OBSERVATIONS

Case Report of Klinefelter's Syndrome With Severe Diabetes, Dyslipidemia, and Stroke

The effect of pioglitazone and other anti-inflammatory agents on interleukin-6 and -8, tumor necrosis factor-α, and C-reactive protein

Klinefelter's syndrome is a sex chromosomal aberration of male infertility. Most diabetes of this syndrome shows insulin resistance. Chronic proinflammation is involved in the pathogenesis of diabetes, and cytokines play a role in insulin resistance (1–3). Interleukin (IL)-8 is a cytokine secreted by monocytes and endothelial cells (6). IL-6 is associated with insulin resistance and is an inducer of C-reactive protein (CRP) (1,2,7). IL-8, IL-6, and CRP are higher in diabetes (1–5). We report a 30-year-old man with Klinefelter's syndrome and diabetes. He was diagnosed with Klinefelter's syndrome from 47 XXY at 27 years of age and was taking testosterone.

Serum samples for high-sensitivity CRP, IL-6, IL-8, and tumor necrosis factor (TNF)-α were stored at −30°C. IL-8 and IL-6 were measured with immunoassays from Bio Source and Fuji Rebio, respectively. Normal control values for IL-8, IL-6, and TNF-α were ≤2.0 pg/ml, ≤4.0 pg/ml, and ≤40.0 pg/ml, respectively.

The patient was admitted to Toyonaka Municipal Hospital in June 2004. His BMI was 26.2 kg/m^2. Although he injected 120 units/day of insulin (aspart and glargine), his fasting blood glucose (FBG) (14.4 mmol/l), HbA_{1c} (A1C) (12.9%), cholesterol, and triglycerides were severely elevated. Urinary C-peptide was 98 μg/day, and glucagon tests showed normal insulin response (ΔC-peptide 4.0 ng/ml). Insulin secretion was preserved and sensitivity was decreased. He had a stroke at the beginning of July. CRP, IL-6, IL-8, TNF-α, A1C, FBG, and insulin dose were 1,020 ng/ml, 1.5 pg/ml, 9.4 pg/ml, 14.3 pg/ml, 10.0%, 6.6 mmol/l, and 98 units/day, respectively. He was administered aspirin (100 mg/day) and atorvastatin (10 mg/day). At the end of July, CRP, IL-6, IL-8, TNF-α, FBG, and insulin dose were 1,140 ng/ml, 2.4 pg/ml, <2.0 pg/ml, 9.9 pg/ml, 8.4 mmol/l, and 90 unit/day, respectively. We then added pioglitazone and increased atorvastatin (20 mg/day). In October, CRP, IL-6, A1C, and insulin dose decreased to 247 ng/ml, 0.9 pg/ml, 5.3%, and 26 units/day, respectively. IL-8 was <2.0 pg/ml, and FBG was 7.8 mmol/l. TNF-α increased to 22.7 pg/ml. Pioglitazone therapy reduced levels of proinflammation and insulin sensitivity, although other anti-inflammatory agents might have also reduced those markers. IL-8 had a tendency to decrease during glycemic improvement. Stroke might have increased those markers. The mechanism of diabetes in this syndrome was reported to be low testosterone and impaired mitochondrial function promoting insulin resistance, but a detailed mechanism remains to be elucidated. Pioglitazone also preserves β-cell function and has an anti-inflammatory effect in type 2 diabetes (8). We suggest that examinations of IL-6, IL-8, and CRP are informative and this anti-inflammatory therapy is useful. In summary, proinflammatory states could contribute to glucose metabolism and insulin resistance in a case of Klinefelter's syndrome with severe diabetes.

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Regression of Pancreatic Diabetes in Chronic Hereditary Pancreatitis

Pancreatic diabetes is believed to be an irreversible sign of progressive pancreatic failure (1). We report here on a girl with chronic hereditary pancreatitis and the R122H-mutation of the cationic trypsinogen gene (2), in whom pancreatic diabetes regressed in the course of the disease.

The girl initially presented at 6.3 years of age with acute pancreatitis. Episodes of diarrhea occurred shortly after initial presentation. The cholecystokinin-secretin stimulation test revealed global exocrine insufficiency. Oral pancreatic enzyme supplementation was initiated with porcine pancreatic extracts. Until the