Improvement of glucose metabolism by pioglitazone in a patient with lipoatrophic diabetes, increased plasma leptin and adiponectin levels, and subcutaneous axillary lipomas

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Introduction

Generalized lipodystrophies are rare disorders characterized by almost total loss of adipose tissue, and they are often accompanied by metabolic complications such as severe insulin resistance, diabetes mellitus, hypertriglyceridemia, and fatty liver. Lipodystrophies can be classified into two major types: congenital and acquired. At least four molecularly distinct forms of congenital generalized lipoatrophy have been defined by mutations in AGPAT2, BSCL2, CAV1, and PTRF. The three types of etiologies for acquired generalized lipodystrophy are infection (e.g., panniculitis), autoimmune, and idiopathic.

Case Report

We diagnosed a 17-year-old woman whose subcutaneous adipose tissue began to decrease in her late elementary school days with the acquired and generalized types of idiopathic lipoatrophic diabetes. She had no family history of lipoatrophy. She had extreme insulin resistance, fatty liver, hyperlipidemia, and an increased basal metabolic rate in addition to a decreased subcutaneous fat mass, partial white hair, acanthosis nigricans, hyperkeratinized skin of the fingers and toes, and arachnodactyly. On first examination, height was 164 cm, weight was 43 kg, fasting plasma glucose level was 100 mg/dL, glycated hemoglobin (HbA1c) level was 6.7%, and fasting immunoreactive insulin level was 80 IU/mL(Table 1.). Her serum insulin level gradually decreased, her glycemic control worsened, and her HbA1c level increased above 12% even with 1,000 U of insulin per day. To overcome this severe insulin resistance, we added pioglitazone hydrochloride to the insulin therapy. Her glycemic control successfully improved along with an increase in the serum leptin (before and after pioglitazone medication: 4.5 ng/dL and 9.6 ng/dL, respectively) and adiponectin levels (1.24 mg/mL and 3.10 mg/mL, respectively)(Table 2.). After starting pioglitazone, percent body fat was increased(Table 3.), and subcutaneous axillary lipomas on both sides of her body (right 9.7 × 7.6 cm, left 7.1 × 6.4 cm) were found(Fig. 1.), and fatty liver was improved(Fig. 3.). She developed nephrotic syndrome and was diagnosed with silent myocardial ischemia with three vessel disease. She underwent percutaneous coronary intervention. At 31 years old, she died, probably of pulmonary edema.

Table 1. Laboratory findings at first visit

Diabetes related data		
FPG	100	mg/dl
HbA1c	6.3	%
Anti-GAD antibody	<0.2	U/ml
U-CPR	308.4	μg/day
Insulin receptor antibody	(−)	
Insulin antibody	5.2	%

75gOGTT

	before	30	60	90	120	min
PG(mg/dl)	100	201	205	216	201	
IRI(μU/ml)	80	332	321	605	652	

Fig. 1. Chest CT

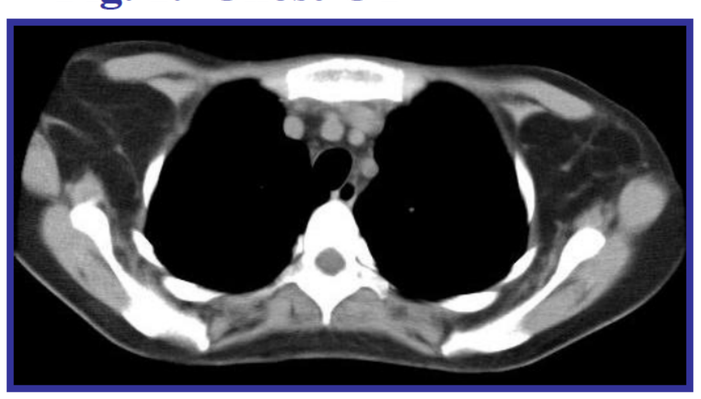


Table 2. Changes in blood levels of leptin and adiponectin

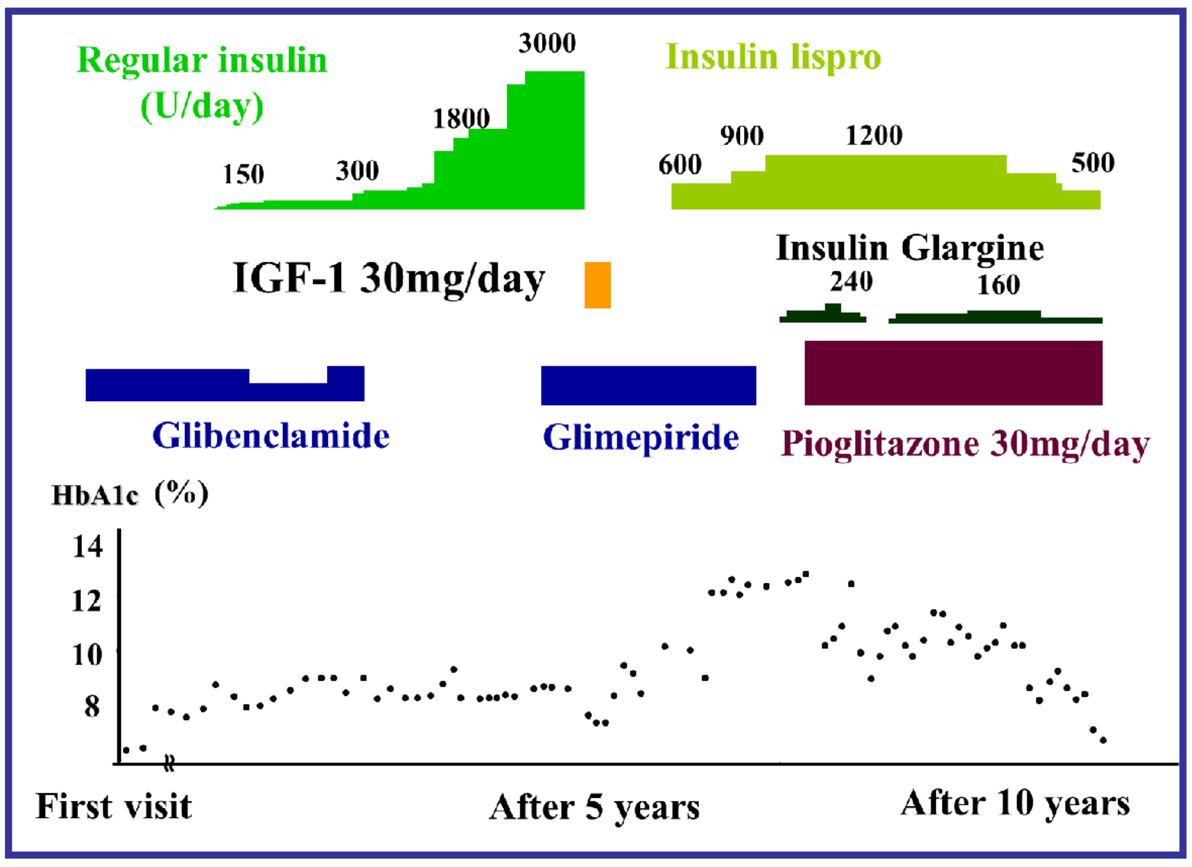
	before	2 years	4 years
Leptin (ng/dl)	4.5	9.6	15.7
Adiponectin (mg/ml)	1.24	3.10	4.39
Weight (kg)	39.0	45.5	51.9
Height (cm)	165.4	165.3	165.5

Table 3. Body fat distribution
dual-energy x-ray absorptiometry

Region	%Fat	
	before	4 years
L Arm	22.6	33.2
R Arm	22.6	40.3
Trunk	9.4	27.6
L Leg	7.8	15.9
R Leg	8.7	15.5
Subtotal	10.4	25.1
Head	17.3	17.9
Total	11.1	24.5

Before : immmediately before pioglitazone treatment
2 years : 2 years after beginning of pioglitazone treatment
4 years : 4 years after beginning of pioglitazone treatment

Fig. 2. Clinical course



CONCLUSIONS

Pioglitazone (thiazolidinedione) is a ligand for peroxisome proliferator-activated receptor-γ a nuclear receptor expressed mainly in adipocytes that promotes their development. In the present case, pioglitazone caused proliferation of the rest of the adipocytes and subcutaneous axillary lipoma growth. Metreleptin replacement therapy can dramatically improve metabolic complications in patients with lipoatrophic diabetes. However, the current case also demonstrated that the metabolic complications of lipoatrophic diabetes can be partially resolved with pioglitazone treatment.

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