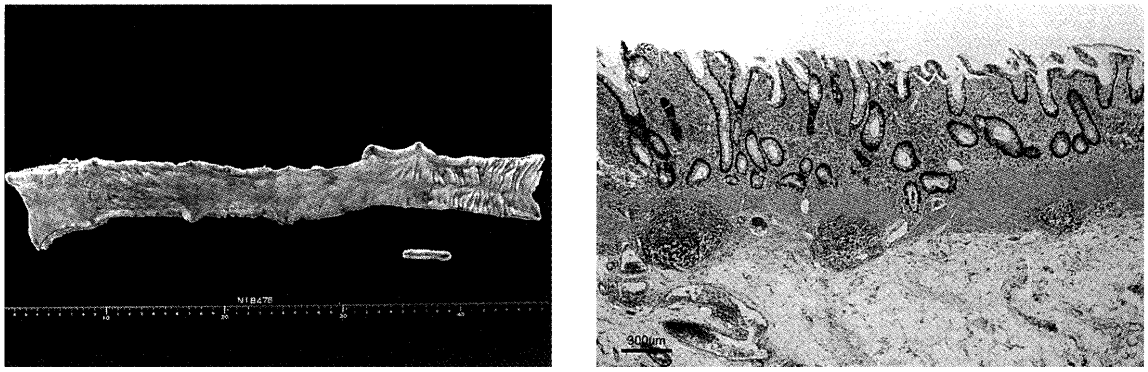

Fig 1. Surgical specimen at the first operation. **A.** The resected colon showing a granular pattern of the mucosa, reduction of the haustral pattern, and a longitudinal ulcer. **B.** Histological examination showing inflammatory infiltration and glandular distortion (HE ×4).

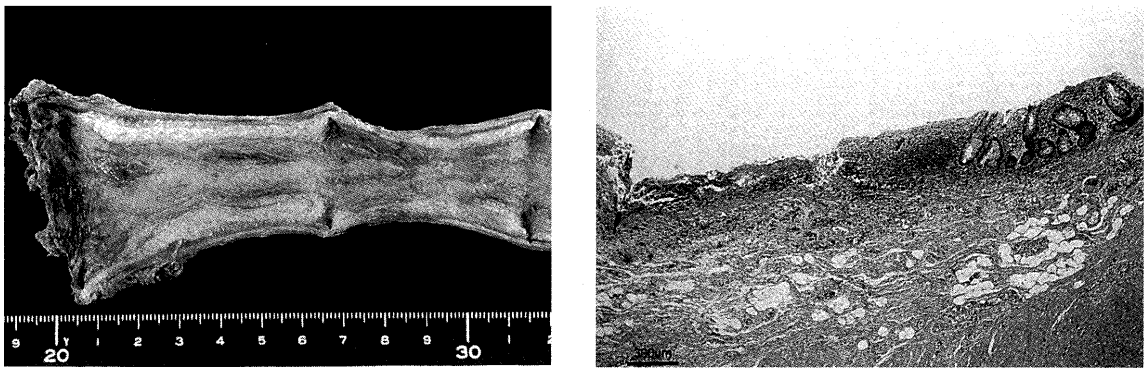

Fig 2. Surgical specimen at the second operation. **A.** The resected rectum again shows a granular pattern of the mucosa and a reduction of the haustral pattern. **B.** Histological findings showing active UC with cellular infiltration and the derangement of glands. (HE ×4).

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' disease[1-5]. 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 family[6], and that the cross-reactivity of this antibody with multiple organs[7-9] 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/μl	Total protein 6.6 g/dl	TSH <0.03 μIU/ml
RBC 523 × 10^4/μl	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 × 10^4/μl	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	Creatinine0.3 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 organs[12]. Corapcioglu et al. reported that a Yersinia enterocolitica infection may play a role in the etiology of Graves' disease[13].

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 UC[2]. 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.

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