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Original Article

Increased prevalence of proliferative retinopathy in patients with acromegaly

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Abstract

Background: This pilot study was carried to determine the prevalence of retinopathy, especially proliferative retinopathy, in patients with acromegaly.
Methods: We analyzed 43 acromegalic patients and 129 age- and gender-matched patients with type 2 diabetes. The retinopathy status was determined from the medical records based on the ophthalmologist consultations of patients with acromegaly. Color photographs of the macula- and disc-centered views were obtained at an angle of 45° with a fundus camera after pharmacologic-induced mydriasis in patients with type 2 diabetes.
Results: Compared with age- and gender-matched patients with type 2 diabetes, the acromegalic patients had lower fasting plasma glucose levels and lower systolic and diastolic blood pressures, but were taller and had higher IGF-1 levels. Any degree of retinopathy was present in 9.3% (4 of 43) of patients with acromegaly and 34.9% (45 of 129) of patients with type 2 diabetes (odds ratio [OR] = 0.191; 95% confidence interval [CI] = 0.064−0.570). Proliferative retinopathy was present in 9.3% (4 of 43) of patients with acromegaly and 9.3% (12 of 129) of patients with type 2 diabetes (OR = 1.000; 95% CI = 0.305−3.281). Non-proliferative retinopathy was absent in patients with acromegaly, but present in 25.9% (33 of 129) of patients with type 2 diabetes.
Conclusion: The high proliferative, but absence of non-proliferative retinopathy in our patients with acromegaly may reflect the pathogenic effect of IGF-1 on neovascularization. IGF-1 may play an important role in proliferative retinopathy, but may play no role in non-proliferative retinopathy.

Keywords: Acromegaly; Growth hormone; IGF-1; Proliferative retinopathy

1. Introduction

Acromegaly is a rare chronic disease that is characterized by hypersecretion of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) and is caused by pituitary adenomas in >95% of patients.[1] GH hypersecretion leads to excessive skeletal growth, soft tissue enlargement, insulin resistance or diabetes, and cardiovascular, cerebrovascular, and respiratory diseases.[1]

Neovascularization is the final common pathway in diabetic retinopathy and IGF-1 has been associated with retinal neovascularization.[2] The retina has also been identified as a target of excessive IGF-1, and increased serum and intraocular IGF-1 have been reported in acromegalic patients with diabetic retinopathy.[3,4] IGF-1 modulates the function of retinal endothelial precursor cells, drives retinal angiogenesis in response to hypoxia, and may play a role in the pathogenesis of

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proliferative diabetic retinopathy.[5] There is a significant amount of data to suggest that an increase in IGF-1 activity may contribute to retinal neovascularization, which is characteristic of conditions, such as proliferative diabetic retinopathy.[6,7] Some studies have reported an association between the plasma or intraocular levels of IGF-1 and the occurrence or progression of diabetic retinopathy.[8–10]

Although there is strong experimental evidence that IGF-1 plays a role in the development of proliferative retinopathy, the prevalence of retinopathy in patients with acromegaly has not been well-documented.[2–10] This pilot study was conducted to determine the prevalence of retinopathy, especially proliferative retinopathy, in patients with acromegaly.

2. Methods

2.1. Subjects

This analysis combined two study populations (acromegalic patients and a diabetes control group). The acromegalic patients were recruited first then the gender- and age-matched controls were selected from a cohort of type 2 diabetes at a 1:3 ratio.

There were 163 patients with acromegaly admitted to the Taipei Veterans General Hospital for trans-sphenoidal surgery between 1979 and 2007. Forty-three patients (16 males and 27 females) had undergone examinations by an ophthalmologist during the hospitalization. Another 480 type 2 diabetic patients consented to participate in the study and were enrolled between 1 August 2001 and 31 December 2002. All participants provided a medical history and underwent a physical examination, biochemical assessment, and fundus examination. We selected 129 gender- and age-matched controls from this diabetes cohort. The Medical Ethics Committee of Taipei Veterans General Hospital approved the two study protocols.

2.2. Clinical examination

Height and weight were measured while each participant wore light indoor clothes without shoes. The body mass index (BMI) was calculated as the body weight in kilograms divided by the square of the height in meters. Blood pressure was measured with a sphygmomanometer and calculated as the mean of two measurements from the left arm of subjects who had been resting for 5 min in a sitting position. We also queried the participants for disease duration, cigarette use, and medications prescribed. The disease duration was defined from known diagnosis of diabetes or acromegaly to the time of fundus examination.

2.3. Eye examinations

The retinopathy status was reviewed from the medical reports prepared by ophthalmologists of patients with acromegaly. In patients with type 2 diabetes, color photographs of the retinas were obtained according to the ETDRS.[11] Macula- and disc-centered views were taken at an angle of 45° with a fundus camera after pharmacologic-induced mydriasis. The fundus photographs were evaluated by one ophthalmologist who was unaware of the medical conditions. The scale has 17 steps, ranging from no retinopathy in either eye to high-risk proliferative retinopathy in both eyes. We combined the severity of retinopathy into three categories in both study populations, as follows: no apparent retinopathy; non-proliferative retinopathy; and proliferative retinopathy.

2.4. Statistical analysis

SPSS for Windows (version 18.0; SPSS, Inc., Chicago, IL, USA) was used to perform data analysis. All data are described as the mean ± SD unless stated otherwise. The nadir GH level was defined as the lowest value at any time after oral ingestion of glucose. Non-normally distributed values were log-transformed. The differences in the prevalence of retinopathy were evaluated using a χ^2 test. Statistical significance was defined as a p value < 0.05.

3. Results

Among the 43 acromegalic patients, there were 7 patients who had visual field defects and 4 had proliferative retinopathy. Another 2 patients had optic neuropathy, but had normal visual field tests. The mean age at diagnosis was 45.1 ± 15.9 years, the mean fasting GH level was 31.38 ± 36.35 μg/L, the mean fasting IGF-1 level was 506.0 ± 308.4 μg/L, and the mean SD score for IGF-1 was 5.21 ± 5.31. According to the results of the oral glucose tolerance tests, 16 patients had normal glucose tolerance, 11 patients were glucose intolerant, and 16 patients had diabetes. Among the 129 type 2 diabetes controls, the mean age was 48.7 ± 6.2 years, the mean diabetes duration was 6.5 ± 5.7 years, the mean fasting plasma glucose level was 165.3 ± 47.8 mg/dL, and mean the HbA1c was 8.07 ± 1.56% (Table 1). Compared with age- and gender-

Table 1
Clinical characteristics of patients with acromegaly and type 2 diabetes.

	Acromegaly (N = 43)	Type 2 diabetes (N = 129)	p
Age (years)	45.1 ± 15.9	48.7 ± 6.2	0.350
Gender (male/female)*	16/27	48/81	1.000
Fasting GH (μg/L)	31.38 ± 36.35	NA	
Fasting IGF-1 (μg/L)	524.4 ± 301.9	216.7 ± 118.7	<0.001
IGF-1 SD score	5.21 ± 5.31	0.97 ± 2.42	<0.001
Fasting plasma glucose (mg/dL)	109.7 ± 37.1	165.3 ± 47.8	<0.001
2-h glucose during OGTT (mg/dL)	196.4 ± 90.8	NA	
HbA1C (%)	6.65 ± 1.12	8.07 ± 1.56	<0.001
Disease duration (years)	0.6 ± 0.6	6.45 ± 5.7	<0.001
Body height (cm)	165.6 ± 9.9	160.6 ± 9.1	0.004
Body weight (kg)	71.6 ± 13.6	67.5 ± 13.1	0.086
Body mass index (kg/m^2)	25.96 ± 3.42	26.45 ± 4.14	0.491
Systolic BP (mmHg)	128.1 ± 18.2	137.4 ± 16.1	0.002
Diastolic BP (mmHg)	77.5 ± 8.4	84.3 ± 10.1	0.001

GH, growth hormone; IGF-1, insulin-like growth factor-1; OGTT, oral glucose tolerance test; HbA1C, glycated hemoglobin; BP, blood pressure. * Fisher's Exact test. Data are described as the mean ± SD.

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