Cutaneous manifestations of acromegaly

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Abstract

Acromegaly is a rare syndrome, usually with insidious manifestations. Cutaneous changes are precocious. The dermatologist may be the first to suspect this early diagnosis and thus prevent the high morbidity of this disorder. The present paper describes dermatological findings in acromegaly (Dermatol Argent 2009; 15(3):186-190).

Key words: *acromegaly, cutaneous manifestacions.*

Introduction

Acromegaly is a syndrome resulting from an excess of growth hormone or somatotropin (GH), whose biological activity is mediated by insulin-like growth factor 1 (IGF-1). Most cases are secondary to a GH-secreting pituitary adenoma. Diagnosis is usually delayed, and 60 percent of the cases show disease remission; therefore, the tissues are usually exposed to excessive growth hormone for a long period of time. The most common clinical manifestations are hypertension, diabetes, hypertriglyceridemia, and cardiomyopathy.[1] The cutaneous manifestations include skin thickening and increase of eccrine, apocrine, and sebaceous gland secretion. Hypertrichosis and/or hirsutism may be found in the early phase, and hair rarefaction and miniaturization may appear in the late phase.[2] Onychodystrophy is described as ungual alteration.[3]

In rare cases, the acromegaly may be associated with multiple endocrine neoplasia type I, McCune-Albright syndrome, and Carney's syndrome.[1]

Objectives

To describe dermatologic manifestations of acromegalic patients and the behavior of some signs and symptoms with treatment.

Material and methods

Population and sample

The study included 19 patients from Hospital de Clínicas "José de San Martín" consulting at the Endocrinology Division and subsequently referred to the Dermatology Division of the same hospital (patients were always assessed by the same medical dermatologist). Diagnosis of acromegaly was reached by clinical evaluation and biochemical abnormalities (loss of GH sup-

Reception date: 17/11/08 | **Approval date:** 5/2/09

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pression in the oral glucose tolerance test, and/or increase of IGF-1).

A prospective, observational, and transversal study was conducted between January 2006 and September 2006).

Study variables

Data were obtained from ambulatory consulting patients and analyzed taking into account the following study variables:

- *Age*: in years
- *Gender*: male - female
- *Most common dermatologic manifestations*, such as acromegaloid facies; increased size of hands and feet; increased size of the nose, external ear and lower lip; the presence of macroglossia, prognathism, onychodystrophy, acanthosis nigricans, soft fibromas or acrochordons, eruptive seborrheic keratoses. Reference of oily skin or hyperhidrosis was also assessed.
- *Behavior of some signs and symptoms after treatment*. The definition of "cured and/or with controlled acromegaly" included those patients with normal serum IGF-1 concentracion according to age and gender, and "active" were the patients without normal serum IGF-1 concentracion according to age and gender.[4,5]

Processing and statistical analysis

Data were entered into a database (Excel-type) and then analyzed with a Pentium III microprocessor and the Epi Info version 6.00 statistical package. Frequency distribution and percentage to total cases were established for categorical variables.

Results

The study included 19 patients (11 female y 8 male) between 25 and 87 years of age, averaging 52.6 ± 17.8. The dermatologist carried out a thorough dermatologic clinical examination.

Of these 19 patients, 8 are cured, 7 are controlled, and 4 are active. "Cured" patients were surgically treated; "controlled" patients were subjected to transeptosphenoidal surgery with partial adenoma removal and/or radiotherapy plus octreotide for disease persistence (**Table 1**).

All patients showed increased size of hand and feet, independently of the acromegaly status. Only 15 (79 percent; 95 percent confidence interval [95% CI]: 54.4-93.9) had increase size of the nose, 4 (21 percent; 95% CI: 6.1-45.6) had increased size of external ear, and 4 (21 percent; 95% CI: 6.1-45.6) had

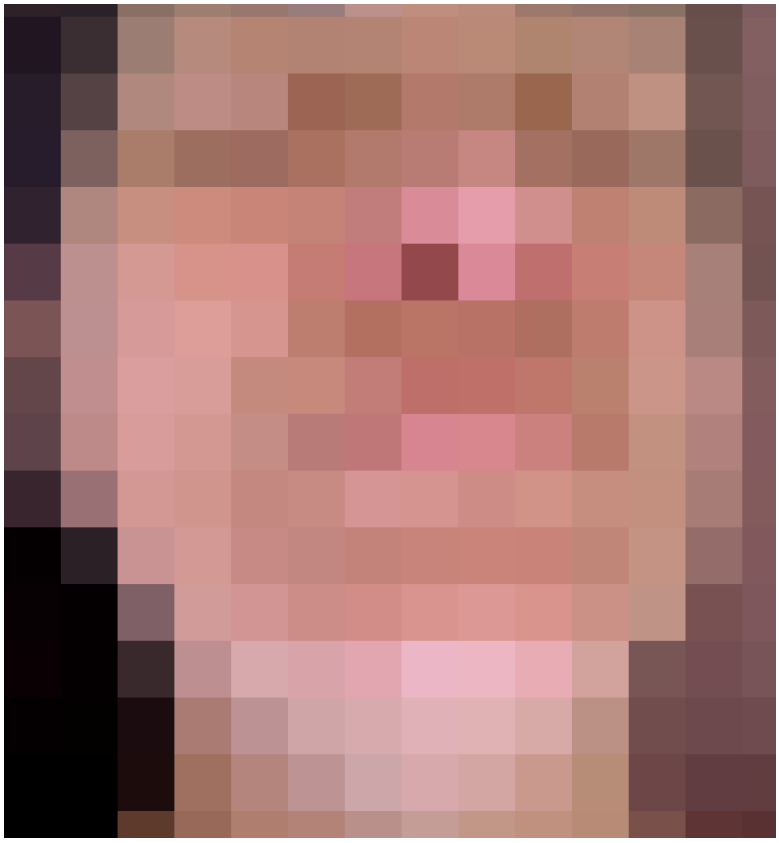

Figure 1. *Acromegaloid facies.*

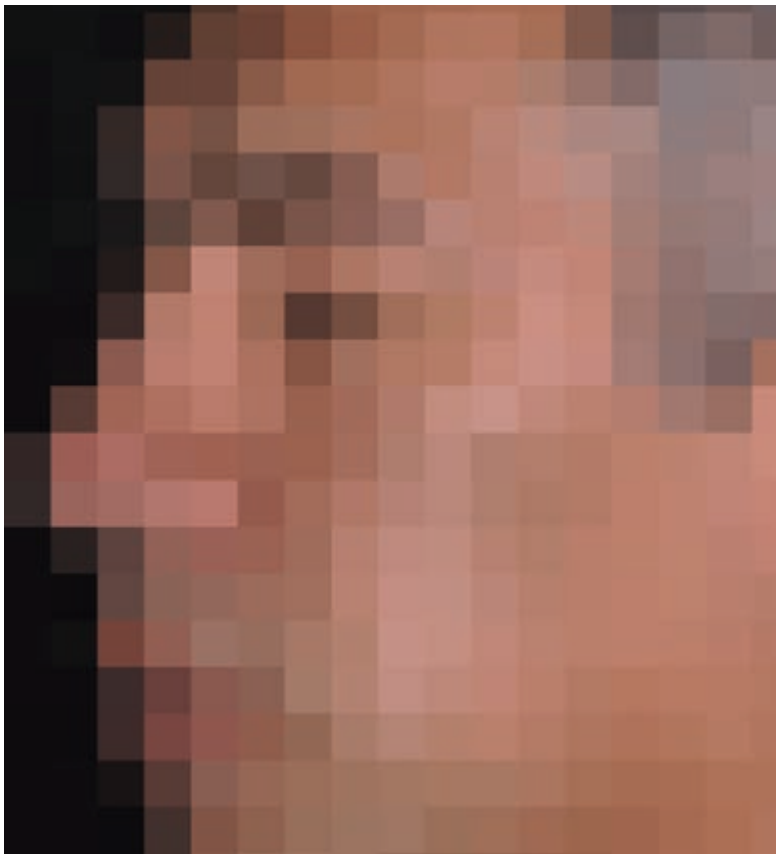

Figure 2. *Acneiform lesions.*

increased size of lower lip. Just 4 showed macroglossia (21 percent; 95% CI: 6.1-45.6) and 5 showed prognathism (26 percent; 95% CI: 9.1-51.2). Fifteen patients had oily skin (79 percent; 95% CI: 54.4-93.9). All showed partial post-treatment improvement (data reported by patients). Acneiform lesions are uncommon; they appeared in 2 of our patients (11 percent; 95% CI: 1.3-33.1), whereof 1 remains active and the other is controlled.

Only 8 of 19 patients (42 percent; 95% CI: 20.3-66.5) had soft fibromas, 1 (5 percent; 95% CI: 0.1-26) had hypertrichosis, and 1 (5 percent; 95% CI: 0.126) had eruptive seborrheic keratoses, with no association to neoplasias.

Seven (37 percent; 95% CI: 12.6-56.6) had toenail onychodystrophy (onycholysis and ungular plate thickening). Seven of the 19 (37 percent; 95% CI: 16.3-61.6) referred history of hyperhidrosis at the time of the acromegaly diagnosis. All referred disappearance of the symptom, even in the active remaining patient, where serum GH concentration decreased from 88.7 ng/ml at onset to 13 ng/ml.

Acanthosis nigricans was found in 2 patients (11 percent; 95% CI: 1.3-26) currently cured. Patients referred decrease in hyperpigmentation without complete post-treatment regression of the acanthosis.

Comment

The incidence of acromegaly is estimated in 3-4 cases per million population per year.[1] Occurrence is most frequent in middle-aged patients, with an average of 40 years in males and 45 years in females.[1] Average age of our patients was 52.6 ± 17.8 years.

Growth hormone (GH) stimulates production of insulin-like growth factor (IGF-1), which binds to the IGI-1 receptor and leads to the growth and differentiation of several skin cell lines such as keratinocytes, fibroblasts, and hair unit cells.[1]

Clinical aspects

The most common general complications of growth hormone (GH) excess are hypertension, diabetes mellitus, hypertriglyceridemia, and cardiomyopathy,[1] with a 2-4 times higher mortality than in the general population.[6]

Cutaneous manifestations

Skin involvement was described in 1899 by Steinberg.[1] Skin changes have been considered a classic finding in acromegaly.[1] However, few published reports related to skin manifestations of this disease were found.[1,3,7] Progression of the condition is characteristically slow and insidious; thus, the diagnosis is tardive. Skin changes may remain stationary or decrease when the disease activity diminishes.[1,7]

Cutaneous manifestations in acromegaly (Table 2)

One of the earliest signs is an edematous and doughy feeling most noticeable in face, palms and soles.[3] Patients have acromegaloid facies consisting of prominent frontal area, hypertelorism, eyelid edema, increased size of the nose and the external ear, prognathism, and macroglossia. In the studied population, 15 (79 percent) had increased size of the nose, 4 (21 percent) had increased size of the external ear, and 4 (21 percent) had increased size of the lower lip. Only 4 (21 percent) showed macroglossia, and 5 (19 percent) had prognathism.

Patients usually have oily skin with dilated pores; but, interestingly, acne is only rarely found.[7] In this aspect, we noticed that 15/19 (79 percent) patients had oily skin at assessment and all referred partial improvement with the indicated treatments. Two of the 15 patients (11 percent) with oily skin had acneiform lesions. Hyperhidrosis, usually with bromhidrosis, is important and is found in 50-88 percent of the cases.[7] Analysis of our patients showed that only 7 of 19 (37 percent) had hyperhidrosis of hands and feet at diagnosis (data referred by the patients). It was not present at the time of the clinical dermatology examination and the patients referred regression of the symptom at onset of treatment. Although one of the patients remained active, noteworthy after two pituitary surgeries with partial tumor excision, radiotherapy and current treatment with octreotide LAR, the patient reduced serum GH concentration. Hypothetically, improvement of hyperhidrosis may be caused by improvement of acromegaly, even though it is not yet controlled. Some skin changes, such as hyperhidrosis, improve readily when the disease activity is controlled. This finding was reported in our patients and correlated in the literature.[3]

Soft fibromas or acrochordons are a common finding in up to 45 percent of acromegaly patients.[8] They were found in 42 per-

TABLE 1.

19 patients were included (11 female and 8 male)	
Age range	25 to 87 years
Cured	8 (42.10 percent)
Controlled	7 (36.80 percent)
Active	4 (21.10 percent)

TABLE 2. CUTANEOUS MANIFESTATIONS OF ACROMEGALY PATIENTS.

Cutaneous manifestations	n	Prevalence	95% CI
Increased size of hands and feet	19	100%	82.4-100
Increased size of the nose	15	79%	54.4-93.9
Oily skin	15	79%	54.4-93.9
Soft Fibromas	8	42%	20.3-66.5
Hyperhidrosis	7	37%	16.3-61.6
Onychodystrophy	6	32%	12.6-56.6
Prognathism	5	26%	9.1-51.2
Increased size of external ear	4	21%	6.1-45.6
Increased size of lower lip	4	21%	6.1-45.6
Macroglossia	4	21%	6.1-45.6
Acneiform lesions	2	11%	1.3-33.1
Acanthosis nigricans	2	11%	1.3-33.1
Eruptive seborrheic keratoses	1	5%	0.1-26
Hypertrichosis	1	5%	0.1-26

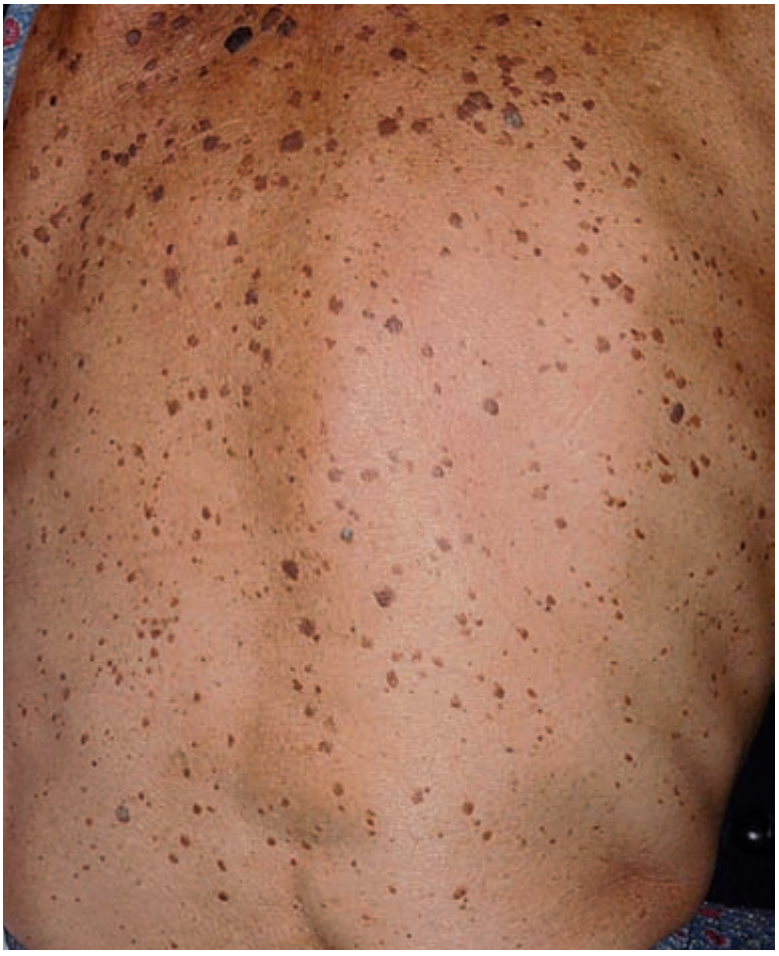

Figure 3. *Eruptive seborrheic keratoses.*

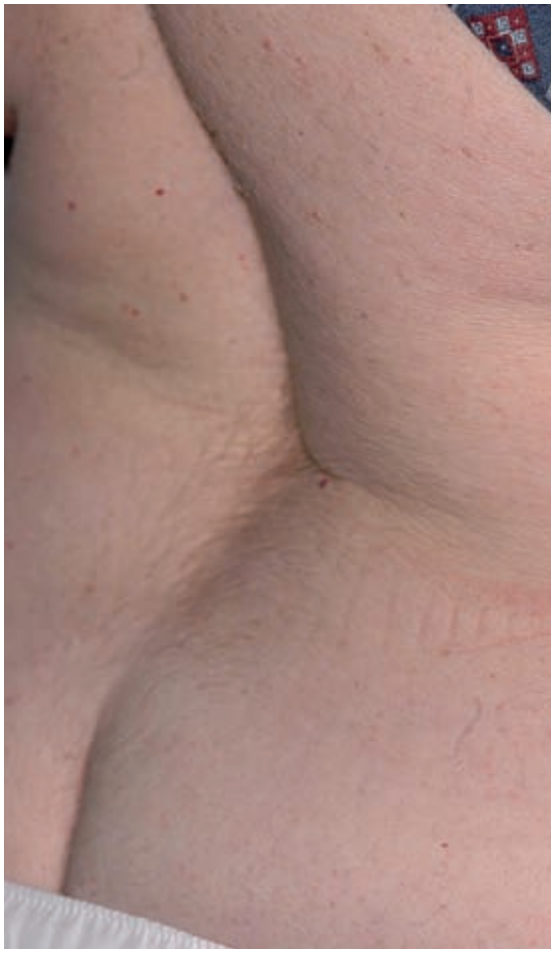

Figure 4. *Hypertrichosis.*

cent of patients in our case material (8 of 19), a finding similar to the literature.[8] Soft fibromas also occur in the general population in patients with diabetes mellitus, dyslipidemia, and other metabolic disorders appearing in acromegaly.[8,9] The search of colonic polyps is recommended if multiple soft fibromas are found.[10]

Acanthosis nigricans occurs in 10 percent of the cases, in the literature.[3] It appeared in 11 percent of our patients, who referred decreased hyperpigmentation after starting treatment, without complete regression of acanthosis (data reported by the patients). Hyperpigmentation, especially on photoexposed areas, is probably caused by an increase of melanocyte-stimulating hormone; these findings are not specific, and are also seen in other metabolic disorders, as mentioned above.

Hypertrichosis and/or hirsutism are detected in the early phase, and hair rarefaction and miniaturization tend to appear in the tardive phase (hirsutism and hyperhidrosis may be caused by a higher level of free testosterone).[3] Hypertrichosis was found in one woman (5 percent) of the 19 patients (cured).

In patients with acromegaly, nails show onychodystrophy.[3] Prevalence in our patients was 32 percent. The main cause of this sign is secondary to trauma. Patients without onychodystrophy had most likely made appropriate shoeware adaptations as the size of the feet increased.

None of our patients showed cutis verticis gyrata, a finding described in the literature.[11] In addition, 2/19 patients (5 percent) showed trichilemmal and eruptive cysts with a similar frequency to the general population. Only one patient (5 percent) showed sudden appearance of multiple seborrheic keratoses not associated with neoplasia.[3]

Conclusion

Some cutaneous manifestations may remain stationary with treatment and not regress (as occurs with acromegaloid facies, increase in size of hands and feet, soft fibromas, hypertrichosis, seborrheic keratoses), while others may decrease partially (such as oily skin and acanthosis nigricans). Above all, it must be remembered that skin alterations are precocious and that hyperhidrosis is an activity marker that may lead to diagnosis of the disease and thus reduce morbility and mortality; therefore, the dermatologist's observation and clinical suspicion are essential.

Acknowledgement

To Dr. Castiglia, for her contribution of statistical data.

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