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The Impact of Gut Microbiota Modulation on Bone Health and Rheumatoid Arthritis: A Case Report and Literature Review

Case Report

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Abstract

Background: The gut-bone axis represents a novel paradigm in which gut microbiota influences bone metabolism and systemic inflammation. Dysbiosis has been implicated in the pathogenesis of rheumatoid arthritis (RA), suggesting that microbiome-targeted therapies could offer adjunct benefits.

Case Presentation: A 52-year-old female presented with seropositive RA and concomitant irritable bowel syndrome (IBS). Stool analysis confirmed gut dysbiosis, characterized by an overgrowth of *Prevotella copri* and reduced commensal *Lactobacillus* and *Bifidobacterium*. In addition to initiating standard pharmacological therapy (methotrexate and adalimumab), a targeted microbiome modulation regimen was introduced, comprising a daily probiotic (*Lactobacillus reuteri*, 1×10^9 CFU) and prebiotic (inulin, 10g). After three months of combined therapy, the patient reported significant improvements in joint pain, stiffness, and gastrointestinal symptoms. Objective biomarkers showed marked reduction: CRP decreased from 12 mg/L to 3.2 mg/L, IL-6 from 8.5 pg/mL to 2.1 pg/mL, rheumatoid factor (RF) decreased from 58 IU/mL to 32 IU/mL, and anti-citrullinated protein antibody (ACPA) levels decreased from 145 U/mL to 95 U/mL.

Conclusion: This case demonstrates significant clinical and serological improvement in a patient with RA following a combined pharmacological and microbiome-targeted intervention. It provides supportive evidence for the role of the gut-joint axis in RA and suggests that probiotics and prebiotics may be a beneficial adjunct to conventional therapy, warranting further investigation in controlled trials.

Keywords: Gut Microbiota; Rheumatoid Arthritis; Dysbiosis; Probiotics; Prebiotics; Gut-Bone Axis; Prevotella copri; Lactobacillus reuteri

Introduction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disorder characterized by erosive synovitis, progressive joint destruction, and systemic bone loss [1]. While the etiology remains incompletely understood, a complex interplay between genetic predisposition and environmental triggers is widely accepted.

Emerging research has identified the gut microbiota as a critical environmental factor modulating immune homeostasis [2,3]. The concept of the “gut-bone axis” and “gut-joint axis” describes the biochemical communication between gut microbial communities and distant organ systems, including bones and joints [4,5]. This communication occurs via mechanisms including immune cell priming, regulation of systemic inflammation, production of microbial metabolites (e.g., short-chain fatty acids, SCFAs), and modulation of nutrient absorption [2,4,6].

A state of microbial imbalance, or dysbiosis, is frequently observed in RA patients [7,8]. This dysbiosis is often marked by a reduction in microbial diversity, a decrease in beneficial SCFA-producing bacteria, and an expansion of pathobionts such as *Prevotella copri*, which has been specifically linked to RA pathogenesis and disease activity [9,10,11]. This altered microbiota can compromise intestinal barrier integrity, leading to increased translocation of microbial products (e.g., lipopolysaccharide, LPS) into systemic circulation, thereby potentiating chronic inflammation and accelerating bone erosion through upregulated osteoclast activity [2,4,12].

Consequently, therapeutic strategies aimed at restoring eubiosis, including the use of probiotics and prebiotics, have garnered significant interest for their potential anti-inflammatory and bone-protective effects [4,13,14]. We present a case of a patient with RA and confirmed gut dysbiosis who exhibited a robust clinical and serological response to a combination of conventional disease-modifying antirheumatic drugs (DMARDs) and a targeted microbiome modulation regimen.

Case Presentation

A 52-year-old female presented to the orthopaedic clinic with a chief complaint of progressive pain, swelling, and morning stiffness in her wrists and knees, persisting for over four months. She also reported significant fatigue and long-standing bowel irregularities consistent with a prior diagnosis of irritable bowel syndrome (IBS), including bloating and diarrhoea. She was on no prior medications.

Physical examination revealed symmetric swelling and tenderness in both wrists and knees. Morning stiffness lasted more than 60 minutes. Initial diagnostic investigations were significant for:

- **Serology:** Elevated inflammatory markers (C-reactive protein [CRP] 12 mg/L; normal <3 mg/L) and positive serology for rheumatoid factor (RF; 58 IU/mL) and anti-citrullinated protein antibodies (ACPA; 145 U/mL). Interleukin-6 (IL-6) was elevated at 8.5 pg/mL.
- **Stool Microbiome Analysis:** A comprehensive stool analysis (via 16S rRNA sequencing) revealed significant gut dysbiosis [15]. Key findings included a notable overgrowth of the genus *Prevotella*, with *Prevotella copri* identified as the dominant species [9,10]. Furthermore, there was a substantial reduction in the abundance of beneficial genera, including *Lactobacillus* and *Bifidobacterium* [7,16].

Diagnosis

Based on the 2010 ACR/EULAR classification criteria, a diagnosis of seropositive rheumatoid arthritis (RA) was confirmed, supported by the positive RF and ACPA (anti-CCP) results. The concomitant gut dysbiosis was diagnosed in the context of her IBS symptoms and microbiological findings.

Therapeutic Intervention

A multi-faceted treatment plan was initiated by orthopaedic surgeon, Lifestyle medicine expert and a clinical nutritionist:

1. **Pharmacological Therapy:** Standard RA treatment was commenced with oral methotrexate (15 mg weekly) and a subcutaneous TNF-α inhibitor (adalimumab, 40 mg every two weeks).
2. **Microbiome-Targeted Therapy:** To address the underlying dysbiosis, an adjunctive regimen was introduced:
    a. **Probiotic:** A commercially available formulation of *Lactobacillus reuteri*, providing 1×10^9 colony-forming units (CFU) per capsule. One capsule was administered orally once daily in the morning on an empty stomach [17,18].
    b. **Prebiotic:** A purified **chicory root-derived inulin powder**. The patient was instructed to dissolve **10 g** (approximately one level tablespoon) in water or a cold beverage and consume it daily before breakfast [19,20].
3. **Lifestyle Modifications:** The patient was counselled on adopting an anti-inflammatory diet rich in fiber (from diverse fruits, vegetables, and legumes), and low in processed foods and added sugars. She was also encouraged to maintain adequate hydration and engage in regular, low-impact physical activity (e.g., walking, swimming) as tolerated.

Follow-up and Outcomes

At the three-month follow-up, the patient reported a substantial improvement in her clinical symptoms. Joint pain and swelling were significantly reduced, and morning stiffness decreased to less than 30 minutes. Her gastrointestinal symptoms, including bloating and diarrhea, had resolved. Repeat laboratory studies demonstrated remarkable improvement:

- CRP decreased to **3.2 mg/L** (normal: <3 mg/L)
- IL-6 decreased to **2.1 pg/mL** (normal: <1.5 pg/mL)
- RF decreased to **32 IU/mL** (normal: <14 IU/mL)
- ACPA decreased to **95 U/mL** (normal: <20 U/mL)

This represented a significant reduction in systemic inflammation and autoantibody levels.

Discussion

This case illustrates the potential synergistic benefit of combining conventional RA therapy with a gut microbiome modulation strategy. The patient's significant clinical and serological improvement, alongside the resolution of GI symptoms, suggests a positive systemic effect beyond standard care alone. The existing body of literature, as summarized in Table 1, provides a strong scientific rationale for this combined interventional approach and the mechanisms behind the observed outcomes [7,9,17,19].

The observed dysbiosis, featuring *Prevotella copri* overgrowth and depleted *Lactobacillus* and *Bifidobacterium*, aligns with the described microbial signature in RA patients [7,8,9]. *P. copri* has been shown to promote Th17-mediated immune responses, leading to increased production of pro-inflammatory cytokines like IL-6 and IL-17, which are central to RA pathogenesis and osteoclast activation [9,11,21].

The intervention with *Lactobacillus reuteri* and inulin likely acted through several

Complementary mechanisms:

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Table 1: Serological Biomarker Response to Combined Therapy and Supporting Literature

Biomarker	Pre-Intervention Value	Post-Intervention Value (3 Months)	Reference Range	Clinical Significance of Change	Validating Studies
C-Reactive Protein (CRP)	12 mg/L	**3.2 mg/L**	<3 mg/L	Reduction indicates a significant decrease in systemic inflammation. Normalization of CRP is a key treatment goal in RA.	Mohammed AT, et al. (2017) [13]: A meta-analysis found probiotic supplementation significantly reduced CRP levels in RA patients, supporting its role as an adjunct therapy for inflammation control.
Interleukin-6 (IL-6)	8.5 pg/mL	**2.1 pg/mL**	<1.5 pg/mL	Marked reduction in a key pro-inflammatory cytokine directly involved in RA synovitis, systemic symptoms, and bone erosion.	Liu Y, et al. (2022) [18]: Demonstrated that *L. reuteri* reduces IL-6 production by modulating the Th17/Treg balance. Schepper JD, et al. (2019) [4]: Reviews the role of probiotics/prebiotics in reducing pro-inflammatory cytokines like IL-6.
Rheumatoid Factor (RF)	58 IU/mL	**32 IU/mL**	<14 IU/mL	A significant decrease in autoantibody titer, suggesting a modulation of the underlying autoimmune response. While not a primary target, reduction often correlates with improved disease control.	While DMARDs are the primary drivers of RF reduction, the synergistic immunomodulatory effect of probiotics may contribute to a more robust response, as shown in clinical improvements in trials [13].
Anti-Citrullinated Protein Antibody (ACPA)	145 U/mL	**95 U/mL**	<20 U/mL	A notable decrease in this highly RA-specific autoantibody. This is a particularly interesting finding, suggesting a potential impact on the citrullination-dependent immune pathway.	The reduction of ACPA is less commonly reported and is a novel finding. It suggests a potential high-level immunomodulatory effect, possibly through gut-mediated regulation of autoimmunity [26, 27].

Table 2: Review of Literature on the Gut-Joint-Bone Axis and Therapeutic Modulation

Thematic Area	Key Finding	Reference	Implication for Current Case
Dysbiosis in RA Pathogenesis	Patients with early RA show altered fecal microbiota, including reduced microbial diversity.	Vaahtovuo J, et al. 2008 [7]	Provides context for the patient's confirmed dysbiosis and its link to her RA diagnosis.
	The abundance of *Prevotella copri* is correlated with new-onset untreated RA and promotes Th17-driven inflammation.	Scher JU, et al. 2013 [9]	Directly supports the finding of *P. copri* overgrowth in our patient and its potential role in her disease activity.
	P. copri can activate human antigen-presenting cells and induce arthritogenic T-cell responses, providing a mechanistic link.	Pianta A, et al. 2017 [11]	Explains a potential immunological mechanism by which the patient's dysbiosis may have contributed to RA development.
Mechanisms: Gut-Bone-Joint Axis	The gut microbiota regulates bone remodeling through immune modulation, influencing osteoclastogenesis and osteoblast activity.	Pacifici R. 2018 [2]	Establishes the fundamental "gut-bone axis" concept that underpins the report's primary focus.
	Gut-derived short-chain fatty acids (SCFAs), like butyrate, protect from pathological bone loss by regulating osteoclast metabolism.	Lucas S, et al. 2018 [6]	Provides a mechanistic rationale for using prebiotics (inulin) to boost SCFA production for bone health.
	Intestinal dysbiosis and barrier breakdown can systemically fuel inflammation and joint pathology in RA (the "gut-joint axis").	Zaiss MM, et al. 2021 [5]	Connects the patient's IBS and dysbiosis directly to her systemic inflammation and joint symptoms.
Therapeutic Interventions: Prebiotics	Prebiotic fibers, such as inulin, enhance mineral absorption (Ca, Mg) and exert chronic beneficial effects on bone metabolism in models of bone loss.	Legette LL, et al. 2012 [20]	Justifies the choice and dosage of inulin (10g) as a bone-targeted prebiotic intervention.
Therapeutic Interventions: Probiotics	Specific probiotic strains, including *Lactobacillus reuteri*, can modulate host immunity, promote Treg differentiation, and suppress pro-inflammatory pathways.	Mu Q, et al. 2018 [17]	Supports the selection of *L. reuteri* for its documented immunomodulatory properties.
	Lactobacillus reuteri DSM 17938 was shown to alleviate RA severity in a model by restoring the Th17/Treg balance and reducing pro-inflammatory cytokines.	Liu Y, et al. 2022 [18]	Provides direct preclinical evidence for the specific probiotic strain's potential efficacy in RA.
Clinical Evidence & Reviews	A meta-analysis of RCTs concluded that probiotic supplementation can significantly reduce disease activity (DAS28) and inflammatory markers (CRP) in RA patients.	Mohammed AT, et al. 2017 [13]	Strengthens the argument for probiotics as an adjunct therapy and mirrors our patient's reduction in CRP.
	A systematic review confirms that probiotics and prebiotics influence bone metabolism by reducing inflammation, improving barrier function, and enhancing mineral absorption.		

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1. **Competitive Exclusion and Barrier Fortification:** *L. reuteri* can inhibit the growth of pathobionts, produce antimicrobial compounds (e.g., reuterin), and enhance mucin production, thereby strengthening the intestinal epithelial barrier and reducing bacterial translocation [17,22].
2. **Immunomodulation:** Certain probiotic strains, including *L. reuteri*, can modulate the host immune system by promoting regulatory T-cell (Treg) differentiation and downregulating pro-inflammatory Th17 responses, leading to decreased systemic levels of TNF-α, IL-6, and IL-17 [18,23,24].
3. **Metabolic Effects:** The prebiotic inulin is fermented by colonic bacteria into SCFAs (e.g., butyrate, propionate). Butyrate is a crucial energy source for colonocytes, further enhancing barrier function [25]. More importantly, SCFAs have demonstrated direct immunomodulatory and bone-protective effects by suppressing osteoclastogenesis and promoting osteoblast activity [4,6,19,20].

The parallel improvement in both musculoskeletal and gastrointestinal symptoms underscores the interconnectedness of the gut-joint axis. The reduction in ACPA levels is particularly intriguing, as it suggests a potential modulation of the autoantibody response, possibly via effects on citrullinating enzymes or the presentation of autoantigens, a mechanism proposed in recent studies [26,27].

Limitations

As a single case report, our findings cannot establish causality or be generalized to the broader RA population. The observed improvements cannot be definitively disentangled from the effects of the potent DMARD therapy (methotrexate and adalimumab). The placebo effect, particularly on subjective symptoms, must also be considered. Furthermore, while stool analysis showed a microbial shift, sequential microbiome sequencing would be required to confirm a direct correlation between the intervention and microbial changes. Finally, the use of specific commercial products, while detailed for reproducibility, may limit the generalizability of the results to other probiotic strains or prebiotic sources.

Conclusion and Future Directions

This case adds to the growing body of evidence supporting the role of the gut microbiome in RA and highlights the potential of microbiome-targeted therapies as a safe and promising adjunct to standard treatment. It provides a strong rationale for designing robust, randomized, placebo-controlled clinical trials to rigorously evaluate the efficacy of specific probiotic and prebiotic strains, both in improving RA disease activity and in mitigating the systemic bone loss associated with chronic inflammation.

Declarations

- Written informed consent was obtained from the patient for the publication of this case report and any accompanying data.
- Competing Interests: The authors declare no competing interests.
- Funding: No funding was received for this work.
- Availability of Data and Materials: The data supporting this case report are available within the article. Further details are available from the corresponding author upon reasonable request.
- Disclaimer: The views expressed in this case report are solely those of the authors. The specific interventions described (including the use of Lactobacillus reuteri and inulin) are for informational and reproducibility purposes only and do not imply endorsement of any specific product or brand. The information contained herein is presented for academic and educational purposes and is not intended to replace professional medical advice, diagnosis, or treatment.

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