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ORIGINAL ARTICLE

Absence of periodontitis in acromegalic patients

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Abstract Acromegaly is a metabolic disorder caused by increased growth hormone (GH) secretion. Common oral features are prognatism, increased interdental spaces, macroglosia, and dental mobility. However, not much is known about the periodontal status of acromegalics. The periodontal status of 16 acromegalic subjects was investigated and compared with 20 controls (similar socioeconomic profile and age). Periodontal probing, followed by the assessment of gingival overgrowth, tooth loss and mobility, and malocclusion was performed. Acromegalic patients' did not present periodontitis and all of them had complete absence of periodontal pockets, while 50% of the control group presented periodontitis. All acromegalic patients presented dental mobility degree 1, mainly in the anterior inferior teeth. Malocclusion (100%) and diastemas (93.75%) were also present in these patients. It was concluded that acromegalic patients may be less prone to periodontal diseases than control subjects.

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Introduction

Acromegaly is a chronic disease due to growth hormone (GH) hypersecretion, mostly caused by a benign adenoma of the pituitary gland. This adenoma usually measures over 10 mm [31]. It is a rare condition, with an estimated annual incidence of three to four cases per million and a prevalence of 40–60 cases per million worldwide [12, 15]. The GH hypersecretion increases insulin-like growth factor (IGF-I) which affects bone metabolism [1].

The change in appearance, characterized by enlargement of the feet, hands, and mandible, is remarkable, but cardiovascular, metabolic, and respiratory complications as well as neoplasias are also present in patients with this disorder [12]. These systemic problems are responsible for the reduced quality of life. In these patients, life expectancy is shortened by an average of 10 years. When diabetes or heart disease are already present at the time of diagnosis the life expectancy is even shorter [25].

Acromegaly exhibits various oral characteristics, most commonly prognathism, macroglossy, everted and edematous lips, tooth mobility, interdental spaces (diastemas) and tooth loss [14, 16], and more rarely, gingival overgrowth[9]. Diastemas, and more significantly tooth mobility, are oral clinical manifestations that suggest the presence of periodontitis. Although these alterations are often observed in acromegalic patients, there is a lack of information regarding the periodontal status of these patients in the literature.

Periodontal diseases are the second major cause of tooth loss and this disease is a common finding in some systemic diseases [6]. Evidence suggests that periodontitis may be a

risk factor to ischemic cardiovascular disease, pulmonary disorders, preterm births, and low birth weight [13, 29]. Risk factors associated to periodontal disease include tobacco use, traumatic occlusion, and diabetes mellitus [35]. The last one affects 19 to 56% of acromegalic patients [26]. Thus, the aim of the present study was to assess the periodontal status of patients with acromegaly attended at a reference hospital in the state of Ceará, Brazil.

Materials and methods

This investigation is a cross-sectional study of 16 acromegalic patients, randomly selected among thirty patients attending the Neuroendocrinology Clinic of the Endocrinology and Diabetes Service at the Federal University of Ceará (UFC). The control group consisted of 20 individuals, who were randomly selected from a group of patients with similar age and socioeconomical status, seeking treatment at the University of Fortaleza (UNIFOR) dental clinic facilities.

All ethical aspects were rigidly observed, being the study conducted after its approval by the UNIFOR Research Ethics Committee. All patients gave informed consent to participate in this study.

Patients' clinical data were obtained using their hospital charts and dental examinations were performed at UNIFOR dental clinic. Glucose tolerance status of all patients was evaluated to diagnose the presence of diabetes mellitus.

Diagnosis of acromegaly was performed through basal determinations of GH (Quimiluminescence), insulin-like growth factor, IGF-I (IRMA), and GH level after oral glucose tolerance test (OGTT)—75 g of glucose orally [20]. It was considered diagnostic a GH nadir greater than 1 ng/L during OGTT, which was indicated when IGF-1 was above the reference range for sex and age and/or GH>0.4 ng/L, except for patients with diabetes, where only basal values were obtained [20]. Glucose tolerance of acromegalic patients was evaluated using diagnostic criteria from the American Diabetes Association [36].

All dental examinations were performed by the same experienced periodontist. Periodontal pockets depth were evaluated using a UNC—15 periodontal probe at six different points of each tooth. Individuals with probing depth (PD< 4 mm with no clinical attachment loss (CAL) were deemed healthy; those with PD between 4 and 6 mm and CAL of up to 4 mm as having chronic periodontitis with slight to moderate loss of periodontal support [3] and those with PD≥6 mm and CAL greater than 4 mm as having chronic periodontitis with advanced loss of periodontal support [4]. Using clinical criteria, subjects were also classified as having or not aggressive chronic periodontitis [5].

Bleeding on probing (BOP), considered an objective inflammatory parameter in periodontitis establishment, was measured using gingival bleeding index (GBI). GBI≤0.1 was considered as low risk for the development of periodontitis [27]. Tooth mobility levels were evaluated and classified as degrees 1, 2, and 3 [10]. Tooth loss, diastemas, and malocclusion were also assessed. Additionally, individuals from both groups were asked about oral hygiene and dietary habits.

Results were described using mean±standard deviation for continuous variables and proportions for cathegoric variables. Significance level was set at $p=0.05$. Independent t test was used to compare periodontal status between the acromegalic and the control group. The statistical software SPSS 12.0 (SPSS Inc, Chicago, IL, USA) was used for statistical analysis.

Results

A total of 16 acromegalic patients were assessed, eight (50%) male and eight (50%) female, with mean age of 45.8± 11.8 years, being 13 above 40 year of age. The mean age at diagnosis was 41.4±10.3 years (Table 1). Control group mean age was 41.5±10.5 years, ranging from 23 to 65 years, and consisting of 11 (55%) females and nine (45%) males. None of the patients were tobacco users.

On magnetic resonance imaging (MRI), 13 (81.25%) of the acromegalic patients presented pituitary macroadenomas and three (18.75%) pituitary microadenomas (6.25%). Seven patients (43.75%) were diabetics, four (25%) presented impaired glucose tolerance (prediabetes), and five (31.25%) normal glucose tolerance; 10 patients also presented hypertension (Table 1). No patients in the control group presented metabolic disorders including diabetes.

Trans-sphenoidal hypophysectomy (surgical adenoma removal) was performed on 10 (62.5%) of the acromegalic patients, four (25%) underwent radiotherapy, and 13 (81.25%) used or were using 10 to 30 mg of octreotide (Sandostatin-LAR®) per month. Octreotide is a synthetic form of a brain hormone, somatostatin, which stops GH production [33] Four patients (25%) used all three treatment modalities, five (31.25%) up to two treatment modalities and only two (12.5%), recently diagnosed patients, had not received any treatment at that time of this investigation.

When evaluated periodontal status in the acromegalic patients; it was observed that none of the patients presented periodontitis (Table 2). None of them had periodontal pockets, once they all presented probing depth lower than 4 mm. In the control group, 10 patients (50%) had periodontitis, four (20%) chronic periodontitis with advanced loss of support, and six (30%) chronic periodontitis with slight/moderate loss of support ($p=0.00$) (Table 2). No difference was noted between acromegalic patients and the control group regarding oral hygiene and dietary habits.

All 16 acromegalic patients presented tooth mobility (degree 1), notably in the lower anterior teeth. Malocclusion

Table 1 Clinical presentation at the time of evaluation of the 16 acromegalic patients studied

Patient	Sex	Age (years)	AD (years)	MRI	Therapeutics			GH (ng/L)	IGF-I (ng/ml)	Comorbidities
					Sur	Rx	Octr			
I	M	41	38	Macro	+	−	+	0.30	0.67 (0.34–1.9)	H, DM
II	F	41	40	Macro	+	−	+	0.10	0.8 (0.45–2.2)	H
III	F	44	37	Micro	+	+	+	0.89	2.05 (0.45–2.2)	DM
IV	F	30	25	Macro	+	−	+	2.96	1.23 (0.45–2.2)	H, DM
V	M	51	50	Macro	−	−	+	3.46	534 (80–283)	H, DM
VI	M	35	33	Macro	+	−	+	0.33	1.12 (0.34–1.9)	H
VII	M	60	42	Macro	+	+	+	37,5	2.4 (0.34–1.9)	H, IGT
VIII	M	42	53	Macro	+	−	−	36.7	696 (87–283)	DM
IX	F	41	40	Macro	−	−	+	64.2	2.55 (0.45–2.2)	IGT
X	F	31	30	Macro	−	−	+	2.00	1.62 (0.45–2.2)	H, IGT
XI	F	68	58	Macro	+	+	+	2.68	379 (78–258)	H, DM
XII	F	71	61	Micro	−	−	+	4.58	2.02 (0.45–2.2)	−
XIII	M	42	42	Micro	−	−	−	2.54	3.52 (0.34–1.9)	H
XIV	M	42	35	Macro	+	+	+	1.66	541 (101–303)	IGT
XV	M	49	49	Macro	−	−	−	77.0	2.99 (0.34–1.9)	H, DM
XVI	F	44	30	Macro	+	−	+	2.45	732 (101–303)	−

AD Age at diagnosis, *MRI* magnetic resonance imaging, *Sur* surgery, *Rx* radiotherapy, *Octr* octreotide, *M* male, *F* female, *Macro* macroadenoma, *Micro* microadenoma, *GH* growth hormone, *IGF-I* insulin-like growth factor, *H* hypertension, *DM* diabetes mellitus, *IGT* impaired glucose tolerance

showing Angle's class III or crossbite were also noted in all these patients. Diastemas were found in 15 (93.75%) of the 16 patients.

The control group presented 23.5±6.1 teeth while acromegalics presented 20.1±8.1 teeth. Bleeding on probing with GBI>0.1 was observed in 12 patients (60%) of the control group with a mean of 0.27±0.30 and in nine (56.2%) acromegalics with a mean of 0.23±0.32. No statistic difference was observed between these two groups ($p>0.05$).

Discussion

Many orofacial features of acromegalic patients have been reported in the literature. Pronounced mandibular prognathism, macroglosia, diastemas, and tooth mobility are the most evident findings [14, 16], with gingival overgrowth being rarely reported [9]. However, to date, not much is known about the periodontal status of these patients.

Table 2 Frequency of periodontal disease of acromegalic patients and controls

Periodontal disease	Control		Acromegalic	
	Number	Percent	Number	Percent
Absent	10	50.0	16	100.0
Chronic periodontitis (Slight to moderate)	6	30.0	–	–
Chronic periodontitis (advanced)	4	20.0	–	–
Total	20	100.0	16	100.0

Chi-square. $p=0.00$

The most significant finding of this study was the complete absence of periodontitis in the acromegalic patients despite the presence of an important risk factor, such as diabetes mellitus [2].

Diabetes mellitus is a clear risk factor for periodontal disease [35]. However, in this study, even with the high prevalence of acromegalic patients with glucose metabolism abnormalities and half of the acromegalic patients presenting diabetes mellitus, no sign of periodontitis was noted in any of the patients.

As related in the literature, the presence of diastemas was also observed. One of the causes of diastemas is pathologic tooth migration (PTM) which is a frequent finding in periodontitis. Studies have demonstrated a variation in PTM between 30.03% and 55.8% in the lower anterior sextant of patients with periodontitis [30, 37]. Many factors, such as periodontal tissue support loss, malocclusion, periapical inflammation, and lip and tongue pressure may influence the onset of PTM [8]. The results of this study suggest that the presence of diastemas in the acromegalic patients is not related to periodontitis. In this case, one factor that may favor diastema is the increased mandibular volume found in most of these patients [14]. Macroglosia, commonly found in acromegalic patients, may also promote the onset of interdental spaces and dental mobility through the pressure of the tongue on the teeth [34].

Tooth mobility is also a common dental finding in acromegalics. All patients studied exhibited class-1 mobility, found mainly in the lower incisor region, and nearly all presented it with diastemas, confirming literature data [16]. However, when probing depth was performed to verify the presence of periodontitis, no acromegalic patient presented periodontal pocket depth over 4 mm. Many patients related that due the mobility many teeth were extracted, showing that teeth are still lost due to incorrect diagnosis.

Severe occlusal trauma, due to malocclusions, which, in these patients, varied from simple crossbites to Angle's class III may be yet another component that favors dental mobility. The significant masticatory force resultant from exaggerated mandible enlargement and muscle hypertrophy is an additional factor [19].

The destructive action on the alveolar bone caused by periodontopathies has made periodontal aesthetic and functional reconstruction one of the main objectives of periodontics. Several biomaterials and proteins have been tested over the last 20 years for the preservation of periodontal structures and regeneration of lost support tissue. Guided tissue regeneration and growth factors such as fibroblast growth factor, platelet-derived growth factor (PDGF), transforming growth factor, bone morphogenic proteins, and insulin-like growth factor are among the materials tested [18].

The effects of many hormones in periodontal tissues have been studied. The results suggest that gingival tissues and alveolar bone may be influenced by the action of sex hormones like estrogen and testosterone [32], parathyroid and thyroid hormones [7, 17] as well as cortisol [24]. The GH is a hormone with anabolic effects on bone tissue that promotes IGF-I secretion [38]. GH increases bone formation via a direct interaction with GH receptors on osteoblasts and via local production of IGF-I (autocrine/paracrine action) [23]. Thus, in the presence of GH excess, a high alveolar bone formation may occur [21, 28]. IGF-I plays an important role in skeletal development by promoting chondrocyte proliferation and maturation, while inhibiting apoptosis to form bone of appropriate size and strength [39], being like this an important growth factor for the skeleton. Additionally, a possible beneficial role of IGF-I combined with PDGF in the treatment of periodontal bone defects and IGF-I impact on specific cells, such as periodontal ligament fibroblasts, have been recently postulated, which may explain the apparent protective effect for periodontitis in the acromegalic patients seen in this study [11, 22]. Like this, the anabolic effects of GH and IGF-I on bone might generate a protective effect in the periodontium, explaining the absence of periodontitis in acromegalic patients.

As acromegaly diagnosis generally occur very late, the changing of oral aspects can make the dentist or the periodontist an important health professional in the early detection of this disease, through early detection of these alterations. Improvement in the treatment and the control of acromegaly can happen when the disease is diagnosed early, further improving the life of these patients.

Conflict of interests The authors declare that they have no conflict of interest.

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