HYPERTHYROIDISM AND ULCERATIVE COLITIS: REPORT OF TWO CASES AND A REVIEW OF THE LITERATURE

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Two cases of coexisting ulcerative colitis and hyperthyroidism are discussed. In both patients, thyrotoxicosis preceded the development of the ulcerative colitis. Exacerbations of the thyroid disease led to exacerbations of ulcerative colitis and consequent difficulty in the management of the patients. Although a review of the literature reveals a possible connection with abnormalities of iodine metabolism in the ulcerative colitis patient, no definite conclusions are drawn.

Coexisting ulcerative colitis and hyperthyroidism have not been discussed extensively in the literature. One report in 1968 noted an increased difficulty in controlling ulcerative colitis in a patient with an exacerbation of hyperthyroidism.[1] Three cases with associated thyroid disease, ulcerative colitis, and diabetes mellitus were reported in the Australian literature.[2] An in-depth study in Sweden revealed a history of thyrotoxicosis in patients with ulcerative colitis in 3.7 percent of 300 studied[3] and Edwards and Truelove[4] noted thyroid disease in 2.4 percent of 624 cases. The present report reviews two cases with associated hyperthyroidism and ulcerative colitis.

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CASE REPORTS

Case 1

A 46-year-old black woman entered Kings County Hospital with chief complaints of heat intolerance, palpitations, nervousness, diarrhea, and weight loss. Physical examination revealed exophthalmos, lid lag, and a 60-gm thyroid without bruit. The right lobe was larger than the left. The T_4 was 16.2 ng/ml and the T_3RU 44 percent. Thyroid scan showed a diffusely enlarged gland (Figure 1 left). Radioactive iodine uptake was 78 percent. The patient was begun on propylthiouracil and propranolol (Inderal) prior to discharge. She was maintained on propylthiouracil, 100 mg tid, and symptoms diminished over the next seven months. At that time the patient noted the onset of intermittent non-bloody diarrhea, quantitated as two to three bowel movements per day. She was seen in the gastrointestinal (GI) clinic where the following work-up was done: The SMA-12 was normal except for a slight elevation

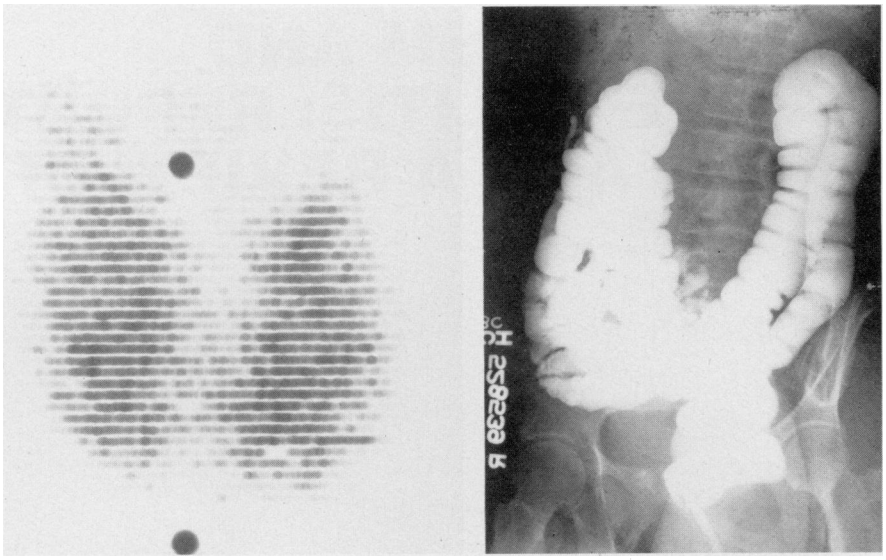

Figure 1. Thyroid scan of Case 1 showing enlarged gland and increased activity (left). Barium enema of Case 1 which is normal (right)

of the SGPT to 60; stools for culture and ova and parasites were negative; amebic titers were normal; HB_sAg was negative; and upper gastrointestinal series with small bowel follow-through and barium enema were normal (Figure 1 right). Sigmoidoscopy revealed friability and multiple severe ulcerations of the colon and biopsy revealed crypt abscesses and edema of the mucosa, consistent with ulcerative colitis. The patient was placed on sulfasalazine (Azulfidine) 500 mg qid with relief of symptoms.

The patient did well for one year and four months but then began noticing increasing palpitations and bowel movements. The thyroid measured 45 gm on physical examination. Sigmoidoscopy revealed friability and purulence up to 10 cm, but granularity with decreased friability was seen at 15 cm. The hematocrit level was stable at 36. The patient reported family problems at this time.

A repeat thyroid evaluation revealed TSH-l, T_4-10.5 ng/ml, T_4I-6.8, and I^{131} uptake-66 percent. Azulfidine was increased to 4 gm per day and propylthiouracil was continued at 300 mg qid. The bowel movements decreased to normal and symptoms cleared over several weeks. Her personal problems were resolved. Thyroid studies repeated were normal. The patient is currently maintaining her weight with her "normal" of two to three bowel movements per day on the same regimen. The WBC has been maintained at 5,700.

Case 2

This 18-year-old Hispanic male patient entered Kings County Hospital complaining of increasing prominence of his eyes, blurring of vision, increased dyspnea on exertion, palpitations, hand tremors, fatigue, and multiple daily bowel movements. He had been seen by a private physician several weeks before who started him on propylthiouracil but this was discontinued when the patient's WBC dropped to 2,100. The physical examination revealed exopthalmus, a diffusely enlarged thyroid of 100 gm with the right lobe greater than the left, a thyroid bruit, and fine hand tremors. Laboratory studies showed: hematocrit 39, WBC 5,900, 30 polymorphonuclear leukocytes, 58 lymphocytes, 6 monocytes, 6 eosinophils, and alkaline phosphatase 320. The remainder of the SMA-12 and SMA-6 was normal. T_4 was 13.3 and $T_4I=8.6$. Thyroid scan showed a diffusely enlarged gland with 71 percent uptake of I^{131} (Figure 2). A diagnosis of hyperthyroidism was made

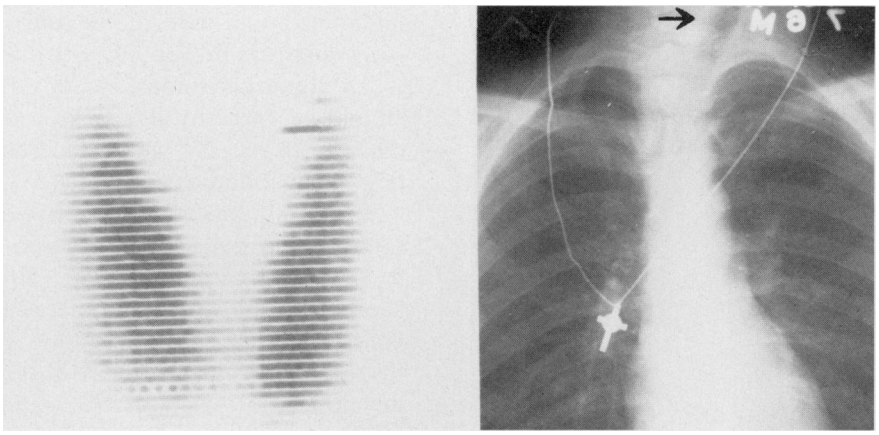

Figure 2. Thyroid scan of Case 2 showing enlarged gland and increased I^{131} uptake (left). Chest x-ray of Case 2 showing tracheal deviation from enlarged thyroid (arrow, right)

and the patient was discharged on Inderal 20 mg qid, propylthiouracil 100 mg qid, and phenobarbital 30 mg tid. The goiter decreased in size and after three months of therapy the T_4 fell to 9. Phenobarbital was discontinued and propylthiouracil was decreased to 300 mg qid. At this time the WBC was 4,400. Five months later the patient noted the onset of diarrhea described as seven to ten bowel movements per day with occasional blood and associated with diffuse abdominal pain. He was admitted to Kings County Hospital for further work-up. On admission the physical examination revealed a temperature of 99.4 F, a palpable thyroid without bruit, an unremarkable abdomen, and gross blood on rectal examination. Sigmoidoscopy revealed hyperemia with oozing of blood. Laboratory results showed: hematocrit 36, WBC 7,100 with 44 polymorphonuclear leukocytes, 6 bands, 36 lymphocytes, 14 eosinophils, and alkaline phosphatase 130 (decreased to a normal level of 85 while in the hospital). The remainder of the laboratory data were normal, including stool for culture, ova and parasites, and amebic titers. Barium enema revealed straightening of the descending colon with loss of haustral markings and ulcerations in the descending and transverse colon (Figure 3). The patient was initially placed on 5 gm Azulfidine daily but was decreased after one month to 2 gm per day. The patient had one mild exacerbation of his ulcerative colitis five months later which responded to an increase of Azulfidine to 4 gm per day. Five months after this, the patient was seen in the GI clinic where the hematocrit was 29 (previously 45), and the WBC, 10,000. The patient was complaining of abdominal cramps and said he had forgotten to take his Azulfidine for one week. Sigmoidoscopy revealed grossly hemmorhagic mucosa. A one-week trial with Azulfidine 4 gm per day and methylprednisolone sodium succinate (Solu-Medrol) enemas were not effective and the patient was admitted to the hospital where he was placed on prednisone 40 mg in addition to Azulfidine.

Colonoscopy showed diffuse involvement and biopsy revealed acute and chronic inflammation (Figure 4). Thyroid reevaluation was normal. The patient responded to treatment.

DISCUSSION

Little has been written about the coexistence of ulcerative colitis and hyperthyroidism. Powell[1] et al noted the apparent refractoriness to therapy in ulcerative colitis patients when thyroid disease was not diagnosed or inadequately treated. He did not postulate any connection between the two diseases. Diarrhea and steatorrhea have been documented in patients with hyperthyroidism but the pathological and laboratory abnormalities documented were in the small bowel.[5-8]

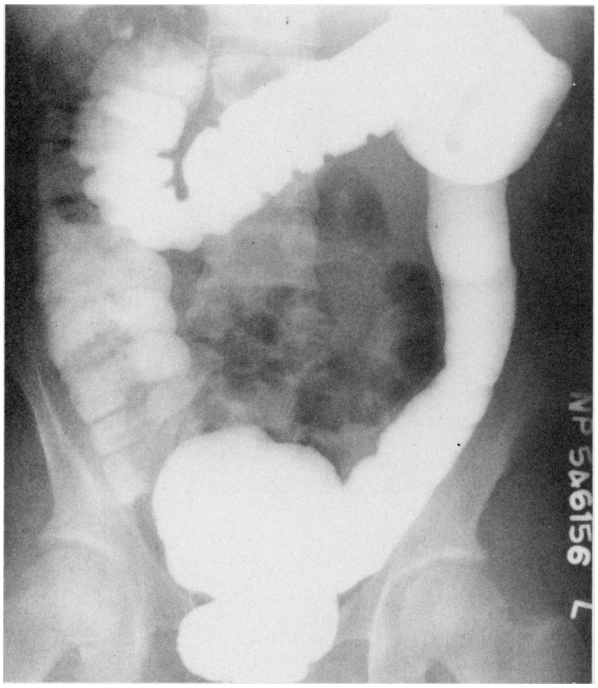

Figure 3. Barium enema of Case 2 revealing loss of haustrations and ulcerations in descending and transverse colon

Clubb[2] et al, in Australia, felt that the association of ulcerative colitis, thyroid disease, and diabetes mellitus in three young patients was sufficiently unusual to postulate a possible similar genetic etiology. Autoimmunity was also mentioned as a possible etiology, but tissue antibodies could not be documented in all their patients.

Jarnerot[3] has done the most extensive work in this area. He postulated an increased iodine deficiency in inflammatory bowel disease patients after noting decreased 24-hour urine iodine excretion and increased 24-hour I^{131} uptake as compared to controls. T_4 is protein bound and there is evidence that increased loss of albumin occurs in the gut lumen in inflammatory bowel disease.[9,10] Jarnerot[11] postulated this as a mode of iodine depletion in patients with this disorder. He also noted a lower level of thyroxine binding pre-albumin (TBPA) and albumin, and a higher thyroglobulin (TBG) in inflammatory bowel disease patients as compared to normal.[12] Thus, the increased I^{131} uptake, decreased urinary iodine excretion, and falsely elevated T_4 (bound to TBG, TBPA, and albumin) could incorrectly suggest hyperthyroidism in patients presenting with diarrhea and weight loss. Radioimmunoassay of thyroid hormone should be used for all cases of suspected thyroid disease, especially where ulcerative colitis might be a diagnostic possiblity.

In 300 patients with ulcerative colitis, Jarnerot[13] noted simple goiter in 6.3-8.7 percent as compared to 3.3-4.3 percent of controls. Thyrotoxicosis was seen in 3.7 percent as compared to 0.8 percent of controls. In greater than one half, the hyperthyroidism occurred before the ulcerative colitis developed (as seen in our patients). Jarnerot's work appears to show a relationship between thyroid function and inflammatory bowel disease but no clear-cut etiology is suggested.

There have been suggestions made as to the etiologies of each disease that are similar in both, eg, psychogenic, but while psychological stress seems to accompany exacerbations of both ulcerative colitis and hyperthyroidism, there is no proof that this is causal. An immune basis has been postulated in both diseases, either as a primary problem or as seen with other autoimmune disorders—but this also has not been proven.[14-21] A genetic etiology has been postulated for both conditions, and abnormalities in sera, such as an increased incidence of antinuclear antibody, have been seen in the relatives of ulcerative colitis patients, but no specific conclusions can be drawn from these observations.[22]

The two cases presented here correlate with the data presented; with exacerbations of thyroid disease, the ulcerative colitis became more difficult to manage. Thyroid disease preceded the development of the ulcerative colitis. In Case 1, there was an exacerbation of both thyroid symptomatology and ulcerative colitis with psychological stress, as reported in the literature.

The possibility of a relationship between these two diseases is interesting to consider, especially in view of Jarnerot's findings of palpable thyroids in patients with ulcerative colitis and Crohn disease even without active thyrotoxicosis. Exacerbations of ulcerative colitis may be a response to the hypermetabolic state resulting from elevated levels of thyroxine, or both diseases could be attributable to common, eg, autoimmune mediators. However, further studies are required to clarify the exact relationship between thyroid disease and inflammatory bowel disease.

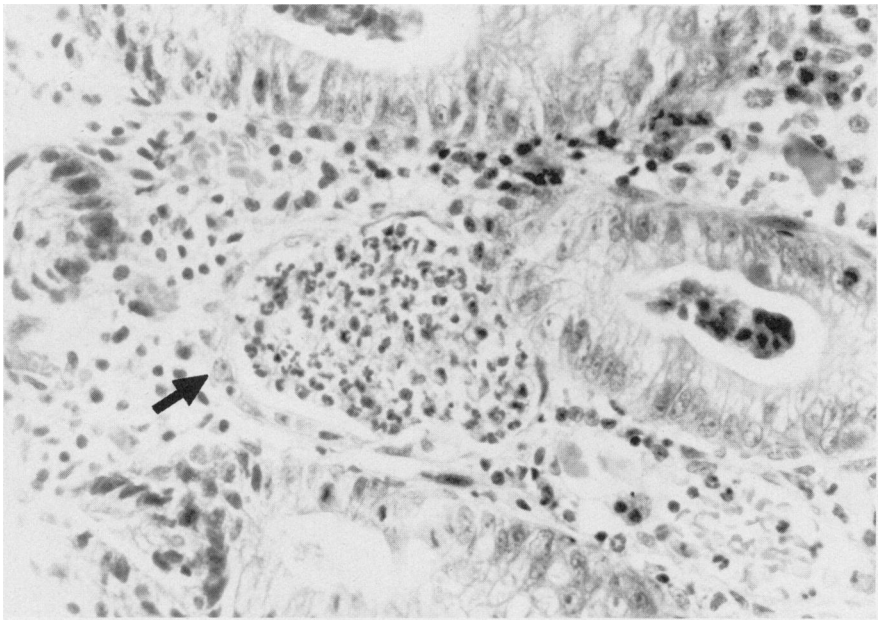

Figure 4. Colon biopsy of Case 2 revealing a crypt abscess (Arrow)

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