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Impaired Metabolic Response to Regular Insulin in the Presence of a High Level of Circulating Insulin-binding Immunoglobulin G

It is only recently that the clinical importance of circulating anti-insulin antibodies has come into focus.[1] In this context we would like to report on a case of a 24-yr-old type I diabetic woman in whom an elevated level of circulating insulin-binding immunoglobulin G (IgG_I) was associated with an impaired efficacy of regular insulin during continuous subcutaneous insulin infusion (CSII).

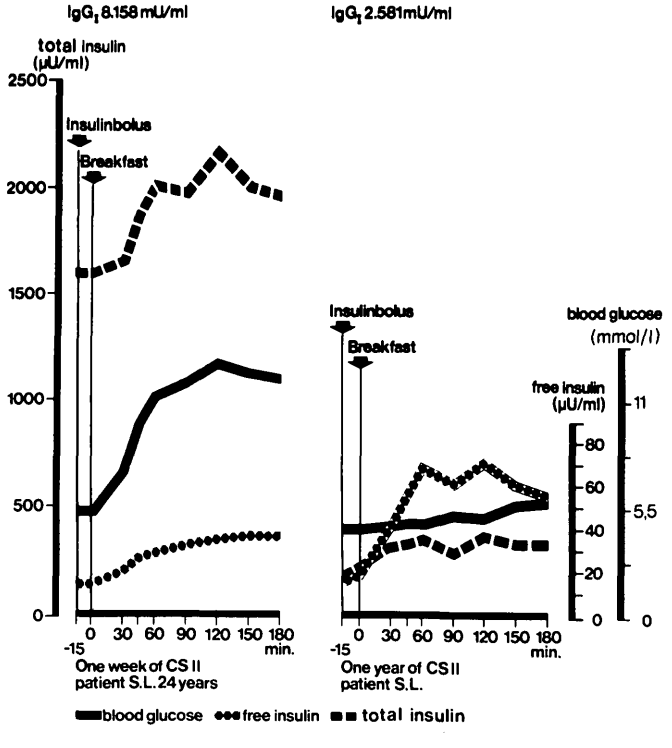

FIG. 1. Serum levels of free insulin (·····), total insulin (e.g., free plus antibody-bound insulin, -----), and blood glucose (——) in a type I diabetic patient on CSII with a high level of insulin-binding immunoglobulin G (IgG_I) shown in the left panel, and with decreased IgG_I 1 yr later (right panel) during test breakfasts.

The patient had been treated before CSII with two daily injections of a bovine-zinc insulin preparation (Depot Insulin Hoechst CR, West Germany); her insulin dose was 62 U/day. Duration of diabetes was 3 yr, basal C-peptide level was below 0.2 ng/ml, and HbA_{Ic} was 10.9% (thiobarbiturate method, normal range 4.1–7.8% of total hemoglobin) when she changed to CSII in October 1981. CSII was performed using Actrapid MC insulin (Novo Industri, Copenhagen, Denmark) diluted in 0.9% saline, and administered by a Mill-Hill Infuser Model HM 1001 (Muirhead, London, United Kingdom).

One week after initiation of CSII, while on a basal insulin infusion rate of 0.9 U/h and a total insulin dosage of approximately 45 U/day, she had a test breakfast consisting of 72 g carbohydrate (125 g white bread), butter, one egg, and coffee 15 min after she had given an insulin bolus of 11 U (Figure 1, left panel). During the next 3 h, her blood glucose rose from a baseline value of 5.7 mmol/L to 12.5 mmol/L despite the premeal insulin bolus, while the serum free insulin level[2] increased only gradually. The level of total (e.g., free plus antibody-bound) insulin,[3] however, exhibited a substantial rise. At that period of CSII treatment, the patient experienced late postprandial hypoglycemia rather frequently.

One year later the test breakfast was repeated with the basal insulin infusion rate, the premeal insulin bolus, and the composition of the test meal being identical.

During that year interval, the serum concentration of insulin-binding immunoglobulin G (IgG_I, determined according to Christiansen[4]) had fallen from 8.16 to 2.52 mU/ml, and the HbA_{Ic} to 7.43%, respectively. This time the serum free insulin level rose sharply after the administration of the premeal insulin bolus, reaching approximately 70 mU/L, whereas total (e.g., free plus antibody-bound) insulin increased only slightly. Glycemia remained perfectly normal throughout the test breakfast (Figure 1, right panel). At that period of treatment, the total daily insulin requirement was about 45 U.

From this observation we conclude that the binding of exogenous insulin to IgG_I[5] may have clinical importance, particularly for patients taking regular insulin. The impaired metabolic response to regular insulin in the presence of high concentration of circulating IgG_I, as has been shown in this case report, is in accordance with previous reports recently reviewed by Kruse.[6]

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Chlorpropamide Alcohol Flushing in Indian Patients with Non-insulin-dependent Diabetes in the Young

Previously we have characterized the syndrome of non-insulin-dependent diabetes in the young (NIDDY) in the South African Indian population, highlighting the strong familial aggregation; 84% had a positive family history with evidence of three-generation transmission of diabetes in some families.[1–3] Because of the conflicting reports concerning the phenomenon of chlorpropamide alcohol flushing (CPAF) in patients with NIDDY,[4–7] we investigated this phenomenon in a group of 15 Indian patients with NIDDY, after obtaining informed consent. The procedure was identical to that recommended by Leslie and Pyke.[8] A CPAF response was defined positive only when there was unanimity between both patient and observer assessment coupled with a significant rise in skin temperature. Of the 15 patients who underwent this procedure, 6 had a positive CPAF test (40%): 2 of these patients had evidence of diabetic retinopathy. Only one of the nine patients who had a negative CPAF test had evidence of diabetic vasculopathy. Thus, our findings are at variance with those of Pyke and co-workers, who recorded a positive CPAF test in 90% of their patients[4] with NIDDY, but are in accord with the data of three other groups who reported a much lower frequency (20%, 29%, and 67%) of positive CPAF tests.[5–7]

Using the expression NIDDY instead of MODY (maturity-onset diabetes in the young), as recommended by Keen[9], we cannot concur with Pyke and co-workers that CPAF is a good marker for NIDDY or that it affords a relative immunity to vascular complications.[4,10]

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Bismuth Subsalicylate—an Aid to the Diagnosis and Treatment of Reflux Esophagitis

A 50-yr-old woman, diabetic for several decades, presented with a complaint of occasional severe retrosternal burning pain. The symptom had been present for about 4 yr, over