tion, given that his fasting plasma glucose values never exceeded 6 mmol/l while only on diet.

His homeostasis model assessment of insulin resistance (HOMA-IR) (fasting serum insulin [μU/ml] × fasting plasma glucose [mol · l^{-1}/22.5]) was 1.8, and an oral glucose tolerance test performed with 75 g glucose was absolutely normal. His PSA value was 0.3 ng/ml.

After surgery there was very little change in body weight. His BMI before the operation was 26.6 kg/m^2 and after the operation 26.5 kg/m^2. This minimal change in body weight could not account for the observed euglycemia, nor could his diet given that it was virtually unchanged.

Combined androgen blockade therapy was initiated with goserelin acetate and bicalutimide. Three weeks later his plasma testosterone level fell well in the hypogonadotropic range (80 ng/ml) with a simultaneous, abrupt worsening of his glycemic control. Fasting plasma glucose ranged from 10 to 15 mmol/l and HOMA-IR rose to 15, indicating an insulin-resistant state. Again there was no significant change in his body weight; his BMI was 26.5 kg/m^2.

Treatment with metformin and rosiglitazone was reinstituted with a significant euglycemic response (fasting plasma glucose 5.5 mmol/l).

The presence of diabetes in the preoperative hypogonadal state, the remission of it in the immediate postoperative eugonadal phase, and the reappearance of insulin resistance after the institution of androgen deprivation treatment indicate that in this patient, the effect of testosterone was insulin sensitizing.

Marked hyperglycemia in prostatic cancer patients, after initiation of androgen deprivation therapy, has been reported in the literature with good response to pioglitazone (1). In the present case, prostatic carcinoma presented as hypogonadotropic hypogonadism. Schaeffer and Walsh (2) eloquently suggested that adenocarcinoma of the prostate should be considered in the differential diagnosis of hypogonadism based on the suppression of the hypothalamic-pituitary-testicular axis occasionally caused by this carcinoma. Undifferentiated prostatic carcinomas may yield normal PSA values, and this should be kept in mind when considering testosterone replacement therapy in men with hypogonadism. Another point of significance is that our patient was receiving rosiglitazone and peroxisome proliferator–activated receptor-γ ligands, which may modify PSA levels (3).

Based on the above information, it is clear that in diabetic patients presenting with sexual dysfunction, prostatic carcinoma should be considered in the differential diagnosis, regardless of the PSA level. Further research is needed to examine the possible relationship between testosterone and insulin resistance and the possible role of hyperinsulinemia in the course of prostatic carcinoma disease, given that in recent years it has become clear that there are multiple androgen-independent routes.

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A Case of Type 1 Diabetes Followed by Methimazole-Induced Hypersensitivity Syndrome

Viruses have generally been considered to be a major environmental factor in the etiology of type 1 diabetes. Drug-induced hypersensitivity syndrome (DIHS) is characterized by a severe drug eruption and multiorgan involvement, and reactivation of human herpesvirus-6 (HHV-6) may contribute to its pathology (1). This is the first reported case of type 1 diabetes followed by DIHS.

Recently, we have reported a case of DIHS induced by methimazole for Graves' disease (2). This patient developed type 1 diabetes during treatment of DIHS. Briefly, a 50-year-old Japanese male subject was diagnosed as having DIHS caused by methimazole in November 2003, based on the physical manifestations and laboratory findings including elevated anti–HHV-6 IgG titer. The administration of glucocorticoids gradually improved his clinical manifestations.

In December 2003, fasting plasma glucose was 4.9 mmol/l. His glycemic control, thereafter, gradually worsened despite treatment with nateglinide (270 mg/day). In March 2004, laboratory studies showed fasting plasma glucose to be 14.4 mmol/l; HbA_{1c}, 12.1%; fasting serum C-peptide, 0.35 ng/ml (normal range 0.5–2.73); and urinary excretion of C-peptide (which means integrated intrinsic insulin secretion), 17.24 mg/day (normal range 40–120). Basal level of serum C-peptide was finally undetectable. Anti-GAD antibody was 24.1 unit/ml (normal range <1.5). Response of serum C-peptide to glucagon was blunted. Thus, we diagnosed the patient as having type 1 diabetes. He started insulin injections immediately. His glycemic control gradually improved.

The coexistence of type 1 diabetes and Graves' disease is not infrequent. The onset age of type 1 diabetes in this case is fairly later, and anti-GAD antibody titer is relatively low, although type 1 diabetes with autoimmune thyroid disease was reported to be clinically characterized as high titer (609 ± 166 units/ml) of anti-GAD antibody and later-onset age (~30 years) compared with the general type 1 diabetic population (3). Therefore, these findings cannot exclude the possibility that the coexistence of type 1 diabetes and Graves' disease may be not incidental.

It is possible that viral infections such as coxsackie B4 virus and cytomegalovirus can trigger autoimmune reactions against pancreatic β-cells, which leads to type 1 diabetes. Molecular mimicry has been considered as a pathogenetic mechanism for autoimmune disease (4).

GAD65-reactive T-cells have been postulated to recognize the peptide derived by coxsackie B4 virus, leading to autoimmune type 1 diabetes (4). Furthermore, sequence homology between GAD65 and cytomegalovirus might participate in the onset of type 1 diabetes and stiff-man syndrome (5). Interestingly, HHV-6 is closely related to cytomegalovirus genomically and antigenically, and GAD65-reactive T-cells also recognize an epitope derived by HHV-6 (5), suggesting that reactivation of HHV-6 might contribute to the onset of autoimmune type 1 diabetes by the molecular mimicry.

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Favorable Effects of Early Insulin Secretion by Nateglinide on Postprandial Hyperlipidemia in Patients With Type 2 Diabetes

Severe postprandial hyperlipidemia is observed in and substantially contributes to the progression of atherosclerosis in type 2 diabetic patients, especially those with insulin resistance and compensatory hyperinsulinemia (1–4). As with postprandial hyperglycemia, increased lipid levels in type 2 diabetic patients peak late, and the magnitude of the increase is greater than that seen in healthy people (2,4). To determine whether early insulin secretion by nateglinide can suppress postprandial hyperlipidemia in type 2 diabetic patients, 20 Japanese patients (10 men and 10 women, [means ± SE] aged 56.4 ± 2.5 years, with BMI and HbA_{1c} 25.6 ± 1.2 kg/m^2 and 5.7 ± 0.1%, respectively) with newly diagnosed type 2 diabetes performed a 75-g oral glucose tolerance test and oral fat tolerance test (OFTT) twice. A 90-mg dose of nateglinide was administered immediately before fat loading in one of the two OFTTs. In the OFTT, each subject ingested 17 g fat/m^2 surface area (OFTT cream; Jomo Food Industry, Takasaki, Japan) (2). Plasma glucose and serum insulin, triglycerides, and remnant-like particles cholesterol (RLPC) concentrations were determined before and 30 min and 1, 2, and 4 h after fat loading.

When nateglinide was not administered (Nate−), triglycerides and RLPC continued to increase during OFTT, while no significant changes in plasma glucose or insulin were noted. In OFTT with nateglinide administration (Nate+), increases in triglycerides and RLPC after fat loading were significantly lower than in Nate− by ANOVA ($P < 0.001$). The average increments of triglycerides and RLPC from baseline to 4 h were 1.1 mmol/l and 0.31 mmol/l in Nate− and 0.46 mmol/l (−58%, $P < 0.01$) and 0.05 mmol/l (−84%, $P < 0.01$) in Nate+, respectively. Plasma glucose levels in Nate+ were gradually decreased by 1.6 mmol/l on average after 2 h. Insulin levels in Nate+ peaked after 30 min and then decreased to below baseline level by 4 h. Furthermore, in Nate−, the regarding rates of increase for triglycerides and RLPC during OFTT had significant correlations with Σinsulin during the oral glucose tolerance test ($r = 0.63$ and 0.72, respectively), which is a surrogate measure for insulin resistance, while in Nate+, there were no significant correlations among them.

Early insulin secretion following nateglinide administration was thus proved to inhibit postprandial hyperlipidemia in type 2 diabetic patients. Improvements in insulin resistance over a short period of time seem to exert substantial influence on lipid parameters. Insulin secretion patterns appear to play a major role in postprandial hyperlipidemia as well as hyperglycemia.

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