ORIGINAL RESEARCH—ERECTILE FUNCTION

Erectile Dysfunction Is Common among Men with Acromegaly and Is Associated with Morbidities Related to the Disease

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ABSTRACT

Introduction. The prevalence of erectile dysfunction (ED) and its correlates in men with acromegaly has never been investigated.

Aim. The aim of this study was to evaluate sexual function in men with acromegaly.

Methods. Multicenter-based, retrospective analysis of a nonselected series of 57 acromegalic subjects (mean age: 52.7 ± 14.2 years) was performed. Acromegalic subjects reporting ED ($n = 24$) were compared with matched ED patients without acromegaly or pituitary disease (controls), selected from a cohort of more than 4,000 subjects enrolled in the Florence Sexual Medicine and Andrology Unit.

Main Outcome Measures. Patients were interviewed using Structured Interview on Erectile Dysfunction (SIEDY) structured interview, a 13-item tool for the assessment of ED-related morbidities. Several clinical and biochemical parameters were taken. Penile color Doppler ultrasound (PCDU) was performed in a subgroup of 37 acromegalic subjects.

Results. ED was reported by 42.1% of acromegalic subjects. After adjusting for age and testosterone, acromegalic subjects with ED had a higher prevalence of hypertension and more often reported an impairment of sleep-related erections and a longer smoking habit. Accordingly, acromegaly-associated ED was characterized by a higher organic component and worse PCDU parameters. No relationship between ED and testosterone levels or other acromegaly-related parameters was found. However, acromegalic subjects with severe ED reported a longer disease duration. In a case-control analysis, comparing acromegalic subjects with ED-matched controls free from acromegaly (1:5 ratio), acromegalic men had a worse ED problem and a higher organic component of ED, as derived from SIEDY score. In line with these data, acromegalic patients with ED had a higher prevalence of major adverse cardiovascular events history at enrollment and lower PCDU parameters.

Conclusions. Subjects with complicated acromegaly are at an increased risk of developing ED, especially those with cardiovascular morbidities. Our data suggest including a sexual function evaluation in routine acromegaly follow-up.

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Key Words. Men with Acromegaly; Sexual Function; Erectile Dysfunction; Penile Color Doppler Ultrasound; Major Adverse Cardiovascular Events; Cardio-Metabolic Morbidities

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Introduction

The role of growth hormone (GH) and insulin-like growth factor-1 (IGF-1) on male reproductive function has rarely been investigated. In rodents, the lack of GH action is associated with impaired spermatogenesis [1]. In humans, GH/IGF-1 status seems to influence male gonadal function in a biphasic fashion, as GH replacement treatment improves sperm volume and Leydig cell function in men with isolated GH deficiency [2], but GH excess leads to sperm abnormalities in male patients with acromegaly [3]. Less is known about the role of GH on male sexuality in humans [4–6]. In men with GH deficiency, GH replacement treatment has no effect on sexual function as evaluated by questionnaires [7], whereas no data are available on sexual function in male patients with GH excess [4–6].

Acromegaly is characterized by increased GH secretion [8,9] and therefore represents a useful in vivo model to study the effects of GH excess on several physiological functions. Moreover, patients with acromegaly have a considerable burden of complications and coexisting morbidities [8–10]. In particular, acromegaly is associated with cardiovascular (CV) and metabolic diseases, such as hypertension, glucose intolerance or diabetes, cardiomyopathy, and sleep apnea which all lead to an increased risk of morbidities and mortality [8–10]. In the general population, CV disease is also strongly associated with male sexual dysfunction, especially erectile dysfunction (ED) [11–15].

The aim of the present study is to investigate the prevalence of ED and its correlates in men with acromegaly.

Materials and Methods

The study was designed as a multicenter-based, retrospective analysis of a nonselected series of 57 endocrinology outpatients with acromegaly, to assess the prevalence of ED and its determinants. The enrollment period lasted about 2 years (2013 and 2014), and the baseline characteristics of the subjects included in the study are reported in Table 1. All patients enrolled underwent the usual diagnostic protocol applied to subjects with sexual dysfunction, in agreement with current guidelines [16], as previously reported [17]. An informed consent to the study was obtained from all subjects enrolled. All subjects were asked to respond to Structured Interview on Erectile Dysfunction (SIEDY), a 13-item tool made up of three scales,

Table 1 Socio-demographic and clinical characteristics of the patients with acromegaly

	Acromegalic patients (N = 57)
Age (years)	52.7 ± 14.2
Marital status (%)	
Stable relationship living together	63.2
Stable relationship not living together	14.0
No stable relationship	22.8
Education (%)	
None/primary school	19.3
Secondary school	29.8
Secondary higher	40.4
University	10.5
Morbidities (%)	
Current smoker	28.1
Arterial hypertension	36.8
Diabetes mellitus	43.9
MACE	26.3
Acromegaly parameters	
Acromegaly duration (years)	10.8 ± 9.2
Pituitary surgery (%)	84.2
Pituitary radiotherapy (%)	15.8
Current medical therapy for acromegaly (%)	64.9
Lanreotide	26.3
Octreotide	29.8
Pegvisomant	12.3
Dopaminergic drugs	7.0
Current active acromegaly (%)	45.6
Overall hypogonadism (TT < 12 nmol/L)* prevalence (%)	64.9
Anterior pituitary tropins defect (%)	68.3
Isolated tropins defect	52.6
Hypogonadotropic (LH < 9.4 U/L)† hypogonadism	50.9
Hypocortisolism	1.7
Multiple tropins defect	15.7
Hypogonadism, hypocortisolism, and hypothyroidism	10.5
Hypogonadism, hypothyroidism	3.5
Hypocortisolism, hypothyroidism	1.7
Clinical, laboratory, and instrumental parameters	
BMI (kg/m^2)	29.2 ± 5.6
SBP (mm Hg)	126.4 ± 15.6
DBP (mm Hg)	81.0 ± 9.5
Glycemia (mg/dL)	104.3 ± 29.6
Total cholesterol (mg/dL)	195.8 ± 41.1
Triglycerides (mg/dL)	107.5 [77.5–158.3]
HDL cholesterol (mg/dL)	52.0 ± 14.1
LDL cholesterol (mg/dL)	122.2 ± 31.8
GH (mcg/L)	1.03 [0.41–3.88]
IGF-1 (ng/mL)	231.9 [174.8–318.7]
LH (U/L)	2.70 [1.50–4.16]
FSH (U/L)	4.10 [2.94–7.35]
TT (nmol/L)	12.0 ± 5.8
PRL (mU/L)	135.5 [96.0–195.0]
TSH (mU/L)	1.10 [0.57–1.63]
FT4 (pmol/L)	16.41 ± 3.54
FT3 (pmol/L)	4.64 ± 0.98
ACTH (ng/mL)	18.0 [11.8–25.1]
Cortisol (nmol/L)	451.6 ± 130.5
Basal penile color Doppler ultrasound PSV (cm/second)‡	16.6 ± 5.0
SIEDY scale score	
Scale 1 (organic domain of ED)	3.69 ± 2.35
Scale 2 (relational domain of ED)	2.21 ± 1.96
Scale 3 (intrapsychic domain of ED)	3.07 ± 1.93
Intrapsychic parameters as derived by MHQ questionnaire	
Σ MHQ score	29.0 ± 14.1
MHQ-A score	5.2 ± 3.8
MHQ-P score	5.2 ± 3.1
MHQ-O score	6.2 ± 3.7
MHQ-S score	3.4 ± 3.1
MHQ-D score	4.4 ± 2.8
MHQ-H score	4.7 ± 2.5

*According to reference Buvat et al. [26] †According to reference Tajar et al. [27]
‡Performed in a subset of 37 subjects
Data are expressed as mean ± standard deviation or as median [quartiles], when appropriate, and as percentage, when categorical
Σ MHQ score = total score; A = anxious; ACTH = adrenocorticotropic hormone; BMI = body mass index; D = depressive; DBP = diastolic blood pressure; ED = erectile dysfunction; FSH = follicle-stimulating hormone; FT3 = free triiodothyronine; FT4 = tetraiodothyronine; GH = growth hormone; H = hysteric traits; HDL = high-density lipoprotein; IGF-1 = insulin-like growth factor 1; LDL = low-density lipoprotein; LH = luteinizing hormone; MACE = major adverse cardiovascular event; MHQ = Middlesex Hospital Questionnaire; O = obsessive; P = phobic; PRL = prolactin; PSV = peak systolic velocity; S, somatized; SBP = systolic blood pressure; SIEDY = Structured Interview on Erectile Dysfunction; TSH = thyroid stimulating hormone; TT = total testosterone