

## CASE STUDIES

# Co-occurrence of rheumatoid arthritis with ulcerative colitis: A rare case

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### Abstract

Ulcerative colitis (UC), an autoimmune disorder with unknown etiology, is a systemic disease with various extraintestinal manifestations such as arthritis, kidney and liver disease, and eye disorders. The present case study focuses on the co-occurrence of UC and rheumatoid arthritis (RA) in a 60-year old female patient. Although the co-existence of RA with autoimmune disease is common, its association with inflammatory bowel disease is rare. The present study highlights the significance of further research to identify the factors and interactions that influence and contribute to the co-existence, which may assist in early diagnosis. Moreover, it focuses on the need to consider the chance of co-occurrence during the differential diagnosis, though the association is rare.

Keywords: rheumatoid arthritis, ulcerative colitis, colonoscopy

### Introduction

Ulcerative colitis (UC), a systemic inflammatory disease of unknown etiology, is fundamentally autoimmune in nature. The disease mainly affects the colon and rectum, resulting in chronic diarrhea. Although the association between autoimmune diseases is identified, the co-occurrence of UC and rheumatoid arthritis (RA) is rare.<sup>1</sup> Moreover, very few studies have explored the mechanism underlying the association of autoimmune diseases and UC. Certain literature evidence indicates that the association is indirect and might be a result of common predisposition to both the diseases.<sup>2</sup>

### Case report

A 60-year-old elderly female patient, diagnosed with rheumatoid arthritis (RA) around 10 years ago, presented to the clinic with flexion deformities in the left elbow and right wrist. She had occasional loose stools since one year, which used to subside with antibiotics and probiotics. Since last 3 months, she had frequent bloody loose stools with abdominal pain, which persisted even after treatment with ofloxacin and ornidazole for 1 week. The routine examination of stools showed numerous pus cells with RBCs without any motile organisms. Her blood culture was negative, but she was positive for rheumatoid

factor and anti-cyclic citrullinated peptide. She was on methotrexate (10 mg/week), hydroxychloroquine (200 mg), and calcium citrate (500 mg) once daily. Abdominal ultrasound examination was unremarkable. Colonoscopy showed multiple ulcerative lesions in hepatic flexure and multiple erosions from mid transverse colon till hepatic flexure (Fig. 1).

Microscopic evaluation of the colonic biopsy showed focal ulcer lined by granulation tissue. Lamina was expanded and showed increase in mixed inflammatory cells to include neutrophils, lymphocytes, plasma cells with crypt distortion, crypt abscess, and cryptitis. There was no evidence of malignancy or granuloma.

The diagnosis of UC was made on the basis of the clinical course, and microscopic and colonoscopic findings. The results of clinical and lab investigations are given in table 1. Overlapping RA was concluded on the basis of high titers of anti-CCP, and the presence of elbow and wrist deformities.

The patient was treated with intravenous methyl prednisolone 125 mg daily for 3 days and later with tapering dose of oral steroids (tapered from 60 mg to 5 mg/day) for 2 weeks. The patient had improved symptomatically

and subsequently restarted methotrexate (7.5 mg/week) treatment. Hydroxychloroquine was replaced with sulfasalazine 1.5 mg daily, as it is effective for both UC and RA. One month of treatment had significantly improved the arthritis and bowel symptoms.

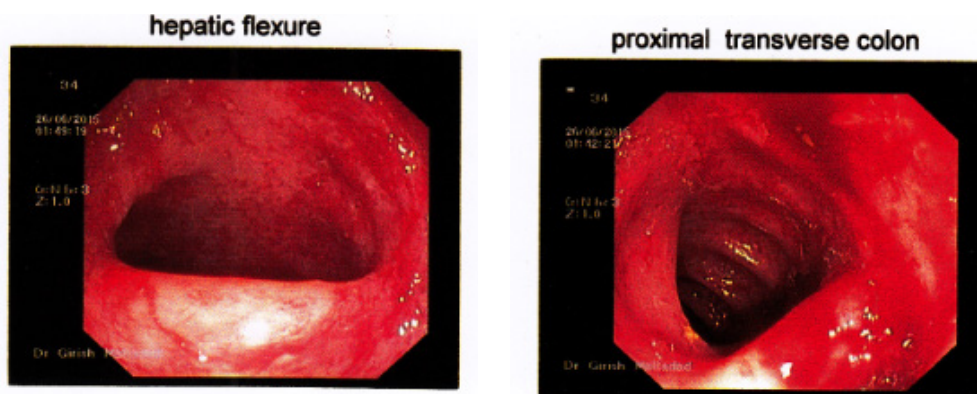
### Discussion

RA co-exists with autoimmune diseases such as SLE, Sjögren's syndrome, thyroiditis, and vitiligo; however its co-existence with inflammatory bowel disease such as UC has been rarely reported.<sup>3,4</sup> The central role of HLA-DR4 gene in both the diseases could explain this rare co-existence. Studies carried out in patients with UC have suggested that HLA-DR4 may confer protection against colitis, whereas it has been identified as one of the susceptibility genes

in RA. RA is a typical TH1-mediated disease, whereas UC is TH2-mediated. The probability of co-existence is reported to be very rare, due to the suppressive action of the predominant TH1 response on the TH2 response and vice versa.<sup>4</sup> Certain studies have reported the occurrence of abnormal immune response against intestinal bacteria in various types of arthritis. Moreover, studies in animal models have demonstrated that the bacterial cell wall components, mainly polysaccharide complexes may induce the development of colitis through T-cell activation. However, further research explaining the pathogenetic mechanism is warranted to clearly explain this rare co-existence.<sup>4</sup>

A prospective cohort study conducted by Aoyangi *et al.*,

**Fig 1: Colonoscopy of hepatic flexure and proximal transverse colon**



**Table 1: Results of clinical and lab investigations**

Parameters evaluated	Results
Hemoglobin (gm/dL)	10.8
Total WBC count (c/cmm)	7000
Neutrophils (%)	57
Lymphocytes (%)	40
Eosinophils (%)	01
Monocytes (%)	02
Basophils (%)	00
Platelet count (Lakhs/cmm)	2.90
ESR (mm)	90
SGPT (IU/L)	8.0
Serum creatinine (mg/dL)	0.3
Random blood sugar (mg/dL)	98.0
CRP (Turbidimetric method) (mg/dL)	31.0
Rheumatoid factor (IU/ml)	30.0
Anti-CCP (IU/ml)	335

between 1980 and 1989, in UC patients has not found any case of overlapping RA.<sup>5</sup> Utsunomiya *et al.* and Sawada *et al.* have reported a 0.4% prevalence of RA in studies involving 5,833 and 1,433 patients with UC respectively.<sup>6,7</sup> Literature evidence also indicates that UC complicate the course of established RA.<sup>5-7</sup>

UC is commonly associated with arthritic manifestations and the articular features involve either axial joints like the sacroiliac joint or the peripheral large joints, especially the lower limb joints. The differential diagnosis between RA and UC-linked arthritis is often challenging. In the current case, the presence of deformities in elbow and wrist, and high ant-CCP titers suggest the co-existence of RA and UC. Inflammatory bowel disease-related arthritis is generally not associated with deformities and positive anti-CCP. The relationship between RA and UC has not been clearly defined and the literature findings are insufficient to elucidate the mechanism underlying the association. Although literature evidence indicates that certain genes might predispose for the co-occurrence; no specific genetic risk factor has been identified. The case report by Asada *et al.* is touted as the first one reporting the association of RA with UC and IgA deficiency. The study has concluded that apart from genetic predisposition, underlying immune dysfunction might be responsible for the co-occurrence.<sup>8</sup>

A correspondence published in the *Annals of Rheumatic diseases* has reported a severe postpartum relapse of both the diseases, speculating that the termination of the protective effect conferred by the pregnancy would have caused the disease flare. In view of the simultaneous occurrence of the flare, the researchers suggested the existence of common underlying mechanisms of inflammation for both the diseases.<sup>9</sup> A 2006 case study by Amezcua-Guerra *et al.* has reported the development of UC in a patient with severe RA during CTLA-4Ig (abatacept) therapy. The researchers speculated that the alteration of balance of pro-inflammatory mediators and the lymphocytic profile due to the therapy would have caused the emergence of a new autoimmune disease. The drug action is based on the blockage of the interactions between CD80/CD86 on antigen presenting cells and CD28 on T lymphocytes. This would have interfered the maintenance and development of regulatory T cells

involved in controlling/ preventing intestinal inflammation.<sup>1</sup>

Further studies are mandatory to explore the underlying pathogenic mechanisms and factors contributing to the co-existence. It is important to consider the chance of co-occurrence during the differential diagnosis in patients showing systemic and joint manifestations, though the association is rare.

#### Competing interests

The authors declare that they have no competing interests.

#### Citation

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#### References

1. Amezcua-Guerra LM, Hernández-Martínez B, Pineda C, et al. Ulcerative colitis during CTLA-4Ig therapy in a patient with rheumatoid arthritis. *Gut*. 2006;55(7):1059-60.
2. Adachi Y, Hinoda Y, Takahashi H, et al. Rheumatoid arthritis associated with ulcerative colitis. *J Gastroenterol*. 1996 Aug;31(4):590-5.
3. Asada Y, Isomoto H, Shikuwa S, et al. Development of ulcerative colitis during the course of rheumatoid arthritis: Association with selective IgA deficiency. *World J Gastroenterol*. 2006;12(32):5240-3.
4. Cruz VA, Yamaguchi L, Ribeiro CN, et al. Ulcerative colitis and rheumatoid arthritis: a rare association - case report. *Revista Brasileira de Reumatologia*. 2012 Aug;52(4):648-50.
5. Aoyanagi T, Nakajima H, Ozaki M. Inflammatory bowel disease and extra bowel lesions. *Internal Med*. 1990;66(7):1068-71.
6. Utsunomiya T, Kitahara T, Shinohara H, et al. An epidemiological study of idiopathic proctocolitis in Japan. *Gastroenterol (Tokyo)*. 1989;11(18):140-9.
7. Sawada T, Higuchi Y, Shinozaki M. Extra-intestinal complications in IBD. *Annual Report of the Research Committee of Inflammatory Bowel Disease*. 1993;105-8.
8. Asada Y, Isomoto H, Shikuwa S, et al. Development of ulcerative colitis during the course of rheumatoid arthritis: Association with selective IgA deficiency. *World J Gastroenterol*. 2006 Aug 28;12(32):5240-3.
9. Boyer F, Fontanges E, Miossec P. Rheumatoid arthritis associated with ulcerative colitis: a case with severe flare of both diseases after delivery. *Ann Rheum Dis*. 2001 Sep 1;60(9):901-901.