

Hyperthyroidism in Association with Ulcerative Colitis: A Case Report

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Summary. This report describes a case of hyperthyroidism associated with ulcerative colitis (UC). A 47-year-old woman who received a subtotal colectomy for incurable UC was admitted to our hospital to undergo a pouch operation. On admission, palpitation, hypersweating, and a finger tremor were observed, and laboratory examination revealed increases of serum free T3 and free T4 along with the positive thyroid stimulating hormone (TSH) receptor antibody. A diagnosis of Graves' disease was confirmed, and after normalization of the thyroid function by potassium iodide and thiamazole, a remnant total colectomy and ileal pouch-anal anastomosis were performed. The postoperative course was uneventful and the patient is in good condition two years on, showing no symptoms of hyperthyroidism. Association of UC and hyperthyroidism is rare; however, the perioperative condition of a patient with UC might deteriorate without the proper management of hyperthyroidism. Thus, surgeons must be alert to the possible coexistence.

Key words—ulcerative colitis, extraintestinal complication, hyperthyroidism.

INTRODUCTION

It is well known that autoimmune thyroid diseases such as chronic thyroiditis are an extraintestinal complication

of ulcerative colitis (UC). However, hyperthyroidism in association with UC is very rare, with the incidence of hyperthyroidism with UC reported to be 0.82%¹⁾ to 3.7%²⁾. Here we report a case of Graves' disease diagnosed with symptoms such as palpitation on admission for a pouch operation after a subtotal colectomy for incurable UC, with improvement after a remnant total colectomy.

CASE REPORT

A 47-year-old woman was admitted to our hospital to undergo a pouch operation for UC. At age 42, she presented watery diarrhea, and a diagnosis of UC was made. She was put on treatment with 5-aminosalicylic acid and steroid. However, because of the progression of UC in spite of conventional medication therapy, at age 43 she underwent a subtotal colectomy (Fig.1) and construction of an ascending colostomy and rectosigmoid mucous fistula. She had been waiting for the pouch operation for about 42 months because of severe back-wash ileitis. On this admission, palpitation, hypersweating, and a finger tremor were observed; however, exophthalmos and swelling of the thyroid gland were not. The patient had a regular pulse rate of 120 beats per minute and a blood pressure of 148/80 mmHg. Serum free T3 and free T4 were 21.6 pg/ml (NV 2.1-3.8) and 6.3 ng/dl (NV 0.9-1.6), respectively. Thyroid stimulating hormone (TSH) was less than 0.03 μ IU/ml (NV 0.6-4.1), and the anti-thyroglobulin antibody (anti-Tg-Ab), anti-thyroperoxidase antibody (anti-TPO-Ab), TSH-receptor antibody (TRAb), and

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Abbreviations—anti-Tg-Ab, anti-thyroglobulin antibody; anti-TPO-Ab, anti-thyroperoxidase antibody; TRAb, TSH-receptor antibody; TSA, thyroid-stimulating antibody; TSH, thyroid stimulating hormone; UC, ulcerative colitis.

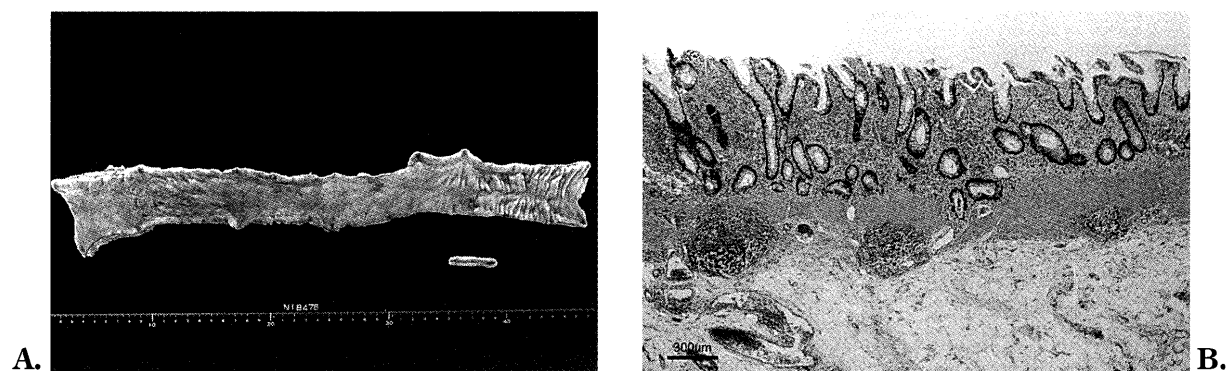


Fig 1. Surgical specimen at the first operation. **A.** The resected colon showing a granular pattern of the mucosa, reduction of the haustral pattern, and a longitudinal ulcer. **B.** Histological examination showing inflammatory infiltration and glandular distortion (HE $\times 4$).

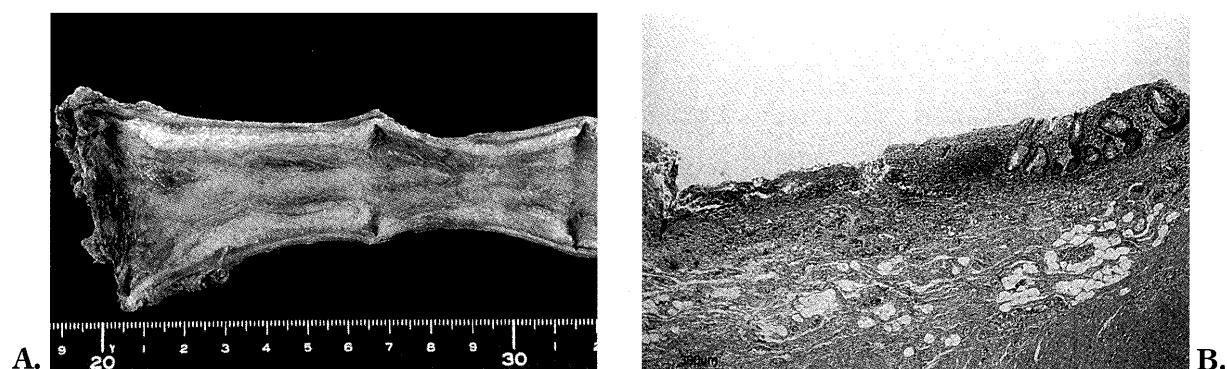


Fig 2. Surgical specimen at the second operation. **A.** The resected rectum again shows a granular pattern of the mucosa and a reduction of the haustral pattern. **B.** Histological findings showing active UC with cellular infiltration and the derangement of glands. (HE $\times 4$).

thyroid-stimulating antibody (TSAb) were all positive (Table 1). These results suggested Graves' disease in association with UC. After normalization of the thyroid function by potassium iodide and thiamazole, a remnant total colectomy, mucosal proctectomy, and ileal pouch-anal anastomosis were performed (Fig.2). The patient was placed on only thiamazole after the surgery, and four months later, her serum free T3, free T4, and TRAb were 1.8 pg/ml, 0.3 ng/dl and 8.6%, respectively. With the diagnosis of hypothyroidism, levothyroxine sodium per os was introduced while the oral administration of thiamazole was continued. The patient continues in good condition two years on, showing no symptoms of hyperthyroidism; her serum free T3, free T4 and TRAb are 2.0 pg/ml, 1.2 ng/dl and 3.3%, respectively, under the oral administration of thiamazole (5 mg. daily).

DISCUSSION

Several reports have addressed the relationship between UC and Graves' disease¹⁻⁵. However, it has not been clarified whether or not Graves' disease is an extraintestinal complication of UC.

Some investigators have suggested that Graves' disease is an extraintestinal complication of UC because of the common immunological etiology of the two diseases^{1, 3-5}. The pathogenesis of both UC and Graves' disease is assumed to involve the autoimmune process. Das et al. reported that patients with active UC have autoantibodies against a 40,000-molecular weight colonic protein -- p40 -- which belongs to the tropomyosin family⁶, and that the cross-reactivity of this antibody with multiple organs⁷⁻⁹ may explain the extraintestinal manifestations of UC. These autoantibodies may also react with the thyroid gland and lead to Graves' disease.

Table 1. Laboratory data on admission

WBC 6,870/ μ l	Total protein 6.6 g/dl	TSH <0.03 μ IU/ml
RBC 523 $\times 10^4$ / μ l	Albumin 3.9 g/dl	F-T3 21.6 pg/ml
Hb 14.8 g/dl	ALT 16IU/l	F-T4 6.3 ng/dl
Ht 43.0%	AST 21IU/l	anti-Tg-Ab 0.8 IU/ml
Platelet 29.3 $\times 10^4$ / μ l	LDH 143IU/l	anti-TPO-Ab 39.9 IU/ml
	ALP 644IU/l	TRAb 57.4%
ESR 8 mm/h	T-Bil 0.8 mg/dl	TSAb 661%
CRP <0.1 mg/dl	Creatinine 0.3 mg/dl	
	Na 138 mEq/l	
	K 3.8 mEq/l	
	Cl 103 mEq/l	

Table 2. Cases with coexisting hyperthyroidism and UC in the Japanese literature

Case	Age	Sex	Order of occurrence		Interval	Author
			First	Second		
1	61	F	UC	HT	7M	Oshitani(1981) ¹⁴⁾
2	46	M	HT	UC	10Y	Ito(1984) ¹⁵⁾
3	66	F	HT	UC	20Y	Chiba(1985) ¹⁶⁾
4	41	F	Simultaneous		0	Hasegawa(1990) ¹⁷⁾
5	50	M	HT	UC	4Y	Nakamura(1993) ¹⁸⁾
6	30	F	HT	UC	2Y	Okai(1999) ¹⁹⁾
7	26	M	UC	HT	12Y	Nishimura(2001) ⁴⁾
8	26	M	UC	HT	2Y	Tomonaga(2001) ²⁰⁾
9	35	F	HT	UC	4Y	Terashima(2001) ²¹⁾
10	47	F	UC	HT	5Y	Our case(2005)

HT, hyperthyroidism; UC, ulcerative colitis.

One of the etiologies suggested for UC and Graves' disease is an imbalance of Th1 and Th2^{10,11)}. UC has been considered a Th2-type autoimmune disease, and these factors may lead to an increase in autoantibodies against the TSH receptor (TSHR), resulting in hyperthyroidism. Bacterial infection also seems to be an essential factor in many autoimmune diseases. Microorganisms such as colonic flora may provide cross-reactive determinants by molecular mimicry, which has been implicated in various human autoimmune diseases involving specific organs¹²⁾. Corapcioglu et al. reported that a *Yersinia enterocolitica* infection may play a role in the etiology of Graves' disease¹³⁾.

On the other hand, some investigators have speculated that Graves' disease is only an incidental disease and not an extraintestinal complication of UC because, in most patients, the onset of hyperthyroidism precedes the development of UC²⁾. Previously, 10 cases – including ours – of the coexistence of hyperthyroidism and UC

have been reported in Japan (Table 2), and half of these cases suffered from hyperthyroidism before the development of UC. In our case, however, UC preceded the onset of hyperthyroidism, and hyperthyroidism improved after a total colectomy for UC under only the oral administration of thiamazol. These results suggest that Graves' disease is an extraintestinal complication of UC and that a successful total colectomy for UC might work towards the suppression of hyperthyroidism.

Management of a patient with UC associated with hyperthyroidism is difficult because hyperthyroidism tends to worsen the clinical features of ulcerative colitis and there is a high level of risk involved in surgery on a UC patient in thyrotoxicosis. In the present case, UC was successfully treated surgically after normalization of the thyroid function using potassium iodide and thiamazole.

In summary, when surgical management for UC is considered, the surgeon must be alert to the possibility of the coexistence of hyperthyroidism with UC.

REFERENCES

- 1) Triantafyllidis JK, Cherakakis P, Zervakakis A, Theodorou M: Coexistence of hyperthyroidism and ulcerative colitis: Report of 4 cases and a review of the literature. *Ital J Gastroenterol* **24**: 494-497, 1992.
- 2) Järnerot G, Azad Khan AK, Truelove SC: The thyroid in ulcerative colitis and Crohn's disease. II. Thyroid enlargement and hyperthyroidism in ulcerative colitis. *Acta Med Scand* **197**: 83-87, 1975.
- 3) Powell JR, Shapiro HA, Carbone JV: Therapeutic problems of ulcerative colitis with hyperthyroidism. *Am J Gastroenterol* **50**:116-124, 1968.
- 4) Nishimura M, Yamamoto T, Iijima H, Moriwaki Y, Takahashi S, Hada T: Basedow's disease and chronic ulcerative colitis: A case report and review of the Japanese literature. *Intern Med* **40**: 44-47, 2001.
- 5) Bonapace ES, Srinivasan R: Simultaneous occurrence of inflammatory bowel disease and thyroid disease. *Am J Gastroenterol* **96**:1925-1926, 2001.
- 6) Das KM, Dasgupta A, Mandal A, Geng X: Autoimmunity to cytoskeletal protein tropomyosin. A clue of the pathogenetic mechanism for ulcerative colitis. *J Immunol* **150**:2487-2493, 1993.
- 7) Das KM, Vecchi M, Sakamaki S: A shared and unique epitope(s) on human colon, skin, and biliary epithelium detected by a monoclonal antibody. *Gastroenterology* **98**:464-469, 1990.
- 8) Bhagat S, Das KM: A shared and unique peptide in the human colon, eye, and joint detected by a monoclonal antibody. *Gastroenterology* **107**:103-108, 1994.
- 9) Das KM, Prasad I, Garla S, Amenta PS: Detection of a shared colon epithelial epitope on Barrett epithelium by a novel monoclonal antibody. *Ann Intern Med* **120**: 753-756, 1994.
- 10) Podolsky DK: Inflammatory bowel disease. *N Engl J Med* **347**: 417-429, 2002.
- 11) Heuer M, Aust G, Ode-Hakim S, Scherbaum WA: Different cytokine mRNA profiles in Grave's disease, Hashimoto's thyroiditis, and nonautoimmune thyroid disorders determined by quantitative reverse transcriptase polymerase chain reaction (RT-PCR). *Thyroid* **6**: 97-106, 1996.
- 12) Das KM: Relationship of extraintestinal involvements in inflammatory bowel disease. New insights into autoimmune pathogenesis. *Dig Dis Sci* **44**: 1-13, 1999.
- 13) Corapcioglu D, Tonyukuk V, Kiyan M, Yilmaz AE, Emral R, Kamel N, Erdogan G: Relationship between thyroid autoimmunity and Yersinia enterocolitica antibodies. *Thyroid* **12**:613-617, 2002.
- 14) Oshitani H, Wakabayashi Y, Sawaguchi Y, Koike H, Yoshino Y: A case of dermatomyositis followed by multiple mononeuritis, with the history of ulcerative colitis and Basedow's disease. *J Kyorin Med Soc* **12**: 47-53, 1981. (in Japanese)
- 15) Ito M, Funauchi M, Fukuma N: A case of hyperthyroidism complicated with ulcerative colitis. *Saishin Igaku* **39**: 167-171, 1984. (in Japanese)
- 16) Chiba M, Naganuma T, Goto M: A case of ulcerative colitis complicated by anti-biotic-induced pseudomembranous colitis with reference to association of Basedow's disease. *Gastroenterol Endosc* **27**: 2797-2805, 1985. (in Japanese)
- 17) Hasegawa H, Hasegawa K, Saito T, Kowa H, Nonaka I: A case of myopathy with ulcerative colitis. *Clin Neurol* **30**: 184-188, 1990. (in Japanese)
- 18) Nakamura M, Okano K, Sekida N: A case of Basedow's disease complicated with refractory ulcerative colitis. *Folia Endocrinol* **69**: 804, 1993. (Abstract in Japanese)
- 19) Okai K, Machida K, Nishi M, Nanjo K: Complications of extraintestinal endocrine disease associated with ulcerative colitis-Association of ulcerative colitis and autoimmune thyroid disease. *Nippon Rinsho* **57**: 2536-2539, 1999. (in Japanese)
- 20) Tomonaga M, Nakamura K, Kinoshita H, Kajiyama H, Isomoto H, Omagari K, Mizuta Y, Murase K, Murata I, Kohno S: A case of ulcerative colitis associated with Graves' disease. *Jpn J Gastroenterol* **98**: 644-649, 2001. (in Japanese)
- 21) Terashima Y, Nishiwaki H, Suzuki T: A case of ulcerative colitis complicated with refractory Basedow's disease. *Hormone to Rinsho* **49**: 78-81, 2001. (in Japanese)