati AS, Dourakis SP, Alexopoulou A, Deutsch M, Archimandritis AJ. Simultaneous development of diabetic ketoacidosis and Hashitoxicosis in a patient treated with pegylated interferon-alpha for chronic hepatitis C. World J Gastroenterol 2007;13:1292–1294
4. Di Bisceglie AM, Shiffman ML, Everson GT, Lindsay KL, Everhart JE, Wright EC, Lee WM, Lok AS, Bonkovsky HL, Morgan TR, Ghany MG, Morishima C, Snow KK, Dienstag JL, HALT-C Trial Investigators. Prolonged therapy of advanced chronic hepatitis C with low-dose peginterferon. N Engl J Med 2008;359:2429–2441

Downloaded from http://ada.silverchair.com/care/article-pdf/33/11/e141/604885/zdc01111000e141.pdf by guest on 17 April 2024