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Cardiac and metabolic effects of chronic growth hormone and insulin-like growth factor I excess in young adults with pituitary gigantism

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Abstract

Chronic growth hormone (GH)/insulin-like growth factor I (IGF-I) excess is associated with considerable mortality in acromegaly, but no data are available in pituitary gigantism. The aim of the study was to evaluate the long-term effects of early exposure to GH and IGF-I excess on cardiovascular and metabolic parameters in adult patients with pituitary gigantism. Six adult male patients with newly diagnosed gigantism due to GH secreting pituitary adenoma were studied and compared with 6 age- and sex-matched patients with acromegaly and 10 healthy subjects. Morphologic and functional cardiac parameters were evaluated by Doppler echocardiography. Glucose metabolism was assessed by evaluating glucose tolerance and homeostasis model assessment index. Disease duration was significantly longer ($P < .05$) in patients with gigantism than in patients with acromegaly, whereas GH and IGF-I concentrations were comparable. Left ventricular mass was increased both in patients with gigantism and in patients with acromegaly, as compared with controls. Left ventricular hypertrophy was detected in 2 of 6 of both patients with gigantism and patients with acromegaly, and isolated intraventricular septum thickening in 1 patient with gigantism. Inadequate diastolic filling (ratio between early and late transmitral flow velocity <1) was detected in 2 of 6 patients with gigantism and 1 of 6 patients with acromegaly. Impaired glucose metabolism occurrence was higher in patients with acromegaly (66%) compared with patients with gigantism (16%). Concentrations of IGF-I were significantly ($P < .05$) higher in patients with gigantism who have cardiac abnormalities than in those without cardiac abnormalities. In conclusion, our data suggest that GH/IGF-I excess in young adult patients is associated with morphologic and functional cardiac abnormalities that are similar in patients with gigantism and in patients with acromegaly, whereas occurrence of impaired glucose metabolism appears to be higher in patients with acromegaly, although patients with gigantism are exposed to GH excess for a longer period.

1. Introduction

Gigantism is a rare disorder due to growth hormone (GH) excess that occurs before fusion of the epiphyseal growth plates in a child or adolescent and causes excessive linear growth and extremely tall stature. In these patients, GH hypersecretion may be due to a somatotroph pituitary adenoma, a mammosomatotroph adenoma, or mammosomatotroph hyperplasia, which may be isolated or part of genetic disorders such as multiple endocrine neoplasia type 1, Carney complex, or McCune-Albright syndrome [1].

Most patients with gigantism also demonstrate clinical characteristics of acromegaly, including large hands and feet, coarse facial features with prognathism and frontal bossing, and excessive sweating. Ten percent of patients with acromegaly also exhibit tall stature indicating a clinical overlap between the 2 disorders [1]. Acromegaly is associated with considerable prevalence of metabolic and cardiovascular complications that account for increased morbidity and mortality [2-4]. Echocardiographic abnormalities have been extensively described in patients with acromegaly and, in particular, left ventricular (LV) hypertrophy (LVH) with variable degrees of diastolic and systolic dysfunction [3,5,6]. Aging and long-term exposure to GH and insulin-like growth factor I (IGF-I) excess are the main

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determinants of acromegalic cardiomyopathy [6], even if structural and functional changes in the heart have also been shown to occur in young patients [7,8]. Visceromegaly and/or impaired glucose metabolism have been reported in isolated patients with gigantism [1,9]; however, no data are available on cardiovascular complications in these patients.

The aim of our study was to evaluate the long-term effects of early exposure to GH and IGF-I excess on cardiovascular and metabolic parameters in adult patients with pituitary gigantism. We therefore studied morphologic and functional echocardiographic parameters, as well as lipid and glucose metabolism, in 6 young patients with gigantism (<40 years) in comparison with 6 age-matched patients with acromegaly and 10 healthy controls.

2. Subjects

Six patients with pituitary gigantism diagnosed during adulthood (all men; mean age, 26.2 ± 3.1 years; range, 19-38 years; body mass index [BMI], 27.6 ± 0.8 kg/m^2) and 6 patients with acromegaly (all men; mean age, 32.2 ± 2.6 years; range, 22-39 years; BMI, 28.7 ± 1.4 kg/m^2) were enrolled to participate in the study. All patients were newly diagnosed and were compared with 10 age- and sex-matched healthy controls (all men; mean age, 30.5 ± 1.8 years; range 22-39 years; BMI 26.1 ± 0.6 kg/m^2). The biochemical diagnosis of acromegaly and gigantism was made based on serum GH level (mean of at least 4 random fasting values) greater than 2.5 μg/L not suppressible below 1 μg/L after a 75-g oral glucose tolerance test and elevated circulating IGF-I levels (age and sex adjusted) [10]. Magnetic resonance imaging showed a pituitary adenoma in all patients (4 macroadenomas and 2 microadenomas in patients with gigantism; 5 macroadenomas and 1 microadenoma in patients with acromegaly). Two patients with gigantism had hyperprolactinemia. The duration of acromegaly was estimated by comparing patients' photographs taken for 1 to 3 decades and by interviews to date the onset of acral enlargement and facial changes. In patients with gigantism, the duration of disease was also estimated by interviews to date the linear growth acceleration and by comparison of the final height with the target height, calculated from parental heights [11]. In 4 patients (2 with gigantism and 2 with acromegaly), anterior pituitary deficiency was adequately replaced before the beginning of the study. All subjects gave their informed consent to participate in the study, which was approved by the ethical committees of the University of Ferrara and of the University of Brescia.

3. Methods

In all subjects, heart rate (HR) and systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements, electrocardiography (ECG), and echocardiography were performed at study entry. Blood pressure was measured with a mercury sphygmomanometer in the right arm, with the subject in a relaxed sitting position, and with the arm supported at heart level, considering the average of 6 measurements (2 measurements in 3 different days). Hypertension was diagnosed in the presence of DBP above 90 mm Hg and/or SBP above 140 mm Hg.

Oral glucose tolerance test was performed after an overnight fast, evaluating serum GH and glucose. Fasting blood samples were assayed for IGF-I, total cholesterol, and high-density lipoprotein cholesterol (HDL-C), tryglicerides (TG), insulin, and fibrinogen levels. Four fasting baseline blood samples were drawn at 15-minute intervals for GH determination. Impaired fasting plasma glucose (IFG) was defined when fasting plasma glucose was ≥100 mg/dL (5.6 mmol/L) but <126 mg/dL (7.0 mmol/L). Impaired glucose tolerance (IGT) was defined by 2-hour postload glucose 140 to 199 mg/dL (7.8-11.1 mmol/L) and diabetes mellitus by 2-hour postload glucose 200 mg/dL (11.1 mmol/L),

Table 1
Clinical characteristics of patients and controls

	Patients with gigantism (n = 6)	Patients with acromegaly (n = 6)	Controls (n = 10)
Sex	Men	Men	Men
Age on study entry (y)	26.16 ± 3.07	32.16 ± 2.56	30.50 ± 1.84
Age at disease onset (y)[a]	15.33 ± 0.42***	28.83 ± 2.05	
Disease duration (y)	10.83 ± 2.91**	4.16 ± 0.87	
Height (m)	1.91 ± 0.02*-**	1.78 ± 0.03	1.76 ± 0.02
Predicted height (m)[b]	1.73 ± 0.02****	1.77 ± 0.03	1.74 ± 0.02
BMI (kg/m^2)	27.64 ± 0.79	28.67 ± 1.35	26.11 ± 0.57
Basal GH (μg/L)	44.73 ± 13.61*	18.58 ± 6.20*	1.13 ± 0.22
IGF-I (μg/L)	918.6 ± 164.1*	828.5 ± 114.7*	233.5 ± 12.2
Testosterone (ng/dL)[c]	424.3 ± 62.1	475.8 ± 46.8	513.4 ± 37.7
GH-secreting adenoma (no.)	4	6	
GH/PRL-secreting adenoma (no.)	2	0	
Gonadotropin deficiency (no. of patients)	2	2	
ACTH deficiency (no. of patients)	0	1	
Thyrotropin deficiency (no. of patients)	0	0	

Values are expressed as mean ± SEM. ACTH indicates adrenocorticotropic hormone; PRL, prolactin.

[a] Age (years) at estimated onset of the disease.

[b] Predicted height (m), calculated from parental heights as follows: [father's height + (mother's height +12)]/2 [11].

[c] Testosterone levels on entry study.

* $P < .05$ vs controls.

** $P < .05$ vs patients with acromegaly.

*** $P < .001$ vs patients with acromegaly.

**** $P < .05$ vs height in the same group.

Table 2
Cardiovascular parameters in young (<40 years) adult patients with pituitary gigantism or acromegaly and in healthy controls

	Patients with gigantism	Patients with acromegaly	Controls
No. of hypertensive subjects	1/6	2/6	0/10
SBP (mm Hg)	126.6 ± 5.1	126.6 ± 6.6	125.8 ± 4.0
DBP (mm Hg)	78.8 ± 2.4	83.3 ± 6.0	77.0 ± 3.9
HR (bpm)	71.8 ± 2.3	64.3 ± 3.3	69.3 ± 1.5
LVEDD (mm)	54.3 ± 2.0	51.5 ± 1.8	47.9 ± 1.7
IVST (mm)	11.8 ± 0.6**	11.7 ± 0.6**	9.1 ± 0.3
PWT (mm)	10.5 ± 0.4**	10.6 ± 1.1**	8.1 ± 0.3
LVM/BSA (g/m^2)	120.2 ± 7.4**	118.4 ± 12.7*	92.1 ± 4.4
LVM/height$^{2.7}$ ($g/m^{2.7}$)	48.0 ± 4.0*	48.8 ± 3.6*	39.8 ± 2.1
IRT (ms)	92.5 ± 3.1	91.5 ± 3.9	87.1 ± 2.2
Peak diastolic E/A ratio	1.18 ± 0.07*	1.17 ± 0.07*	1.37 ± 0.05
LVEF (%)	63.8 ± 2.5	65.5 ± 4.5	65.7 ± 1.5

Values are expressed as mean ± SEM. bpm indicates beats per minute; LVEDD, left ventricular end-diastolic diameter.
* $P < .05$.
** $P < .001$ vs controls.

or by fasting glucose ≥126 mg/dL in 2 determinations [12]. To estimate insulin resistance, homeostasis model assessment (HOMA) index was calculated as follows: [fasting insulin (mIU/mL) × fasting glucose (mmol/L)]/22.5.

3.1. Doppler echocardiography

M-mode, 2-dimensional, and pulsed Doppler echocardiographic studies were performed with ultrasound systems (Sonos 2500, Hewlett-Packard Co, Andover, Mass) using a 2.5- to 3.5-mHz transducer during at least 3 consecutive cardiac cycles. All subjects were studied according to the recommendations of the American Society of Echocardiography [13]. The following measurements were recorded on M-mode tracing: interventricular septum diastolic thickness (IVST) and posterior wall thickness (PWT), frequency-normalized mean velocity of circumferential fiber shortening end-diastolic volume (EDV) and end-systolic volume, and ejection fraction (ejection fraction = EDV − end-systolic volume/EDV%), estimated according to the method of Quinones et al [14]. Left ventricular mass (LVM) was calculated using the formula of Devereux [15]. Indexation of LVM was performed by 2 different methods, adjusting LVM with body surface area (BSA) or with body height to the power of 2.7. Left ventricular hypertrophy was defined by LVM/BSA greater than 134 g/m^2 (men) or LVM/height$^{2.7}$ greater than 50 $g/m^{2.7}$ (men) [16]. Systolic function was evaluated by LV ejection fraction (LVEF; normal above 50%). Diastolic function was evaluated by Doppler studies providing indexes of LV filling: (*a*) the isovolumic relaxation time (IRT) corrected for cardiac frequency (normal IRT <92 milliseconds, <30 years; <100 milliseconds, 30-50 years; <110 milliseconds, >50 years), which represents the interval between the end of aortic valve closure and the onset of mitral valve opening; (*b*) the early (E; cm/s) and late (A; cm/s) transmitral flow velocity, and the ratio between E and A curves (E/A; normal value >1), indicating the pattern of diastolic filling [17].

3.2. Analytical procedures

Growth hormone was measured by immunoradiometric assay with reagents supplied by Nichols Institute Diagnostics (San Juan Capistrano, Calif). The limit of detection was 0.02 μg/L, with intra- and interassay variation coefficients of 4.2% and 7.2%, respectively, at a concentration of 1.4 μg/L, and of 2.8% and 4.6% at a concentration of 12.2 μg /L. Plasma IGF-I was determined by radioimmunoassay using a commercially available kit (Medgenix Diagnostic SA, Fleurus, Belgium), after acid-ethanol extraction from EDTA plasma. The sensitivity of the method was 0.1 μg/L. The intra- and interassay coefficients of variation were 9.6% and 6.1%, respectively, in the concentration range of 125 to 1050 μg/L. The age-specific reference ranges for IGF-I were 135 to 485 μg/L (20-30 years) and 120 to 397 μg/L

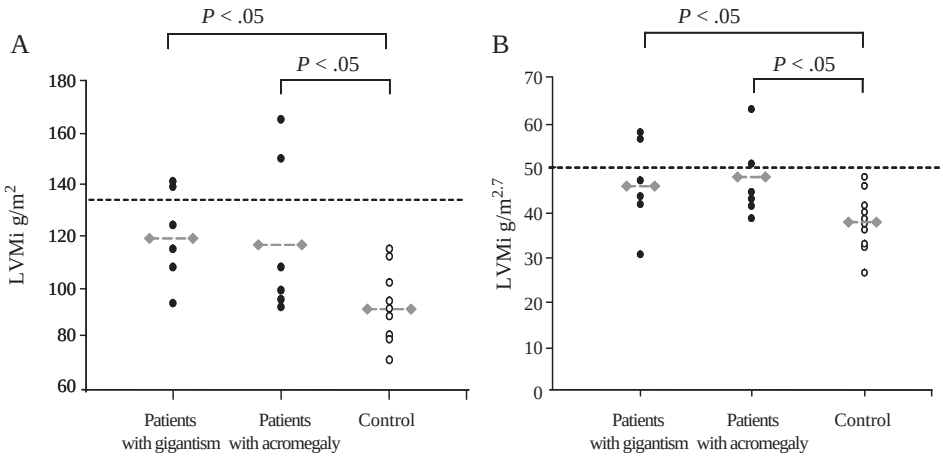

Fig. 1. Left ventricular mass index calculated both by adjustment to BSA (A) and by body height to the power of 2.7 (B), in young (<40 years) patients with gigantism, patients with acromegaly, and healthy controls. Normal LVMi/BSA >130 g/m^2; normal LVM/height$^{2.7}$ >50 $g/m^{2.7}$.

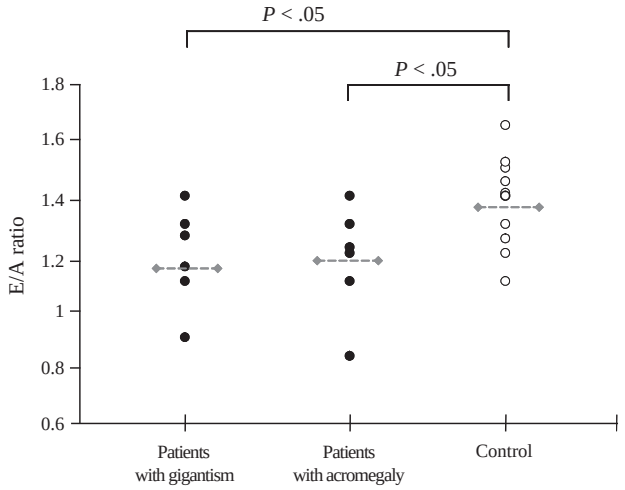

Fig. 2. E/A ratio in young (<40 years) adult patients with pituitary gigantism or acromegaly and in healthy controls. Normal E/A ratio >1.

(31-40 years). Insulin and testosterone levels were determined by using an automatic chemiluminescence immunoassay system. Total cholesterol and HDL-C, and TG levels were determined by enzymatic-colorimetric assay, and low-density lipoprotein cholesterol (LDL-C) was calculated by Friedewald equation. Glucose and fibrinogen levels were measured by standard methods.

3.3. Statistical analysis

All results are expressed as the mean ± SEM. Basal levels of GH were obtained from the mean (±SEM) of the 4 fasting values. Comparison between groups of continuous variables was assessed by using Student *t* test or 1-way analysis of variance and the post hoc analysis of Student-Newman-Keuls test for multiple variables. Correlations between hormonal values and clinical measures were performed by linear regression analysis. Values were considered statistically significant when P was less than .05.

4. Results

Clinical characteristics of patients and healthy controls are shown in Table 1. The mean estimated age of disease onset was significantly ($P < .001$) lower in patients with gigantism (15.3 ± 0.4 years; range, 14-17 years) than in patients with acromegaly (27.8 ± 2.6 years; range, 20-35 years), with longer ($P < .05$) disease duration in patients with gigantism (mean, 10.8 ± 2.9 years; range, 4-23 years) compared with patients with acromegaly (mean, 4.4 ± 0.9 years; range, 1-7 years). The mean age at initial diagnosis was not significantly different from that of control subjects on study entry. The mean basal serum GH and IGF-I concentrations of both patients with gigantism and patients with acromegaly were significantly ($P < .001$) higher than that in controls, with no significant difference between the 2 groups of patients.

4.1. Blood pressure and ECG data

As shown in Table 2, mean SBP and DBP, as well as HR, did not significantly differ among patients with gigantism, patients with acromegaly, and controls. Mild hypertension (blood pressure > 140/90 < 160/100 mm Hg) was detected in 1 patient with gigantism (16%) and in 2 patients with acromegaly (33%).

A first-degree atriovetricular block was observed in 1 patient with gigantism. No ECG alterations were detected in either patients with acromegaly or controls.

4.2. Doppler echocardiography

The mean LVM index (LVMi), calculated by LVM/BSA and LVM/height$^{2.7}$ ratios, was significantly ($P < .05$) higher in patients with gigantism and in patients with acromegaly, as compared with control subjects, whereas no significant difference was observed between patients with gigantism and patients with acromegaly (Table 2).

Left ventricular hypertrophy was detected in 2 (33%) of 6 patients with gigantism and in 2 (33%) of 6 patients with acromegaly, evaluating LVMi adjusted either with BSA or with body height to the power of 2.7 (Fig. 1) The mean IVST and PWT values, detected both in the patients with gigantism and in the patients with acromegaly, were significantly ($P < .05$) higher than those in the controls, without any significant difference between patients with gigantism and patients with acromegaly (Table 2). Moreover, in 1 patient with gigantism, who has normal LVMi, isolated IVST was found.

E/A ratio was significantly ($P < .05$) lower both in patients with gigantism and in patients with acromegaly compared with controls (Table 2). Moreover, a reduced

Table 3
Relationship between echocardiographic parameters and clinical characteristics

	Patients with gigantism		Patients with acromegaly	
	Cardiac alterations (3)[a]	No cardiac alterations (3)[a]	Cardiac alterations (2)[a]	No cardiac alterations (4)[a]
Age at diagnosis (y)	23.3 ± 3.0*	29.0 ± 5.5	38.5 ± 5.5	29.0 ± 2.5
Disease duration (y)	8.0 ± 5.5	13.6 ± 5.5	5.5 ± 1.5	3.5 ± 1.0
Basal GH levels (μg/L)	50.3 ± 20.4	39.0 ± 21.6	9.1 ± 2.1	23.3 ± 8.5
IGF-I levels (μg/L)	1237.3 ± 175.8**	603.3 ± 46.1	938.0 ± 112.0	798.7 ± 159.1

Values are expressed as mean ± SEM.

[a] Number of patients in parenthesis.

* $P < .05$ vs patients with acromegaly with cardiac alterations.

** $P < .05$ vs patients with gigantism with no cardiac alterations.

diastolic filling (E/A ratio <1) associated with LVH was observed in 1 patient with gigantism and in 1 patient with acromegaly (Fig. 2).

The mean IRT and LVEF values did not significantly differ among patients with gigantism, patients with acromegaly, and controls (Table 2).

No valvular abnormalities were detected either in the patients with acromegaly and gigantism or in the controls.

4.3. Relationship between echocardiographic parameters and clinical characteristics

Serum IGF-I concentrations were significantly higher in patients with gigantism who have cardiac hypertrophy compared with patients with gigantism without cardiac abnormalities ($P < .05$). Moreover, patients with acromegaly who have cardiac abnormalities were significantly ($P < .05$) older than patients with gigantism who have cardiac abnormalities (Table 3). However, linear regression analysis failed to demonstrate any significant correlation between either GH or IGF-I levels and patients' age, disease duration, and Doppler echocardiographic parameters.

4.4. Metabolic function

As shown in Table 4, IFG was detected in 1 (16%) of 6 patients with gigantism and in 4 (66%) of 6 patients with acromegaly. Two-hour postload glucose levels were significantly ($P < .05$) higher in patients with acromegaly than in controls, being diagnostic for IGT in 3 (50%) of 6 patients with acromegaly and 1 (16%) of 6 patients with gigantism. Both in patients with gigantism and in patients with acromegaly, HOMA index was higher than in controls, but the difference did not reach statistical significance.

Table 4
Metabolic parameters in patients with pituitary gigantism or acromegaly and in healthy controls

	Patients with gigantism	Patients with acromegaly	Controls
Fasting blood glucose (mg/dL)	95.7 ± 3.5	99.0 ± 5.7	88.4 ± 2.5
Fasting serum insulin (mU/L)	14.8 ± 4.1	15.5 ± 4.4	9.4 ± 1.4
Fasting glucose/ insulin ratio	8.7 ± 1.8	8.5 ± 0.3	11.1 ± 1.3
2-h postload glucose (mg/dL)	125.8 ± 10.1	142.5 ± 11.9*	117.5 ± 3.5
HOMA	4.23 ± 0.96	3.98 ± 1.32	2.12 ± 0.37
IFG, no. of patients (%)	1/6 (16)	4/6 (66)	0/10
IGT, no. of patients (%)	1/6 (16)	3/6 (50)	0/10
Total cholesterol (mg/dL)	186.3 ± 12.0	197.6 ± 12.9	179.5 ± 11.5
HDL-C (mg/dL)	51.0 ± 5.1	52.3 ± 3.4	59.0 ± 3.1
LDL-C (mg/dL)	116.8 ± 10.1	122.4 ± 12.8	103.9 ± 11.5
TG (mg/dL)	137.2 ± 29.2	143.1 ± 41.5	103.7 ± 13.9
Fibrinogen (mg/dL)	361.5 ± 42.2*	348.3 ± 19.8*	274.8 ± 13.9

Values are expressed as mean ± SEM.
* $P < .05$ vs controls.

No significant difference was observed in total cholesterol, HDL-C, LDL-C, and TG concentration between patients with gigantism, patients with acromegaly, and controls. Serum fibrinogen concentrations detected both in patients with gigantism and in patients with acromegaly were significantly ($P < .05$) higher than that in controls (Table 4).

5. Discussion

The present study demonstrates for the first time that adult patients younger than 40 years with pituitary gigantism have the same occurrence of morphologic and functional cardiac abnormalities as age- and sex-matched patients with acromegaly despite a longer duration of disease. In particular, both in patients with gigantism and in patients with acromegaly, LVH was detected in 33% of the patients, associated with inadequate diastolic filling in 2 (33%) of 6 patients with gigantism and 1 (16%) of 6 patients with acromegaly. In contrast, the occurrence of impaired glucose metabolism was higher in patients with acromegaly (66%) than in patients with gigantism (16%).

The role of GH and IGF-I in the development, growth, and function of the cardiovascular system is well known. Chronic exposure to GH and IGF-I excess is responsible for a specific cardiomyopathy that may be reversed by effective reduction in GH/IGF-I levels [3,5,6,18]. Patients with acromegaly with short-term disease duration show cardiac hypertrophy, increased systolic output, and decreased vascular resistance, consistent with the hyperkinetic syndrome. With the persistence of elevated GH levels (after ~5 years of active disease), cardiac abnormalities may include evident hypertrophy and diastolic dysfunction, subsequently progressing to systolic dysfunction and heart failure [6].

Aging and long duration of GH/IGF-I excess appear to be the main determinants of cardiac derangement because 90% of older patients with long disease duration show biventricular cardiac hypertrophy [3,6]. Our patients with pituitary gigantism and younger than 40 years showed a occurrence of LVH (33%) similar to that observed in age-matched patients with acromegaly, even if patients with gigantism had been exposed to GH and IGF-I excess for a significantly longer time. These data are consistent with recent reports suggesting that about 20% of young (<30 years) normotensive patients with acromegaly have cardiac hypertrophy [8]. It is still unclear whether aging may have independent negative effects on the heart in acromegaly. In the present report, patients with gigantism who have cardiac hypertrophy were younger than patients with acromegaly who have LVH. Moreover, we have shown that occurrence of cardiac abnormalities in young adult patients with gigantism with long disease duration (4-23 years) is lower than that generally observed in older patients with acromegaly with similar disease duration [6]. These results underline the role of aging in the development of acromegalic cardiomyopathy.

Testosterone has been shown to promote cardiac hypertrophy [19,20], possibly mediated by IGF-I [21]. Therefore, in patients with gigantism, the exposure to GH excess during adolescence, characterized by low circulating testosterone levels, might not exert the detrimental effect on the heart possibly occurring in adults with higher testosterone levels. Alternatively, it may be hypothesized that, in young age, cardiomyocites and/or smooth muscle vascular cells may better adapt to GH/IGF-I excess due to the greater plasticity in this period of life [22].

Although no statistically significant correlation was found between GH/IGF-I levels and cardiac abnormalities (probably due to the small sample size), patients with gigantism who have cardiac abnormalities had significantly higher IGF-I levels than patients with gigantism who have normal cardiac function and morphology. This observation suggests the presence in gigantism of a relative cardiac resistance to IGF-I, which may be overcome by very high circulating IGF-I levels.

In the general population, LVM is an important independent risk factor of cardiovascular disease morbidity and mortality [16,23]. It is unknown whether this relationship is present also in acromegaly, but it is well known that in patients with acromegaly, normalization of GH and IGF-I can reverse cardiac hypertrophy and reduce mortality to expected levels [2,4,6].

Controversy still exists regarding the best method for indexing LVM in clinical settings. In overweight subjects, LVM corrected for BSA may underestimate the prevalence of LVH, whereas LVH defined by LVM/height$^{2.7}$ criteria appears to be more appropriate for detection of preclinical cardiovascular abnormalities associated with obesity [23]. Accordingly, in overweight patients with acromegaly, the prevalence of LVH detected by LVM/BSA may be lower than that by LVM/height$^{2.7}$ [24].

Most of our patients, whether patients with acromegaly or with gigantism, were overweight; however, we found that the occurrence of LVH was similar in these patients by calculating LVM corrected both for BSA and height$^{2.7}$. On the other hand, we cannot exclude that in patients with gigantism, the greater height could cause an underestimation of the prevalence of LVH as defined by LVM adjusted for height$^{2.7}$. Cardiac hypertrophy was associated with initial LV diastolic dysfunction in 33% of patients with gigantism, in accordance with the generally observed prevalence (~30%) in untreated patients with acromegaly [6]. Because the diastolic impairment remains asymptomatic for several years, Doppler echocardiography should be performed in all young adult patients with GH excess regardless of the estimated disease duration to detect any possible cardiac involvement.

Finally, it is known that arterial hypertension favors the development of cardiac hypertrophy [4,6]. In our patients, hypertension was detected in 1 patient with gigantism who has isolated interventricular septum diastolic thickening and in 2 patients with acromegaly, only one of whom had LVH associated with initial diastolic dysfunction.

None of the patients with gigantism had diabetes mellitus, and the occurrence of altered glucose metabolism (either IGT or IFG) was lower than that found in patients with acromegaly. Homeostasis model assessment index was high both in patients with gigantism and in patients with acromegaly, indicating the presence of insulin resistance in both groups. It is well known that impairment in glucose metabolism or type 2 diabetes occurs in 20% to 50% of patients with acromegaly [3]. Our study demonstrates that the occurrence of impaired glucose metabolism in patients with gigantism is lower than in patients with acromegaly, although patients with gigantism are exposed to a longer-term GH excess. This could imply that the duration of GH hypersecretion does not have a significant role in determining alterations in glucose metabolism in young patients.

In accordance with the literature [25], fibrinogen levels were elevated in patients with GH excess, without any significant difference between patients with acromegaly and patients with gigantism.

In conclusion, our data suggest that GH/IGF-I excess in young adult patients is associated with morphologic and functional cardiac abnormalities which are similar in patients with gigantism and in patients with acromegaly, whereas occurrence of impaired glucose metabolism appears to be higher in patients with acromegaly, although patients with gigantism are exposed to GH excess for a longer period. The higher serum IGF-I concentration in patients with gigantism who have cardiac abnormalities may suggest that, in these patients, IGF-I value, rather than disease duration, could have a predictive value in cardiac complications.

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