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Hashimoto's Thyroiditis Labial Capillary Microscopy

G.A. Scardina and P. Messina
Department of Oral Science, University of Palermo, Italy

Abstract: The aim of this study is to verify labial microcirculation differences among healthy subjects and those with Hashimoto'sthyroiditis. Fifteen healthy patients and 15 patients suffering from Hashimoto's thyroiditis were examined. Labial capillaroscopy was used to investigate the characteristics of microcirculation. For each patient we evaluated visibility, course, tortuosity and the possible presence of microhaemorrhages, average calibre of capillary loops and the number of visible capillary loops per square millimetre. The investigation of the labial mucous was simple, non invasive and repeatable for each patient. In Hashimoto'sthyroiditis patients it was possible to observe a wide vascular architectural disorganisation, morphologic anomalies of the capillary loops, loosening of the U shape, reduced capillary diameter. This study shows that capillary alterations in patients suffering from Hashimoto'sthyroiditis occur in the labial mucous microcirculation.

Key words: Oral capillaroscopy, hashimoto's thyroiditis

INTRODUCTION

Primary hypothyroidism, the most common form, is an autoimmune disease, usually occurring as a result of Hashimoto's thyroiditis and is associated often with a firm goiter or, later in the disease process, with a shrunken fibrotic thyroid gland with little or no function (Lorini *et al*., 2006; Okamoto *et al*., 2006).

The symptoms and signs of primary hypothyroidism are generally in striking contrast to those ofhyperthyroidism and may be quite subtle and insidious in onset. The facial expression is dull; the voice is hoarse and speek is slow; cold intollerance may be prominent; hair is sparse, coarse, and dry. Weight gain is modest and is largely the result of decreased metabolism of food and fluid retention. Patients are forgetful and show other evidence of intellectual impairment, with a gradual change in personality. Some appear depressed (Syrenicz *et al*., 2005; Volpe, 1981). There is often carotenemia, particularly notable on the palms and soles, cause by deposition of carotene in the lipid-rich epidermal layers. Deposition of proteinaceous ground substance in the tongue may produce macroglossia. The pericardial and pleural effusions develop slowly and only rarely result in respiratory or hemodynamic distress. The heart may be enlarged, partly because of dilatation but chiefly because of the accumulation of a serous effusion of high protein content in the pericardial sac (Lorini *et al*., 2006; Volpe, 1981). Paresthesias of the hands and feet are common, often due to carpal-tarsal tunnel syndrome caused by deposition of proteinaceous ground substance in the ligaments around the wrist and ankle, producing nerve compression. The reflexes may be very helpful diagnostically because of the brisk contraction and the slow relaxation time. Women with hypothyroidism often develop menorrhagia, in contrast to the hypomenorrhea of hyperthyroidism. Hypothermia is commonly noted. Anemia is often present, usually normocytic-normochorim and of unknown etiology, but it hypochromic owing to menorrhagia, and sometimes macrocytic because of associated pernicious anemia or decreased absorption of folic acid (Volpe, 1981).

The aim of this study is to observe labial microcirculation in patients suffering from Hashimoto's thyroiditis.

MATERIALS AND METHODS

Fifteen healthy subjects (5 males and 10 females; mean±SD age: 22.2+1.4 years; range: 18-35 years) and 15 patients with Hashimoto's thyroiditis (5 males and 10 females; mean±SD age: 22.8+1.7 years; range: 18-35 years) were examined in our laboratory.

Healthy subjects were included in the study only if the accurate exam of their medical history and the objective examination of their oral mucosa revealed that they were non smokers.

All subjects provided informed consent for the processing and use of their personal medical data in scientific papers, according to the Italian law.

Corresponding Author: G.A. Scardina, Department of Oral Science-University of Palermo, Italy

The patients were examined by computerised videomicroscopic techniques and related software (Videocap 200-DS medigroup MI).

The capillaroscopic investigation was carried out with the patients in a sitting position, with the same light source, at the same room temperature (23°C), in the morning, by the same operator and repeated twice for each examined area.

The examined area was always the same for each patient: - the fraenum area of the lower lip.

Two independent observers examined all the images. The intraobserver and interobserver variability was assessed with the two observers evaluating twice the same randomly selected images.

The following static parameters were used

Nonparametric data: Capillary loop visibility (score from 1 to 4): 1) simple focusing - within 30 seconds from the beginning of the examination; 2) average focusing- over 30 seconds and within 2 min; 3) difficult focusing- over 2 min; 4) impossible focusing; orientation regarding the surface (score A, B or AB): A) capillary loop course parallel to the surface; B) capillary loop course perpendicular to the surface; AB) both parallel and perpendicular; capillary tortuosity (score from 0 to 3): 0) absence of crossing in the capillary loops; 1) presence of crossing; 2) greater presence of crossing; 3) complete distortion of the capillary loops; microhaemorrhages (score 0 or 1): 0) absence; 1) presence; characteristics of the capillary loops (score 0 or 1): 0) absence; 1) presence.

Parametric data: Number of visible capillary loops in every square millimetre (value obtained from the average of the two observations for each examined area); capillary loop calibre (values obtained from the average of the two observations for each examined area).

All patients involved in the study kept a dietary diary for a period of three months, in order to evaluate any dietary differences possibly affecting the oral capillary pattern observed.

The statistical significance of the differences between healthy and Hashimoto's thyroiditis subjects was checked with the Student's t test for independent samples regarding parametric data and with the Mann-Whitney test (MW test) regarding nonparametric data. The level of significance was set to $p<0.05$. Data analysis was carried out with StatView 5.0.1 (SAS Institute Inc., Cary, NC).

The results obtained from each examined area represent the average values of the two observations.

RESULTS

Intrasubject variability satisfied the priori hypothesis of a limited dispersion. For the parametric data, variability ranged from +2% to –2% regarding the mean value. For the non-parametric data, 1 score point difference at most was observed.

No significant differences were detected between healthy and Hashimoto's thyroiditissubjects in age ($p>0.01$, MW test).

Labial microcirculation: The visibility of the microcirculation was simple in both patient and control group.

The microcirculation architecture in healthy subjects was characterised by a network of capillaries in polygonal mesh and a parallel orientation (type A) regarding the surface. The microcirculation architecture in Hashimoto's thyroiditis patients was characterised by an anarchical arrangement of the capillary major axis.

The tortuosity of the capillaries in healthy subjects showed a score = 0 in 10 patients; score = 1 in 5 patients. In patients with Hashimoto's thyroiditis, capillaries t ortuosity showed score=0 in 1 patient; score = 1 in 2 patients; score=2 in 2patients; score 3 in 10 patients ($p<.001$). Rare microhemorrhages (score = 1) were observed in 2 healthy patients. These were identified as reddish stains, that could have been caused by possible microtraumas. No microhemorrhages were observed in Hashimoto's thyroiditis patients.

The calibre of the visible capillary loops was17.84+2.7 μm (mean+SD) in healthy subjects and 6.8+1.4 μm (mean+SD) in patients with Hashimoto's thyroiditis ($p<.001$,MW test). The number of capillaries visible was 8.86+1.85 (mean+SD) in healthy subjects and 7.1+1.6 (mean+SD) in patients with Hashimoto's thyroiditis($p>.001$, MW test) Fig. 1-4.

No significant differences in the alimentary habits of patients were detected.

The results of the labial observations are summarisedin Table 1.

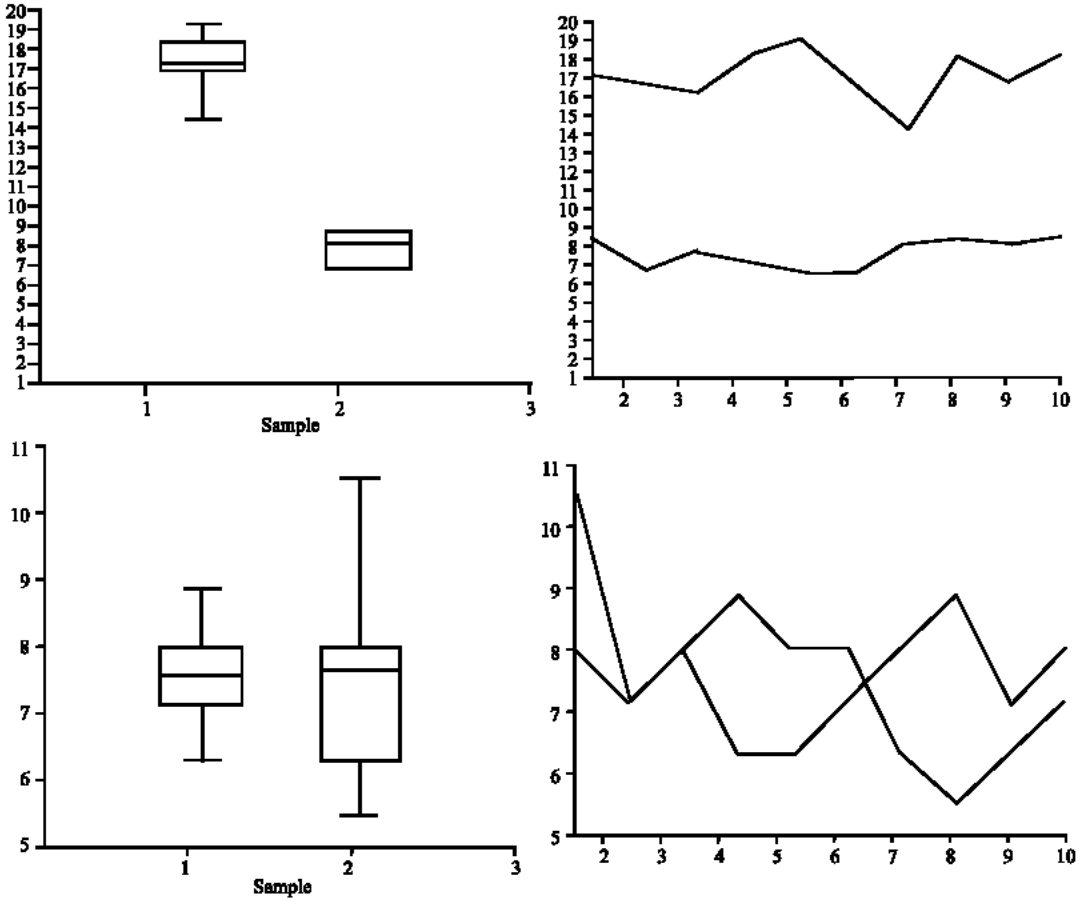

Fig. 1: Box Plot and graph: Differences were tested by Mann-Whitney U test. Calibre of the capillary loop (T = Ub 0; p = 0.0001827); Number of the capillary loop (T=Ub 49.5; p = 1)

Fig. 2: Labial microvascular characteristics in Hashimoto's thyroiditispatients (200X)

Fig. 3: Labial microvascular characteristics in Hashimoto's thyroiditispatients (200X)

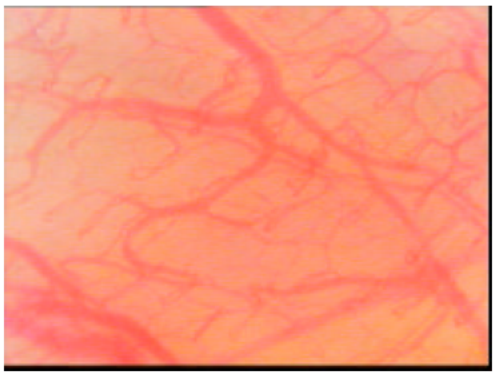

Fig. 4: Labial microvascular characteristics in healthy patients (200X)

Table 1: The characteristics of the microcirculation of labial mucous in healthy subjects and Hashimoto's thyroiditispatients

	Healthy subjects		Hashimoto'sthyroiditis patients	
	Score	Subjects	Score	Subjects
Visibility of the	1	190%	1	190%
capillary loops	2	10%	2	10%
Orientation regarding				
the surface	A	100%	A	100%
Tortuosity	0	10	0	1
	1	5	1	2
			2	2
			3	10
Microhemorraghes				
	1	2	0	100%
Calibre of the capillary loops				
(mean±SD) S	17.84±2.7 µm		6.8±1.4 µm	
N° mm^2				
(mean± SD)NS	8.86+1.85		7.1±1.6	

SD±Standard Deviation; Differences were tested by Mann-Whitney U test; S = significant; NS not significant

DISCUSSION

The authors observe *in vivo* the microvascular characteristics of the labial mucosa inHashimoto's thyroiditis patients.

The investigation method appear quite simple, immediate and permits the extrapolation of parametric and non-parametric data (Cantatore *et al*., 2000; Cinti *et al*., 1984; Curri, 1984; Del Guercio and Piovella, 1995; Grassi *et al*., 1984).

Capillaroscopy is a non-invasive diagnostic technique, fundamental in viewing peripheral circulation and in studying microangiopathies, which are the manifestations of numerous pathologies in both the diagnostic and monitoring phases of the disease.

Affected capillaries are characterized by distorted and irregular loops. The value of capillaroscopic investigation as a diagnostic means for peripheral microcirculation damage is confirmed by numerous studies. It must be mentioned, however, that other studies have used capillaroscopic investigation to evaluate microcirculation damage not as a complication of disease (diabetes), but as its beginning, and therefore for diagnosis (Haak *et al*., 1998; Halfom *et al*., 2003).

Our study shows that capillaroscopy is a reliable method for studying labial microcirculation. The advantages of oral mucous as a capillaroscopic examination area, result in a satisfying evaluation of microcirculation for the excellent mucous transparency, especially at the labial level; in an easily approachable exam area; in the lack of local mechanical or chemical microcirculation stimulation, and in a reduced susceptibility to the "cold stress" due to the contact of the mucous to the probe (Manler *et al*., 1987; Miniati *et al*., 2001; Scardina *et al*., 2004; Scardina and Messina, 2004). This study demonstrates that capillaroscopic alterations during Hashimoto's thyroiditisresult in the oral mucous peripheral circulation.

Labial capillaroscopy in patients with Hashimoto's thyroiditis revealed significant microvascular changes regarding the controls.

Labial capillaroscopic pattern in patients with Hashimoto's thyroiditis is recognisable by a direct evaluation and is characterised by:

- Wide architectural disorganisation;
- Loosening of the U shape capillaries with a high degree of heterogeneity in shapes characterised by reduced calibre.

This study shows that capillary alterations in patients suffering from Hashimoto's thyroiditis occur in the labial mucous microcirculation.

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