Cutaneous manifestations in hypothyroid patients

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Abstract

The aim of this study was to describe the most frequent manifestations in skin, mucosa, and its adnexa in hypothyroid patients, and to compare them to a control group. This is a case-control, prospective, observational, and analytic study of consecutive patients performed at the Dermatology, Endocrinology, and Internal Medicine Departments of the University Clinic "Reina Fabiola", (Córdoba, Argentine Republic) between September 2003 and December 2006. It included 135 hypothyroid patients (cases), and 135 patients without hypothyroidism (controls). The most frequent dermatologic manifestations found in our series, statistically significant in univariate analysis, were melasma, xeroderma, acne, and telogen effluvium. Most results obtained were similar to those described in published data (Dermatol Argent 2008;14(3):196-199).

Key words: *cutaneous manifestations, hypothyroidism.*

Introduction

Endocrine diseases may induce manifestations in skin, and its adnexa, that become relevant where they are the primary expression of a general disorder.[1] Like most systemic pathologies, hypothyroidism is expressed in multiple ways through the skin, and its adnexa.

Hypothyroidism is defined as the presence of insufficient levels of circulating thyroid hormone, or target cell resistance to the hormone activity.[2,3] It is classified as **congenital**, describing a newborn with reduction or, very rarely, absence of thyroid hormone production;[2,4,5] **primary**, caused by an intrinsic defect of the thyroid structure;[2,6] **secondary** to a hypothalamic insufficiency;[2] and **tertiary**, from insufficient secretion of hypothalamic thyrotropin releasing hormone (TRH).[2,6] The most frequent is the primary type, characterized by the presence of low free plasma T4 (thyroxin), below 0.8 ng/dl, and high TSH (thyrotropin), above 4.0 mIU/ml.[2,7,8] Where TSH values exceed 2.5 mIU/ml, we face a "subclinical" hypothyroidism, even though thyrotropin levels are normal.[7,8] According to the seriousness of this hormone deficit, the disease may appear with signs and symptoms of diverse extent.

It is one of the most prevalent pathologies of medical consultation, more frequent in women between 25 and 50 years of age. The most common cause of primary idiopathic hypothyroidism in the United States is the atrophic variant of Hashimoto thyroiditis.[9,10] In Argentina, no research work on its origin exists so far (reviewed in Medline, ProQuest, SciElo, and MdConsult databases).

Deficit of thyroid hormone causes changes in skin and its adnexa, and the most frequent are hyperkeratosis, xeroderma, diffuse hair loss, nail brittleness, tendency to pyodermitis, palm

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and sole keratoderma, yellowish color of the skin, wound-healing delay, and purpura.[9-12]

Objective

The purpose of this work is to describe the most frequent manifestations in skin, mucosa, and their adnexa in hypothyroid patients, and compare them with a control group.

Patients and methods

A case-control, prospective, observational, and analytical study was carried out in consecutive patients consulting the Dermatology, Endocrinology, and Internal Medicine Departments of the University Clinic "Reina Fabiola" (Cordoba, Argentina) during the period between September 2003, and December 2006. The same group of dermatologists, endocrinologists, and internists conducted the study. The population studied (American Caucasian adults' descendants of Spaniards and Italians, and in a lesser degree, the crossing of these with native Indians) belongs to the central area of the Argentine Republic, with temperate climate, 31° 25' 16.4" latitude south, and 439 meters altitude. Two groups were formed: one of cases, or study group (Group A) including all patients with primary and subclinical hypothyroidism at the time of consultation, and those with such diagnosis reached in these Departments. They were compared to a control group (Group B) of patients consulting for other non-dermatologic reasons, where hypothyroidism was ruled out clinically and by laboratory tests. Physicians from the Endocrinology and Internal Medicine Departments completed a standardized questionnaire both for hypothyroid patients and controls, and they referred these patients to the Dermatology Department for a dermatological clinical examination. One control for each case was included, selected randomly with similar age and gender.

All data were included in the Excel worksheet (Microsoft Office 2000®), and analyzed with SPSS 9.0 program for Windows Data Editor®. Analysis of variables was performed with dichotomic result tests; they were compared by Pearson's chi-square test (deemed significant as from 0.05); confidence interval (CI) was computed by Wilson's method for 95 percent; odds ratio (OR) was computed for each variable, and its appropriate 95 percent CI as relative risk estimate. Data is expressed in absolute (n) and relative (%) figures.

This work does not include cutaneous manifestations secondary to thyroid cancer, congenital, secondary or tertiary hypothyroidism, or dosage of anti-thyroid antibodies (Ab).

No assessment was made on the difference between patients with subclinical, and clinical hypothyroidism.

It should be noted that pathologies such as psoriasis, lichen, eczema, acrochordons, lentigines, and nevi evidenced and recorded at the physical examination, have not been included in this work because, although they are common in daily dermatologic practice, they are not related directly to hypothyroidism, and their occurrence frequency did not vary significantly compared to euthyroid patients.

Results

Total number of patients included in the study amounted to 270 (total n= 270) patients: Group A 135 (n=135), and Group B 135 (n=135). Both groups included 10/135 (7.41 percent) males (M) and 125/135 (92.59 percent) females (F) (**Table 1, and Figure 1**). Average age of Group A patients was 39.19 years, 41.80 years for M, and 38.98 years for F (**Table 2**). As regards Group B, average age was 39.96 years, 44.90 years for M, and 39.95 years for F (**Table 3**).

Group A patients showed: xeroderma 40/135 (29.63 percent), telogen effluvium 32/135 (23.70 percent), melasma 23/135 (17.04 percent), vitiligo 18/135 (13.33 percent), acne 14/135 (10.37 percent), nail brittleness 5/135 (3.70 percent), and keratoderma 3/135 (2.22 percent) (**Table 4**, and **Figure 2**). As re-

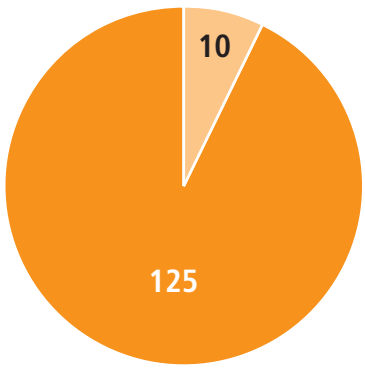

Figure 1. *Distribution by gender.*

TABLE 1. POPULATION DISTRIBUTION BY GENDER.

	n	%
Male	10	7.41
Female	125	92.59
Total	135	100

TABLE 2. AGE OF CASES (GROUP A).

	Average
Global age	39.19
Age M	41.80
Age F	38.98

TABLE 3. AGE OF CONTROLS (GROUP B).

	Average
Global age	39.96
Age M	44.9
Age F	39.95

TABLE 4. MOST FREQUENT CLINICAL MANIFESTATIONS IN GROUP A.

	n	%
Xeroderma	40	29.63
Telogen effluvium	32	23.70
Melasma	23	17.04
Vitiligo	18	13.33
Acne	14	10.37
Nail brittleness	5	3.70
Keratoderma	3	2,22

TABLE 5. CLINICAL MANIFESTATIONS IN GROUP B.

	n	%
No manifestations	73	54.07
Xerodermia	21	15.56
Telogen effluvium	19	14.07
Vitiligo	9	6.67
Nail brittleness	5	3.70
Melasma	5	3.70
Acne	3	2.22
Keratoderma	0	0

TABLE 6. UNIVARIATE STATISTICAL ANALYSIS

Pathology	Odds Ratio	CI95%	p
Xeroderma	2.29	1.26 to 4.14	0.005
Telogen effluvium	1.90	1.01 to 3.55	0.043
Melasma	5.34	1.97 to 14.51	0.0003
Vitiligo	2.15	0.93 to 4.98	0.067
Acne	5.09	1.43 to 18.15	0.005
Nail brittleness	1.00	0.28 to 3.54	[3] 0.999
Keratoderma	N/C	N/C	0.081

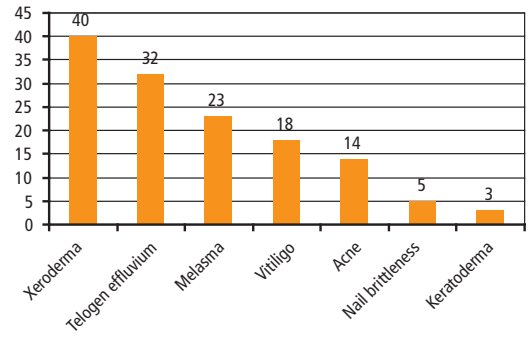

Figure 2. *Most frequent clinical manifestations of Group A..*

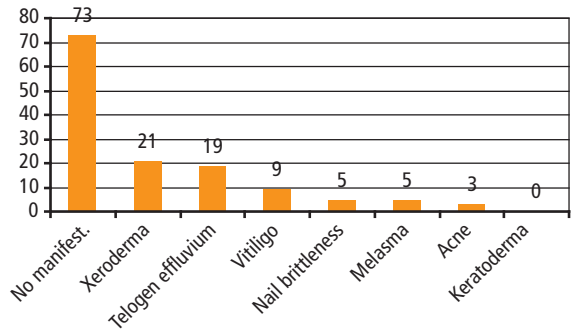

Figure 3. *Clinical manifestation of Group B.*

gards Group B, the findings were: no pathology 73/135 (54.07 percent), xeroderma 21/135 (15.56 percent), telogen effluvium 19/135 (14.07 percent), melasma 5/135 (3.70 percent), vitiligo 9/135 (6.67 percent), acne 3/135 (2.22 percent), nail brittleness 5/135 (3.70 percent), and keratoderma 0/135 (0.00 percent) (**Table 5** and **Figure 3**).

Results of the compared independent variables were as follows (**Table 6**):

1. Xeroderma showed OR 2.29 (95 percent CI: 1.26 to 4.14), p = 0.005.
2. Telogen effluvium showed OR 1.90 (95 percent CI: 1.01 to 3.55), p = 0.043.
3. Melasma showed OR 5.34 (95 percent CI: 1.97 to 14.51), p = 0.0003.
4. Vitiligo showed OR 2.15 (95 percent CI: 0.93 to 4.98), p = 0.067.
5. Acne showed OR 5.09 (95 percent CI: 1.43 to 18.15), p = 0.005.
6. Nail brittleness showed OR 1.00 (95 percent CI: 0.28 to 3.54), p = 0.999.
7. Keratoderma; no OR was computed due to diagnose test limitation, p = 0.081.

Discussion

As in the paper submitted by Ai J, Leonhardt JM, and Heymann W,[9] like most international papers,[10,11] our study reflects a clear dominance of female gender.

Publications by the Dermatology Department of UMDNJ - Robert Wood Johnson Medical School at Candem, in U.S.A.,[11] and the Dermatology Course, UBA School of Medicine Hospital "José María Ramos Mejía,"[13] describe the main cutaneous manifestations of this thyroid disease, which are similar to our results.

The most important findings, by order of frequency appearing in Group A, were: xeroderma, telogen effluvium, melasma, vitiligo, acne, nail brittleness, and keratoderma. Xerodermia, telogen effluvium, melasma, and acne showed significant differences compared to the control group, according to our experience; thus, they may be deemed dermatological manifestation markers of thyroid gland hypofunction, a result matching studies by Ai J et al.,[9] Leonhardt JM et al.[11] and Jabbour SA.[14]

Although vitiligo appears among the four most frequent variables, no significant differences appeared in comparison to Group B. According to world,[9,11] and national[13] report series, vitiligo is more common in relation to thyroid autoimmunity, associated or not with hypothyroidism. No dosage of anti-thy-

roid antibodies was performed, since it is beyond the scope of this study. These findings might be different if a sample with a greater number of patients was evaluated.

Nail brittleness appeared with a similar frequency in hypothyroid patients and in the control group; this differs with the paper published by Achembach, in Revista Argentina de Dermatología, where nail dystrophy was more frequent in hypothyroid patients.[13]

Finally, as regards keratoderma, since the number of cases with this manifestation was minimal, and it was not found in the controls, this constitutes a limitation for the analysis and comparison of both groups; therefore, it would be interesting to widen the sample in future studies.

Conclusion

Like most systemic diseases, hypothyroidism expresses itself in multiple ways through the skin and its adnexa. Therefore, we believe in the usefulness of performing certain local dermatologic studies that enable us to recognize the most frequent signs in our population, which may or may not be different from others, but will help us to reach an early diagnosis, even when changes are very subtle.

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