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The prevalence of hyper- and hypothyroidism in patients with ulcerative colitis

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Abstract

Background: The association between ulcerative colitis and thyroid disorders has been previously reported. However, most reports consist of single case description, and a systematic assessment of this relationship has only sporadically been investigated.
Aims: To study a cohort of patients with ulcerative colitis to establish the prevalence of hyper- and hypothyroidism.
Material and methods: During a four-year period, we studied thyroid function in 162 ulcerative colitis patients (62 men, 100 women, age range 18–78 years).
Results: Thyroid dysfunction was present in 4 patients (2.5%) of the overall population and was represented by both hypo- (3 patients) and hyperthyroidism (1 patient). The incidence of this kind of thyroid dysfunction was significantly ($p=0.03$) lower than that found in a large (more than 5000 subjects) control group.
Conclusions: We conclude that the prevalence of hyper-/hypothyroidism is relatively low in patients with ulcerative colitis, at least in our country, and does not justify a systematic investigation of the thyroid function, except in selected cases, probably those with scarce or no response to standard therapeutic measures.

1. Introduction

The association between ulcerative colitis (UC) and thyroid disease was firstly reported in 1968, with an emphasis on the increased therapeutic difficulties when thyroid abnormalities

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are not recognized.[1] Since then, several reports appeared in the literature, mostly describing single case reports or very small groups of patients,[2–6] and only two studies reported series including more than 10 subjects; one investigated 300 UC patients and the other reported on a mixed series of 31 UC and Crohn's disease patients.[7,8]

The purpose of the present study was to assess the prevalence of hyper- and hypothyroidism in a series of UC patients.

2. Materials and methods

Retrospective data of a five-year period (December 2002–December 2007) on one hundred sixty-two consecutive UC patients (62 men, 100 women, mean age 43 (range 18–78) years) were obtained. The disease was classified according to standard endoscopic and histological criteria.[9,10] Disease activity was defined as mild, moderate and severe according to Truelove and Witt's classification.[11]

Thyroid hormones (fT3, fT4, TSH) were assessed in all UC patients by immunochemiluminescent assay (Roche Diagnostics GmbH, Mannheim, Germany) and, only if hormonal alteration were present, further evaluation was carried out by assessing anti-thyroglobulin and anti-thyroperoxidase antibodies in hypothyroidism (immunochemiluminescent assay, Roche) and anti-TSH receptor (2nd generation TRAb assay TRAK human DYNOtest, BRAHMS Diagnostica GmbH, Berlin, Germany)[12] in hyperthyroidism.[13] These cases were also investigated with ultrasound and nuclear (scintigraphy) imaging.

Incidence data of thyroid dysfunction in UC patients was compared to that obtained in a group of 5721 subjects (1037 men, 4684 women, mean age 48 (range 20–75) years) undergoing a screening program for thyroid disorders with the above methods in the general population of the same geographic area in the period January 2003–December 2007.

3. Statistical analysis

Patients' and controls' data were compared by means of chi-square test with Yates' correction for continuity and Mann–Whitney *U* test, where appropriate. Values of $p<0.05$ were chosen for rejection of the null hypothesis.

4. Ethical considerations

After carefully explaining the aims of the investigation the patients gave informed consent, and the study was carried out in accordance with local ethical guidelines, following the recommendations of the Declaration of Helsinki (Edinburgh revision, 2000).

5. Results

Table 1 summarizes the disease characteristics of the UC study population. Thyroid disorders were present in 4 patients (2.5%) of the overall UC population and were represented by both hypo- and hyperthyroidism. A 60 year old woman had hyperthyroidism, diagnosed 1 year before the onset of UC. Thyroid function showed a marked increase of FT4 (25 ng/ml n.v. 7–12), inhibition of TSH (<0.01 U/L) and the presence of antibodies anti-TSH receptor. Ultrasonographic features and thyroid scintigraphy were consistent with Graves' disease. In this patient the clinical condition improved after the starting of methimazole therapy; however after 5 years of follow-up total colectomy was performed for the presence of severe dysplasia in the left colon. Thyroid function remained stable after surgery. In the other 3 patients (1 woman and 2 men, age range) autoimmune hypothyroidism with the presence of both anti-thyroglobulin and anti-microsomal antibodies was diagnosed. In two cases the diagnosis was made 1 and 10 years after the onset of ulcerative colitis. In these three patients a marked increase of TSH (15 mU/l n.v.0.7–5) and low blood value of FT4 (5 ng/ml n.v.8–19) was documented. Ultrasonography findings revealed a normal size of the thyroid gland with altered ultrasound pattern, suggesting an autoimmune thyroid process, whereas thyroid scintigraphy showed a decreased uptake of the radioisotope. All the three patients have been successfully treated by oral L-thyroxine therapy. None of these three patients had extraintestinal manifestations of UC.

Table 1 Disease characteristics of the UC study population

	UC patients (total)	Subgroup with UC and thyroid disease
	n	*n*
Total number	162	4
Age yr (range)	45 (18–78)	65 (55–77)
Women n	100	2
Duration of disease yr (range)	9 (2–15)	18 (12–26)
Location		
Proctitis	8	
Left-sided colitis	132	3
Extensive colitis	22	1
Surgery		1
Disease activity		
Severe	31 (15 women)	4
Moderate	82 (44 women)	
Mild	49 (41 women)	

As potential predictive factors associated with thyroid dysfunction we were able to identify a more advanced age ($p=0.009$), severity ($p=0.001$) and duration of the disease ($p<0.0001$) (Table 1), in that all four patients with thyroid dysfunction were also more than 55 years old, had severe UC, and the onset of disease was >10 years for each patient.

The incidence of thyroid dysfunction (both hypothyroidism, 360 subjects, and hyperthyroidism, 69 subjects) in the general population was 7.4% (429 out 5721 subjects, mean age 62 (range 54–71) years), significantly higher than that found in the patients' population cohort (chi-square 4.8, $p=0.027$, 95% CI 2.4–7.4).

6. Discussion

An increased prevalence of thyroid disorders (2–4 times higher than in the general population) has been previously reported in UC patients.[1] In subsequent studies on the topic (mostly case reports), both hypo- and hyperthyroidism were

present, and the incidence of thyrotoxicosis ranged from 0.82% to 3.7% in the only study in which more than 100 patients were recruited.[7] Thyroid disorders can often be present before the diagnosis of UC and can also modify the therapeutic response of the inflammatory bowel disease.[14] However, to date, thyroid disorders are not classified as extraintestinal manifestations of UC[15,16] especially because, in most cases, they precede for many years the clinical manifestations of UC.[7] On the other hand, well established extraintestinal manifestations of UC, such as arthritis or sclerosing cholangitis, are often diagnosed months or even years before the clinical onset of UC.[4,17]

Even though the possibility that the coexistence of thyroid disease and UC may be found by chance, a possible link between these two pathological conditions has been previously suggested.[18] In accordance to this view, a higher incidence of thyroid diseases in inflammatory bowel disease patients with colonic involvement (especially those with Crohn's disease) has been claimed.[15]

Inflamed colonic mucosa may be either the source of or a target for disease-producing factors, such as autoantibodies or circulating immune complexes.[18] An important contribution in favour of the concept of an autoimmune basis for UC is the observation that human tropomyosin isoform 5 (hTM5), a cytoplasmic protein mainly expressed in colonocytes, is a potential autoantigen associated with UC.[18–20] The precise role of these antibodies needs to be well defined; however, it is possible that their cross-reactivity with epidermis, biliary epithelium, and chondrocytes may help to explain the basis for some of the extraintestinal manifestations of UC.[18] In addition, hTM5 is capable of inducing T cellular immune response in many patient with UC.[19,20]

A Th1/Th2 imbalance in autoimmune thyroiditis and Graves' disease, resulting in Th2-type cytokine profile disease, has been similarly described in UC patients.[6,21] Therefore, the association of Hashimoto's thyroiditis and/or Graves' disease with UC is not surprising,[22] although it was not supported by the present study.

A further possible factor to be considered is the possibility of an increased occurrence of iodine deficiency in patients with chronic inflammatory bowel disease.[23]

We evaluated the occurrence of hyper- and hypothyroidism in a relatively large series of UC patients. Our results demonstrated a 2.5% prevalence in this population and a 7.4% prevalence in a control group from the general population in the same geographic area. The prevalence of thyroid dysfunction found in iodine-deficient communities in our country is 3.5%[24], and other studies showed a prevalence of 2%–8% in control subjects.[25,26]

The study of thyroid function should be considered in selected patients with UC, particularly in those with long-standing and severe disease and when there is scarce or no response to standard therapeutic approaches (since silent hyperthyroidism in UC has been reported[27]), or if there is the presence of clinical signs of thyroid disease.

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