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Clinical Case of Tofacitinib Therapy in Autoimmune Alopecia in Patient with Ulcerative Colitis

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Abstract
This article presents the clinical case of a patient with a long history of ulcerative colitis. Seven years after the onset of the disease, other autoimmune disorders such as sacroiliitis and alopecia have manifested. Ulcerative colitis is characterized by severe exacerbations, development of steroid resistance, ineffectiveness of mesalazine therapy, and onset of leukopenia when taking azathioprine and 6-mercaptopurine. Janus kinase inhibitor (tofacitinib) administration leads to remission of the disease, reduced activity of ulcerative colitis and sacroiliitis, and a resumption of hair growth was also observed.

Keywords Ulcerative colitis · Alopecia · Autoimmune disease · Tofacitinib · Inflammatory bowel disease

1 Introduction

Inflammatory bowel diseases (IBD), such as ulcerative colitis and Crohn's disease, show a progressive natural history, frequent exacerbations, and many extraintestinal manifestations [1, 2], which can be directly associated with IBD or represent an independent autoimmune disease. All extraintestinal manifestations of ulcerative colitis and Crohn's disease can be divided into three groups: associated with activity of IBD, not associated with activity of IBD, and developed due to prolonged inflammation, metabolic disorders or side effects of drugs [2]. The most common extraintestinal manifestations of IBD involve the joints, skin, and eyes.

Skin manifestations in patients suffering from ulcerative colitis include pyoderma gangrenosum, erythema nodosum, and acute febrile neutrophilic dermatosis (Sweet syndrome) [3]. Some patients may have secondary skin lesions due to nutritional deficiency such as enteropathic acrodermatitis, psoriasis, and other associated autoimmune diseases [4], including alopecia.

Alopecia occurs in 1.12% of patients with IBD [5]. In general, the causes of hair loss in patients with IBD can be divided into three groups: (1) telogen effluvium, aggravated by malnutrition, chronic inflammation, and adverse effects of treatment; (2) alopecia areata, directly associated with autoimmune pathogenesis; (3) primary cicatricial alopecia, characterized by prolonged destruction of hair follicles, probably associated with receptors deficiency activated by peroxisome proliferators [6]. Several studies have suggested that alopecia in IBD patients may be the result of infliximab and azathioprine therapy [6, 7].

IL-2, IL-15, and IFN-gamma play important role in the development of autoimmune alopecia areata. JAK kinase inhibitors can be used in the treatment of alopecia for IBD patients [8, 9].

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2 Clinical Case

Patient M., 33 years old, female, was admitted in to gastroenterology department of the Republican Clinical Hospital in Kazan with complaints of diarrhea 4–5 times a day, sometimes with blood up to 10 mL; cramping abdominal pain associated with defecation; arthralgia of small joints of hands, feet, pain in the lumbar region; and general weakness.

Past medical history is remarkable for first symptoms of the disease developed when the patient was only 5 years old—diarrhea, abdominal pain, and fever. The patient was examined by a doctor 4 years after the onset of the first symptoms. A colonoscopy, histological examination, and laboratory tests were performed. Ulcerative proctitis was diagnosed, sulfasalazine, and prednisone were used. The course of the disease was characterized by exacerbations 1–2 times a year, and each attack was associated with arthralgia of small joints of hands and feet.

At the age of 16, the patient had onset of sacroiliitis with pain in the lumbar region, right hip joint pain, and enthesopathies in the right sacroiliac joint. Additionally, exacerbation of ulcerative colitis was characterized by anemia, eosinophilia, and active proctitis on endoscopy. Steroids and 5-aminosalicylic acid (5-ASA) have been used to induce remission. During that exacerbation, alopecia areata of the scalp was first observed; in 2 months, alopecia had a total character and patient lost all hair of scalp, brows, and eyelashes. Also, abdominal mass was revealed during palpation. CT-scan of abdomen showed some mass $75 \times 50 \times 120$ mm in retroperitoneal area. Diagnostic laparotomy with retroperitoneal biopsy was performed. Histological examination showed the presence of fibrous tissue with eosinophilic inflammation. Lymphoproliferative disease was excluded; the mass was concluded as an eosinophilic retroperitoneal infiltrate. The patient continued to intake 5-ASA, prednisone; also, cyclosporin A was added; however, alopecia, arthropathy, and right-sided sacroiliitis still persisted.

At 24 years, the patient had mild exacerbation of ulcerative colitis with eosinophilic infiltrate of the submandibular area, which resolved by anti-inflammatory therapy of ulcerative colitis.

At 26 years, the patient was admitted with exacerbation of ulcerative colitis during pregnancy. Alopecia was still total, despite the additional vitamin supplements for hair growth. Anti-inflammatory therapy was continued; the pregnancy ended with a safe delivery; and healthy baby was born at 40-week gestation.

At 31 years, the patient had exacerbation of ulcerative colitis with manifestation of eosinophilic infiltrate of lungs, which was resolved by prednisone. Immunosuppressive therapy was added; however, the use of 6-mercaptopurine and azathioprine led to severe leukopenia, which did not allow continuing of this treatment. Biological therapy was also not available at that time.

During the current admission, a complete clinical examination of the patient was carried out. Complete blood count showed anemia (hemoglobin 116 g/L), thrombocytopenia (161×10^9/L), and leukopenia (3.7×10^9/L). Total protein was 74.9 g/L and albumin 49.5 g/L. Colonoscopy showed total ulcerative colitis of moderate activity. Maintenance therapy was performed by 5-ASA and low-dose steroids.

Due to the disease activity, several extraintestinal manifestations and progressive natural history of disease JAK kinase inhibitor tofacitinib were started. Initial dosage was 20 mg/day for 8 weeks with decreasing of dose to 10 mg/day. The tofacitinib therapy resulted in clinical remission of ulcerative colitis. Interestingly, by the end of the 8th week of therapy, the patient's hair began to regrow (Fig. 1).

During the tofacitinib therapy, the patient had mild COVID-19 with successful recovery. The infection was confirmed by nose and throat PCR test; CT-scan of the lungs was not performed.

Now the patient continues tofacitinib therapy; however, she experienced hair loss after lowering the dose to 10 mg/day, while remission of ulcerative colitis was clinically preserved. Further recommendations for the patient include continued tofacitinib therapy to control ulcerative colitis activity.

Fig. 1 Head hair regrowth of patient M. with ulcerative colitis during tofacitinib treatment

3 Discussion

The current report covered a rare clinical case of an early onset of ulcerative colitis with several systemic manifestations. The course of ulcerative colitis was characterized by frequent severe attacks, progressive colon involving, onset of episodes of eosinophilic infiltrates, lack of effectiveness of basic therapy, development of leukopenia while taking immunosuppressive drugs, and development of concomitant autoimmune diseases such as sacroiliitis and alopecia. This led to prescribing the biological therapy.

The severity of ulcerative colitis attack and extraintestinal manifestations is often directly dependent; after stopping activity of ulcerative colitis, we expect a decrease in the activity of other associated conditions. In this clinical case, alopecia was not amenable to adjustment, despite the ongoing basic therapy, supported by vitamin supplements.

Several studies show that a 3-month course of tofacitinib in patients with alopecia is effective in resuming hair growth; however, after stopping therapy, alopecia progresses again [8], which was observed in our patient.

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Declarations

Informed Consent Informed consent was obtained from all individual participants included in the study.

Research Involving Humans and Animals Statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

Conflict of Interest The authors declare no competing interests.

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