Assessment of Nasal Carriage of Staphylococcus Aureus and Axillar Flora in Patients With Acromegaly

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Purpose: Recent study showed that patients with acromegaly have typical skin findings including increased sebum secretion, decreased transepidermal water loss, more alkaline, and colder skin surface correlated with serum growth hormone and insulin-like growth factor 1 levels. Different anatomic localizations and texture of the skin differ in bacterial concentrations.

Nasal carriage of Staphylococcus aureus and axillar flora in patients with acromegaly was compared with normal population with regard to duration of acromegaly as well as the growth hormone and insulin-like growth factor 1 levels.

Methods: This patient-control prospective study was conducted in university hospitals in Mersin, Turkey. The study consisted of 30 active acromegalic patients and 60 healthy adults who had no previously diagnosed chronic illness as a control group. A total of 90 volunteers were enrolled in this study; nasal and axillar cultures were obtained. Axillar and nasal specimens from anterior nares of the individuals were taken using sterile swabs.

Results: Nasal colonization of Staphylococcus aureus was 13.3% in acromegalic patients, but 43.4% in control group. This difference was statistically significant ($P = 0.004$). Patients and control group compared according to axillar cultures, the authors determined proteus colonization 16.7% in patients with acromegaly but no proteus colonization in control group. This result was statistically significant ($P = 0.001$). Proteus colonization was negatively correlated only with disease duration in acromegalic patients ($P = 0.017$).

Conclusion: The authors demonstrated that compared with healthy subjects, acromegalic patients had low percentage of nasal carriage of Staphylococcus aureus and more gram-negative basili in the axillar flora. These nasal and axillar flora changes should be considered for prophylactic antibiotics use before surgery and ampiric antibiotics use after surgery.

Key Words: Acromegaly, axillar flora, GH, IGF-1, nasal carriage

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Acromegaly is a disease caused by excess secretion of growth hormone (GH), which is characterized by enlarged acral parts, coarse facial features, and visceromegaly.[1] Bony and soft tissue changes are responsible for the characteristic appearance of patients with acromegaly. The changes are most prominent on the face, hands, and feet.[1] Skin changes of patients with active acromegaly consist of oily and sweaty skin.[2] These changes correlated with excess GH and insulin-like growth factor 1 (IGF-1) levels. Recent study showed that patients with acromegaly have physiologic and environmental skin findings including increased sebum secretion, decreased transepidermal water loss, more alkaline, and colder skin surface.[3] In addition, patients with acromegaly exhibited craniofacial changes such as diminished dimensions at nasal, uvular, mandibular, pharyngeal levels, and at the narrowest point of the pharyngeal airway space compared with healthy controls.[4]

The composition of skin flora of the body varies from site to site and depends on many factors such as host physiology; environment, immune system; host genotype, lifestyle and pathobiology.[5,6] Different regions of the human skin contain characteristic distributions of different types of glands. These glands produce oily substances such as sebum and other lipid, carbohydrate, and proteinaceous components that may serve as nutrients for the microbiome, as well as inhibitors to particular classes of microbes. Rich sebaceous glands areas are enriched for Propionibacterium spp., whereas moist skin areas are enriched for Corynebacterium spp. and dry skin areas enriched for β-Proteobacteria.[7] Interpersonal variation such as the individual's state of health, age, and sex also influence composition of skin flora.[8,9]

Acromegaly treatment consists of trans-sphenoidal surgery, medical treatment, and radiotherapy.[1] Skin and nasal flora may change after surgery and radiotherapy.[10,11]

These environmental, physiologic, and morphological changes and acromegaly treatment may influence nasal carriage of Staphylococcus aureus and skin flora in patients with acromegaly. Unfortunately, in the literature, there is no study on nasal carriage of Staphylococcus aureus and skin flora in patients with acromegaly.

In light of this background, nasal carriage of Staphylococcus aureus and axillar flora in patients with acromegaly was compared with normal population with regard to duration of acromegaly as well as the GH and IGF-1 levels.

METHODS

Patients

This patient-control study was conducted in hospitals of Mersin University, Turkey, from November to December 2012. Subjects in the patient group were 30 acromegalic patients referred to clinic of Endocrinology and Metabolism. The study samples were consecutively selected from the patient and control groups. Informed consent was obtained from all patients and controls. The study protocol was approved by the Hospital Ethics Committee. The control group consisted of 60 healthy adults who had no previously diagnosed chronic illness and did not use previous treatments and medication that modify skin flora. Control participants were matching in sex, age with the acromegaly patients.

The 30 patients had active acromegaly who have increased IGF-1 levels according to age and sex with or without increased GH levels. All the patients were previously treated by surgery and/or somatostatin analogs. All the patients had underwent transsphenoidal surgery for adenoma removal and 8 of them received radiotherapy previously. Twenty-one patients were on octreotide-long acting release alone (dose change between 20 and 40 mg/mo) and 6 patients were on lanreotide autogel (dose changed between 90 and 120 mg/mo) and 3 patients were on lanreotide autogel (90 mg/mo) plus pegvisomgmant (20 mg/d) at the time of basal evaluation. Eighteen of the acromegaly patients have diabetes mellitus type 2. All of them had controlled with oral antidiabetic drugs. None of the acromegalic patients previously used treatments and medication that modify skin flora. All the patients have normal immune system and normal white blood cell counts in hemogram test.

Nasal and Axillar Culture Taking and Culture Study Method

Different skin sites have different levels of temporal variability. Partially occluded sites, such as the axillar and inguinal areas, had more stable bacterial communities over time, whereas dryer and more exposed skin sites, such as the palm, had higher diversity and more temporal fluctuation.[12] Nasal and axillar cultures were obtained.

All the samples were obtained by the same physician by using a regular cotton swab method. Axillar and nasal specimens from anterior nares of the individuals were taken using sterile cotton swab that was moistened with sterile buffered transport medium (composed of 0.075 mol/L phosphate buffer, pH 7.9; 0.1% polysorbate 80; 0.1% sodium thiosulfate; and 0.3% lecithin), and a quarter-sized area was swabbed in a circular motion, with approximately the same pressure applied when a pencil eraser is used. Each swab was placed in a vial containing 2.0 mL of the transport medium and was plated within 2 hours. Samples were diluted 10-fold with the transport medium and were spread plated onto 5% sheep blood agar and eosin–methilen blue media for isolation of gram-negative rods. Cultures were incubated at 35°C for 24 and 48 hours. Bacteria were identified by means of standard laboratory identification methods.[13] Biological isolates were identified using API (bioM é rieuxsa, Marcy l ' Etoile, France).

Patients' and control' age, sex, clinical presentation, white blood cell and neutrophil counts, hemoglobin levels, GH and IGF-1 levels were recorded.

Statistical Analysis

SPPS 16 (Chicago, IL) packet program was used for statistical analysis. Student t test was used for continuous data, χ^2 test or Fisher exact test was used for categorical data. All statistical analysis were 2-tailed and considered significant at $P<0.05$ (Tables 1 and 2).

RESULTS

Demographic characteristic of patients and controls is shown in Table 1. The mean ages, the sex distribution, height, and weight of the patients and control were found to be similar (Table 1). Acromegalic patients have higher basal GH, IGF-1, fasting glucose, and Hba1c levels than control groups ($P<0.05$). Nasal colony counts and axilla colony counts of patients and controls were found to be similar (Table 2). Nasal carriage of staphylococcus aureus was 13.3% in acromegalic patients, but 43.4% in control group. This differences was statistically significant ($P=0.004$) (Table 2). Patients and control group were compared according to axillar and nasal cultures, we determined Proteus colonization 16.7% in patients with acromegaly but no Proteus colonization in control group (Table 2). This result was statistically significant ($P=0.001$). The culture results of patients and control groups are shown in Table 3. There was no correlation between Staphylococcus aureus carriage and age, sex, height, weight, disease duration, fasting glucose, creatinin, IGF-1 level, GH level in patients with acromegaly. There was no correlation between Proteus colonization and age, sex, height, weight, disease duration, fasting glucose, IGF-1

TABLE 1. Demographic and Clinical Characteristics of Acromegalic Patients and Controls

	Patients (n = 30)	Controls (n = 60)	P
Age (yr)	43.06 ± 15.21	44.01 ± 13.38	>0.05
Sex (male/female)	11 (36.7%)/ 19 (63.3%)	23 (38.3%), 37 (61.7%)	>0.05
Duration of disease (yr)	6.05 ± 11.04	—	
Radiotherapy therapy (n, %)	8 (26.7%)	—	
Medical treatment (n)		—	
Ocreotide long acting release	21		
Lanreotide autogel	6		
Lanreotide autogel plus pegvisomgmant	3		
Height (cm)	167 ± 14.21	168.4 ± 12.87	>0.05
Weight (kg)	84 ± 23.32	85.6 ± 24.81	>0.05
Fasting glucose (mg/dL)	113 ± 42.56	81.4 ± 11.19	<0.001
HbA1c (%)	6.22 ± 0.42	4.91 ± 056	0.021
Creatinin (mg/dL)	0.64 ± 0.36	0.69 ± 0.28	>0.05
IGF-1	673 ± 442.34	184 ± 32.56	<0.001
GH	23 ± 17.34	0.03 ± 0.05	<0.001

GH, growth hormone; IGF-1, insulin-like growth factor 1.

TABLE 2. Comparison of Acromegalic Patients' and Control Groups' Culture Results

Variable	Patients (n = 30)	Controls (n = 60)	P
Staphylococcus aureus nasal colonization	4/30 (13.3%)	26/60 (43.3%)	0.004
Proteus spp. colonization	5/30 (16.7%)	0/60 (0%)	0.001
Nasal colony count (CFU/mL)	44,300	41,400	0.609
Axilla colony count (CFU/mL)	54,600	44,800	0.137

CFU, colony forming units.

TABLE 3. Bacterial Components of Nasal and Axillar Cultures of Acromegalic Patients and Controls

	Patients	Controls
Nasal colonization		
Staphylococcus epidermidis	20	34
Staphylococcus aureus	4	22
S. aureus + S. epidermidis	—	4
Proteus spp.	4	—
S. epidermidis+micrococcus	1	—
Corynabacterium spp.	1	—
Axillar colonization		
S. epidermidis	27	58
S. aureus	—	2
Proteus spp.	2	—
Corynabacterium spp	1	—

level, GH level in patients with acromegaly. But Proteus colonization was negatively correlated with disease duration in acromegalic patients ($P = 0.017$). Disease duration was 2.2 years in acromegalic patients with Proteus colonization but 6.5 years in acromegalic patients with no colonization.

DISCUSSION

The present study has shown that axillar and nasal flora consist of Proteus spp in patients with acromegaly different from normal population. But nasal carriage of Staphylococcus aureus was lower in acromegalic patients than control group.

The presence of the GH receptor in human skin suggests a direct effect of GH,[14] but the exact mechanism by which GH exerts its effect is unknown. However, studies have shown an abundance of IGF-I receptor mRNA in human skin biopsies,[15] which could suggest an IGF-I-mediated action on skin. Elevated GH and IGF-1 in patients with acromegaly changes skin physiology and environment. These changes consist of increased sebum secretion, decreased transepidermal water loss, alkali, and hypothermic skin surface.[3]

Normal skin flora and nasal area consist of Acinetobacter, Firmicutes, Proteobacteria, and Bacteriodes.[16] The flora at these 2 sites is similar qualitatively but may differ quantitatively. Organisms generally considered commensals include coagulase-negative Staphylococci, nonhemolytic and viridans Streptococci, Corynebacterium spp, micrococci, saprophytic Neisseria spp, Haemophilus spp, and a wide range of anaerobes including Propionibacterium, Lactobacillus, Peptostreptococcus, and Veillonella. Other organisms commonly found at these sites but often thought of as pathogens include Staphylococcus aureus, Fusobacterium, Bacteroides, Prevotella, Porphyromonas, and Actinomyces spp.

The present study demonstrated that skin flora in patient with acromegaly consists of Staphylococcus epidermidis, Staphylococcus aureus, Proteus spp, Corynabacterium spp. But in control group skin flora was not consisted of Proteus spp. Gram-negative facultative organisms such as *Escherichia coli*, Proteus and environmental organisms such as Pseudomonas spp are not generally part of the normal flora at these sites in healthy individuals. These differences may be due to functional and environmental skin changes in acromegalic patients. Normally, very little water is present on the skin surface and skin forms an acid mantle with a ph of 5 to 6. Colonization with organism sensitive to desiccation, such as gram-negative bacilli is not favored. But acromegaly associated with increased sebum secretion, decreased transepidermal water loss, more alkaline, and colder skin surface.[3] Skin colonization by proteus in patients with acromegaly may be due to increased skin ph in acromegaly.

Nasal carriage of Staphylococcus aureus in healthy population estimated that 20% are persistent carriers and an additional 30% intermittent carriers, while approximately 50% are noncarriers. But in our study we demonstrated that nasal carriage of Staphylococcus aureus in patients with acromegaly (13.3%) was lower than in control group (43.4%). In carriers, Staphylococcus aureus predominantly colonizes the moist squamous epithelium on the septum adjacent to the nasal ostium.[17] This region is devoid of cilia and subepithelial glands, and thus its protection is mostly derived from the overlying fluid and innate factors from epithelia.[18] The innate immune system, which consists of physiological barriers, pathogen recognition receptors, humoral effectors and innate immune cells, plays a principal role in the elimination of these colonizing pathogens.[19,20] The nasal mucosa can also respond directly to bacterial challenge through the elaboration of cationic polypeptides, which are responsible for the majority of antibacterial activity of nasal fluid.[21] The quantitatively most abundant antimicrobial polypeptides, lysozyme, lactoferrin, and secretory leukoprotease inhibitor contribute to this activity, although certain aureus strains are reportedly resistant to both lysozyme and lactoferrin.[22] Acromegalic patients have a very high incidence of polyp formation and mucosal hypertrophy within nasal mucosa.[23] Different anatomic localizations and texture of the skin differ in bacterial concentrations. Dry skin leads to a low level of colonization, whereas moist areas, such as skin folds and areas with more sebaceous glands, contain large amounts of bacteria.[24] Previous studies demonstrated that among active acromegalic patients, elevated IGF-1 levels and GH influence physiology and environment of skin and nasal mucosa.[3] The low percentage of nasal carriage of Staphylococcus aureus in patients with acromegaly may be due to secretory and anatomical changes within nasal mucosa. Previous study showed that preoperative nasal cavity cultures most frequently consist of Staphylococcus epidermidis and Corynebacterium species in patients with pituitary lesion.[25] In this study, the most common reason for a transsphenoidal operation was a pituitary adenoma, Rathke cyst, chordoma, meningioma, cholesterol granuloma, and giant cell tumor. In contrast to our study nasal carriage of Staphylococcus aureus was found to be 25% in patients with pituitary lesion. But in this study the etiology of pituitary adenomas was not clear. The most commonly reported indications for prophylactic antibiotics were prevention of meningitis and sinusitis .[26] But there is no evidence-based guidelines for preventing surgical site infections in trans-sphenoidal surgery.

CONCLUSIONS

We demonstrated that compared with healthy subjects, acromegalic patients had low percentage of nasal carriage of Staphylococcus aureus and more gram-negative basili in the axillar flora. These nasal and axillar flora changes should be considered for prophylactic antibiotics use before surgery and ampiric antibiotics use after surgery.

Study Limitation

The present study was only moderate size. Further prospective studies are necessary to determine the effect of low-percentage nasal carriage of Staphylococcus aureus and skin flora changes on the development of infection before and after trans-sphenoidal surgery in patients with acromegaly.

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