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Ulcerative colitis with autoimmune thyroid disease results in bilateral auricular ossificans : a case

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ABSTRACT

Background: Patients with ulcerative colitis (UC) often exhibit susceptibilities to multiple autoimmune diseases such as Sjogren's syndrome, primary sclerosing cholangitis, systemic lupus erythematosus, and insulin-dependent diabetes mellitus. This propensity likely stems from common pathogenic mechanisms underlying immune-mediated conditions. This report highlights the occurrence of autoimmune thyroid disease during UC exacerbations. Notably, the patient displayed petrified auricles.

Case Summary.

A 57-year-old male complained of sustained abdominal pain, diarrhea, hematochezia, and mucus for a duration of 20 days. The diagnosis of UC was confirmed via colonoscopy, histopathological examination, and small bowel MRE. Clinical evaluations revealed bilateral ectopic ossification in his ears, which appeared to develop over an unspecified timeframe. Imaging and histological evaluations substantiated the ectopic ossification diagnosis while eliminating the possibility of adrenal insufficiency. The presented case offers a unique instance of bilateral auricular ossification, which is hypothesized to result from hyperthyroidism.

Conclusion: Our case report underscores the necessity of enhancing awareness of the rare complications associated with UC. Medical practitioners should recognize the potential overlap of autoimmune thyroid disorders in UC patients. It is imperative to test for thyroid-related antibodies in such individuals, irrespective of overt thyroid dysfunction.

1. Introduction

The etiology of ulcerative colitis remains elusive, yet emerging research posits that individuals with a genetic predisposition might exhibit a dysregulated immune response to commensal gut bacteria, precipitating intestinal inflammation [1]. Existing studies corroborate that patients diagnosed with ulcerative colitis manifest a heightened predisposition to concurrent immune-mediated disorders, encompassing autoimmune hepatitis, autoimmune thyroiditis, primary biliary cholangitis, polymyalgia rheumatica, and temporal arteritis. This underscores a plausible epidemiological linkage among these ailments, perhaps attributable to a shared immunopathogenic mechanism. These conditions can either manifest in isolation or concur in a synergistic manner. The coexistence or sequential onset of multiple diseases might culminate in an overlapping syndrome.

The coexistence of ulcerative colitis (UC) with autoimmune thyroid disease (AITD) is relatively rare in clinical practice. Autoimmune thyroid diseases (AITD) encompass Graves' disease (GD) and Hashimoto's thyroiditis (HT), presenting clinically at two extremes: hyperthyroidism and hypothyroidism. AITD results from the interplay between multiple environmental factors, genetic predisposition, and epigenetic mechanisms. Immune dysfunctions leading to thyroid tissue damage involve B lymphocytes, T lymphocytes, and regulatory T cells [2].

The concurrent presentation of UC with GD or the thyrotoxic phase of Hashimoto's thyroiditis might exacerbate the incidence of diarrhea and result in pronounced cachexia in affected individuals. The concomitance of both UC and AITD is closely linked to cellular and humoral immunity, with cell-mediated immune processes playing a

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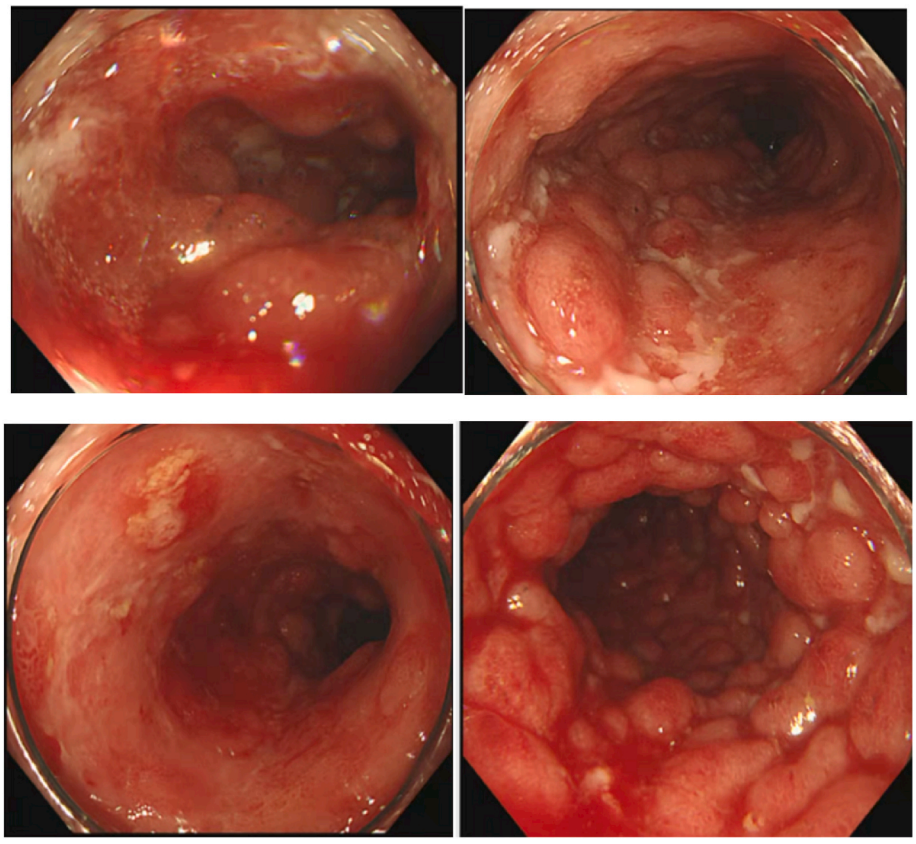

Fig. 1. Colonoscopic presentation of ulcerative colitis. Active phase of ulcerative colitis. Hyperemia, edema, erosion in the descending colon mucosa(A) (B). Inflammatory hyperplasia and ulcers in sigmoid colon, rectum(C) (D).

pivotal role in the pathogenesis. Lymphocytic infiltration of various glands can result in the loss of functional epithelial cells and subsequent scarring. In the diagnostic and therapeutic process, autoantibodies targeting both endocrine and non-endocrine tissues can aid in the diagnosis of autoimmune diseases and identify asymptomatic individuals at risk of developing other associated diseases [3].

2. Case presentation

2.1. Chief complaints

The patient was a 57-year-old man whose chief complaint was abdominal pain, diarrhea, and mucous blood stool for 20 days.

2.2. History of present illness

The patient developed mucous blood stool accompanied by abdominal pain and bowel ringing 20 days ago after working in paddy fields. He also had poor appetite, dry mouth, fatigue, weight loss of nearly 25 kg.

2.3. History of past illness

He had a history of hypertension for 2 years and he was taking 40 mg/day of telmisartan once a day. In addition, he was diagnosed with hyperthyroidism 20 years ago and took methimazole orally for 4 years. The medication was discontinued after the patient's thyroid function recovered, but the thyroidism was not reexamined.

2.4. Personal and family history

He did not abuse substances or alcohol. There was not any family history of disease.

2.5. Physical examination

The patient's vital signs were within normal range, with a body temperature of 36.2 °C, pulse rate of 78 beats per minute, breathing rate of 18 breaths per minute, and blood pressure of 101/57 mmHg. Physical examination revealed thin body habitus and blotchy pigmentation on the upper limbs. The patient exhibited palpable and moderately enlarged thyroid gland with hardened ears. Right abdominal tenderness was present without rebound pain or muscle tension, and bowel sounds were heard at a rate of 4 times per minute.

2.6. Laboratory examinations

The result of routine blood examination was as follows: WBC 2.81 $\times$ 10^9/L, RBC 3.62 $\times$ 10^{12}/L, HGB 99g/L, PLT 281 $\times$ 10^9/L, CRP 8.30mg/L, complement C1q (c1q) 83.70mg/L, We examined his thyroid work: free triiodothyronine (FT3):5.74pmol/L, FT4 32.4pmol/L, TSH $<$0.005, the thyroid globulin antibody (THGAB) was normal, Thyroid peroxidase antibody (TPOAB) $>$ 600IU/ml, Thyroid stimulating receptor antibody (TRAB) was 2.05IU/L.All virus series were negative, including rotavirus (stool), cytomegalovirus antibody IgM, herpes simplex virus antibody IgM, Epstein-Barr virus antibody IgM, hepatitis B and C virus. The antinuclear antibody was positive.

2.7. Imaging and pathologicalexaminations

The colonoscopy reveales hyperemia and edema in the descending colon mucosa, causing a narrow lumen. The endoscopic body located 50cm from the anus was unable to pass through. Additionally, endoscopic observation displayed hyperemia and edema of the colorectal

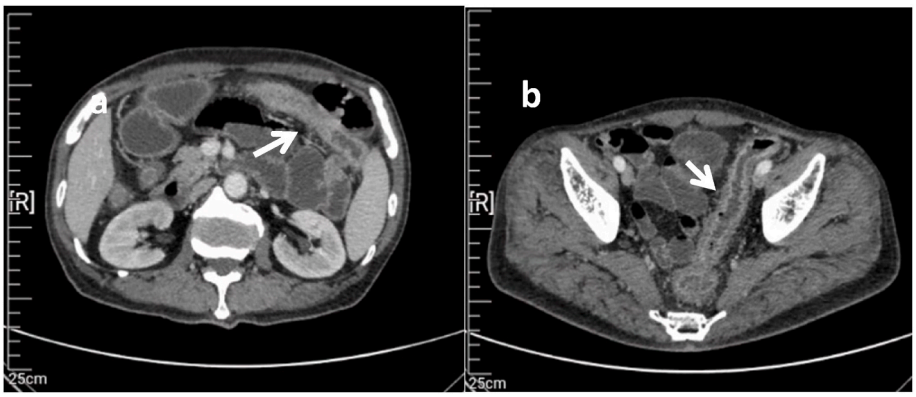

Fig. 2. Small intestinal CT enterography. A thickened stiff colon(A) (B).

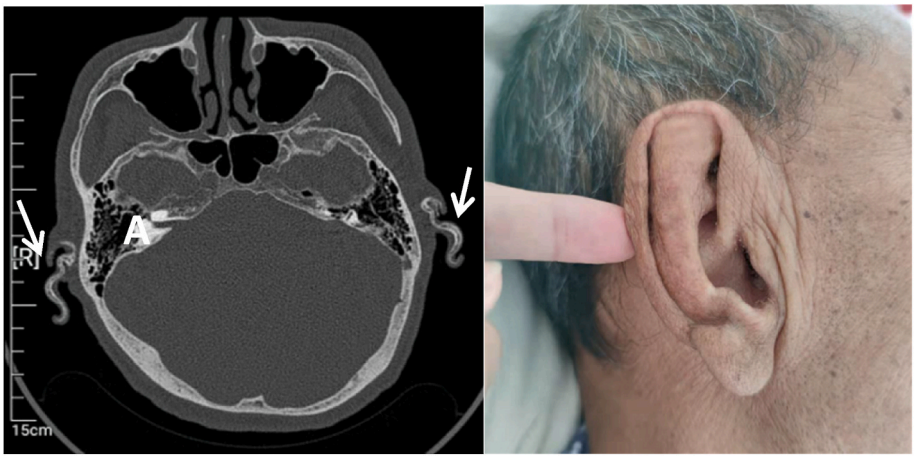

Fig. 3. a. Axial CT images demonstrate ossification along both auricles.
b.The ears are hard as stone against the skull.

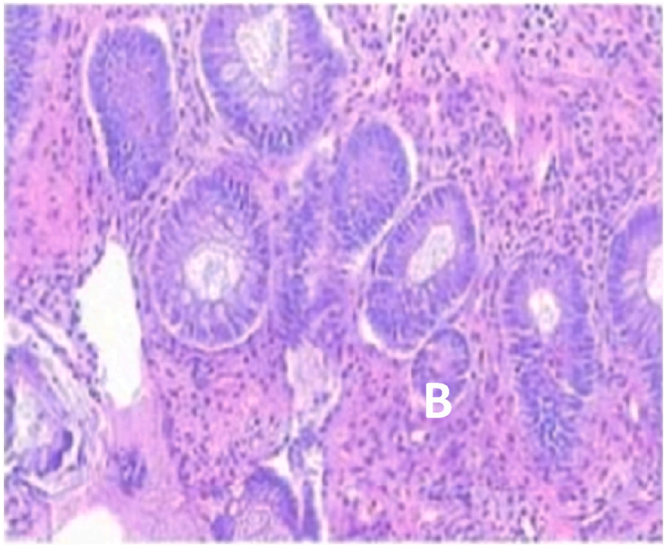

Fig. 4. Colonic mucosal pathology.

mucosa, with some areas exhibiting hyperplastic bulge. (Fig. 1).

Small intestinal CTE showes signs of colonic rigidity, slightly thick local tube wall, uneven enhancement, blurred serosal surface, and multiple fine vascular shadows around (Fig. 2).

Axial CT images demonstrate ossification along both auricles (Fig. 3).

A pathological examination of the colonic suggestes mucositis with erosion (Fig. 4).

Reexamination of the colonoscopy revealed the colonic pocket morphology disappeared, and the colorectal mucosa was scattered with congestion and erosion, and no active bleeding was observed (Fig. 5).

2.8. Diagnostic procedure

To aid in the pathological diagnosis, we sought assistance from Shengjing Hospital Affiliated to China Medical University. Additionally, we requested the endocrinology department's assistance in diagnosing thyroid disease.

2.9. Final diagnosis

After multidisciplinary consultation, the patient was diagnosed with: (1) Ulcerative colitis (extensive colonic type, severe, active stage) with a Mayo score of 11; (2) Autoimmune thyroid disease (hyperthyroidism); (3) Petrified pinna; (4)Hypertension.

2.10. Treatment

The patient was prescribed Mesalazine (2 g bid po) and infliximab (5 mg/kg via IV drip) to treat intestinal symptoms. After a week, the patient reported relief from symptoms of abdominal pain and hematochezia. Upon being discharged from the hospital, the patient was instructed to continue taking Mesalazine (2 g bid po) and to return to the hospital regularly for infliximab treatment at weeks 2 and 6, and then every 8

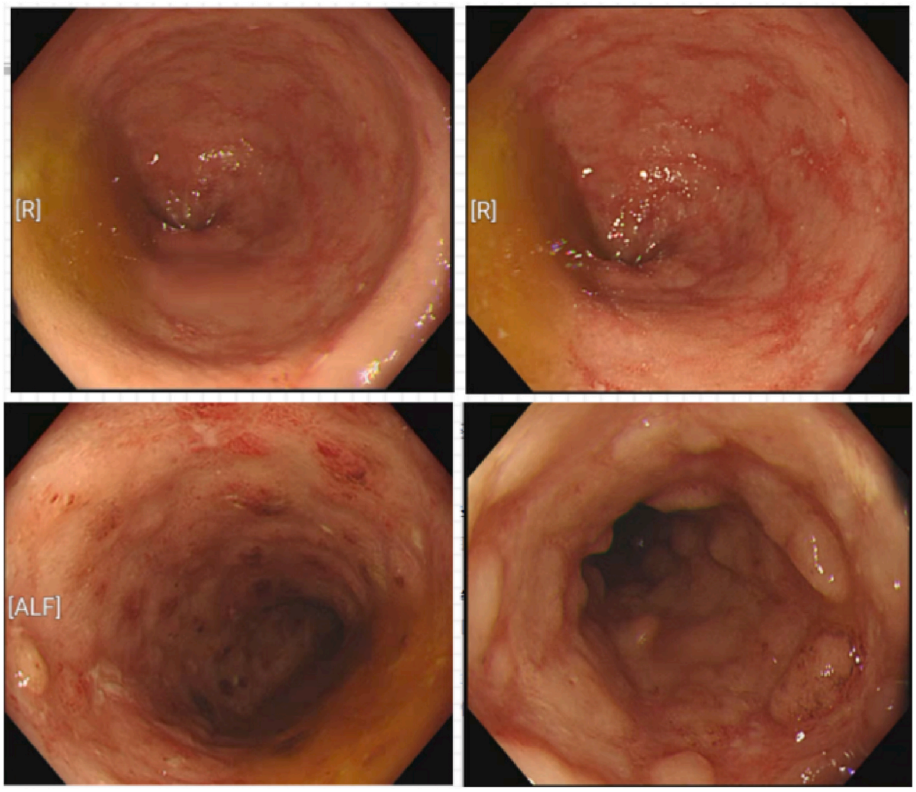

Fig. 5. Colonoscopic presentation of ulcerative colitis. Remission of ulcerative colitis.

weeks after the third treatment. Additionally, Methimazole (5 mg qd po) was given to treat the patient's hyperthyroidism.

2.11. Outcome and follow-up

According to the patient's self-report, his experienced relief from abdominal pain and hematochezia. Additionally, the number of stools decreased to 2–4 times per day and his appetite was restored. A subsequent review of the routine blood test showed that WBC 4.35 $\times$ 10^9/L, RBC 4.27 $\times$ 10^{12}/L, HGB 132g/L, PLT 231 $\times$ 10^9/L. His review of thyroid work:FT3 10.02pml/L, FT4 36.23pmol/L, TSH $<$0.005. As a result, the dosage of methimazole was increased to 7.5mg/day. Additionally, the patient experienced a weight gain of approximately 10kg. Upon re-examination through colonoscopy, no abnormalities were found in the distal ileum and the disease went into remission (Fig. 5).

3. Discussion

Herein, we report a case of a UC patient concomitantly diagnosed with autoimmune thyroid disease. Elevated FT4 levels, decreased TSH, and high titers of thyroid-associated antibodies (TPOAb and TRAb) indicated that the patient exhibited hyperthyroidism with an autoimmune underpinning. Additionally, the presence of the antinuclear antibody ANA further signified an aberration in autoimmune function. Following treatment with mesalazine, infliximab monoclonal antibody, and methimazole, the patient showed significant improvement in symptoms of diarrhea and hematochezia, along with notable weight gain.

According to a study [4], the prevalence rate of ulcerative colitis (UC) in patients with hyperthyroidism is 1.34 %. The first reported case of a patient with both hyperthyroidism and UC dates back to 1968 [5]. The patient was admitted to the hospital due to sudden bloody stools and was eventually diagnosed with UC after 10 months of treatment and follow-up. During the process of intestinal ulcer healing and recurrence, Vitolizumab was chosen as the treatment option. It is worth noting that the onset of hyperthyroidism can manifest as symptoms such as changes in bowel habits, persistent abdominal pain, and weight loss. These symptoms may overlap with those of ulcerative colitis. However, simultaneously managing both conditions can effectively alleviate the patient's bowel symptoms [6]. Furthermore, there are reports suggesting that autoimmune thyroid disease (AITD) may be associated with other organ-specific autoimmune attacks in the same patient [7,8]. In Graves' disease, there is an increase in Th2 activity, and the pathophysiology of UC is also related to the Th2 cytokine phenotype. Both GD and UC are associated with an imbalance in Th1/Th2 responses, with Th2 reactions predominating [9].

Petrified auricle is a rare clinical condition where the ear gradually stiffens and the cartilage is replaced by lamellar bone. The first case was identified in 1866 by Bochdalek [10]. The condition can be caused by various factors such as frostbite, inflammation, and systemic diseases. Calcification of auricle cartilage can occur in primary and secondary adrenal insufficiency, as well as adrenal hormone syndrome [11,12]. Possible mechanisms for this include corticosteroid insufficiency and elevated ACTH status. Auricular calcification has been observed in various endocrine disorders like diabetes, hypothyroidism and acromegaly. It is also linked with rare systemic diseases such as cold allergy, alkalinuria, hypertension, scleroderma and systemic chondromalacia [13,14]. In this particular case, ear sclerosis occurred successively. We conducted tests to assess the patient's adrenal cortex function, which revealed normal levels of ACTH (8:00, 16:00), aldosterone, plasma renin (8:00, 16:00) and cortisol (8:00, 16:00). All six hormones were within normal range. Additionally, the patient had normal parathyroid hormone levels and no diabetes. It is inferred that stone ear is associated with autoimmune thyroid disease-induced hyperthyroidism.

Ear involvement in inflammatory bowel disease is exceptionally uncommon and typically manifests as impaired vestibular function and auricular disease [15]. Recurrent polychondritis, a rare and excruciating condition characterized by inflammation and destruction of cartilage,

has been reported in association with IBD. The etiology of recurrent polychondritis is not fully understood but may be linked to the presence of circulating type II collagen antibodies. Bickford DD et al. documented a case of IBD with recurrent polychondritis involving a 35-year-old Crohn's disease patient who also had autoimmune pancreatitis, a history of primary sclerosing cholangitis (PSC), and suspected RP with auricular and nasal chondritis. The patient exhibited ear deformity, occasional erythema, pain and redness in the outer ear, and intermittent pain in the nasal cartilage [16]. Furthermore, Ko LN et al. reported rare cases of skin reactions, characterized by pain, fissures, and erosive plaques behind the ear, in seven IBD patients following anti-TNF therapy [17].

4. Conclusion

There have been very few reports of UC patients being diagnosed with autoimmune thyroid diseases to date. This case also presents the rare occurrence of bilateral auricular calcification.

Due to the complexity of autoimmune phenomena associated with UC, categorizing concurrent autoimmune thyroid diseases as primary or secondary can be challenging. However, in cases where no other primary cause of autoimmune thyroid disease is known, certain characteristics in some UC and autoimmune thyroid disease patients suggest a direct relationship between these two conditions. Nevertheless, the exact mechanisms require further elucidation in the future.

For patients suspected of UC with concurrent autoimmune thyroid diseases, it is advisable to perform at least one set of thyroid function tests (FT3, FT4, TSH) and thyroid-related antibodies (including TRAb, TPOAb, TGAb). In terms of treatment, standard immunosuppressive agents and biologic therapies can be employed. Methimazole in combination with infliximab is an effective treatment approach. However, it is important to note that auricular ossification caused by hyperthyroidism is irreversible.

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CRediT authorship contribution statement

Jiaqi Zhao: Writing - original draft. **Fangxiao Liu:** Data curation, Formal analysis, Investigation. **Lingshuo Bai:** Methodology, Supervision. **Zheng Jiao:** Investigation, Methodology. **Zihui Meng:** Investigation, Methodology. **Bo Jia:** Investigation, Methodology. **Yu Huang:** Data curation, Supervision. **Lin Liu:** Supervision, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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