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Case report

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Coexistence of Anti-CCP Positive Rheumatoid Arthritis with Autoimmune Hepatitis Type 1

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Abstract

Anti-cyclic citrullinated peptide (anti-CCP) antibodies are highly specific serological markers for rheumatoid arthritis (RA), providing both diagnostic and prognostic value. Autoimmune hepatitis type 1 (AIH-1), a chronic liver disease, is characterized by positive autoimmune markers such as antinuclear antibodies (ANA) and anti-smooth muscle antibodies (SMA). While musculoskeletal symptoms can occur in autoimmune liver diseases, they are rarely associated with high-titre anti-CCP or fulfil diagnostic criteria for RA. The coexistence of RA and AIH is exceptionally rare and presents diagnostic challenges, especially in distinguishing hepatic arthropathy from true RA. We report a case of a 50-year-old woman with a two-year history of biopsy-confirmed AIH-1, who presented with new-onset symmetrical polyarthritis involving small and large joints. Serologic evaluation revealed rheumatoid factor positivity with extremely elevated anti-CCP levels (>25000 U/mL). Inflammatory markers (ESR, CRP) were significantly raised. Her joint symptoms and laboratory profile met the ACR/EULAR criteria for RA. She was already receiving immunosuppressive therapy for AIH (prednisolone, azathioprine), which was adjusted to accommodate RA management. This case underscores a rare yet clinically significant autoimmune overlap syndrome involving AIH-1 and seropositive RA. High anti-CCP titres in patients with autoimmune liver disease should raise clinical suspicion for true RA rather than hepatic-related arthropathy. Interdisciplinary management involving rheumatologists and hepatologists is essential to ensure early recognition, diagnostic classification, and effective treatment of such patients. This case supports the inclusion of anti-CCP screening in AIH patients presenting with persistent joint complaints.

Keywords: Autoimmune hepatitis, Rheumatoid arthritis, Anti-CCP antibody, Overlap syndrome, Autoantibody, Hepatic arthropathy.

Introdction

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease primarily affecting the synovial joints, characterized by persistent inflammation, joint destruction, and systemic manifestations. Among the autoantibodies used in its diagnosis, anti-cyclic citrullinated peptide (anti-CCP) antibodies have emerged as one of the most highly specific biomarkers for RA, with reported specificity rates exceeding 95% in many cohorts.[1] Their presence is not only diagnostic but also prognostic, correlating with more aggressive disease and radiographic progression.[2] The detection of anti-CCP antibodies, especially in the context of early or atypical symptoms, significantly strengthens the diagnostic certainty of RA. On the other hand, Autoimmune Hepatitis Type 1 (AIH-1) is a rare, chronic inflammatory liver disease of unknown etiology, marked by a

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complex serologic profile that includes antinuclear antibodies (ANA), anti-smooth muscle antibodies (SMA), and elevated serum immunoglobulin G (IgG) levels.[3] It commonly affects women and is associated with other autoimmune disorders, ranging from thyroiditis to systemic lupus erythematosus. Hepatic inflammation in AIH is mediated by a loss of tolerance to liver-specific autoantigens, with a robust plasma cell infiltrate seen on histology.

The clinical and serological overlap between RA and autoimmune liver diseases, though uncommon, presents a significant diagnostic challenge. While rheumatoid factor (RF) may be detected in a broad spectrum of inflammatory and hepatic conditions, anti-CCP antibodies are rarely elevated in non-RA autoimmune diseases, including AIH. [4] This distinction becomes clinically relevant in patients who present with joint manifestations and underlying liver pathology raising questions whether the articular symptoms are hepatic-related arthropathy or true RA. Previous studies have identified anti-CCP positivity in AIH, often without clinical evidence of RA; moreover the titers are typically low and of uncertain specificity [5,6] .

In this context, we describe a case of a 50-year-old female patient with previously diagnosed AIH-1, who later presented with classical joint symptoms and markedly elevated anti-CCP levels (>25000 U/mL), strongly suggestive of coexistent RA. This case underscores the importance of distinguishing true RA in the backdrop of autoimmune liver disease and contributes to the limited literature documenting such an overlap. It also highlights the diagnostic value of anti-CCP in differentiating hepatic arthropathy from early RA in patients with autoimmune liver disease.

Case Report

A 50-year-old woman presented to the outpatient rheumatology clinic with a four-month history of symmetrical polyarthritis, involving the knees, wrists, metacarpophalangeal (MCP), and proximal interphalangeal (PIP) joints. The patient reported morning stiffness lasting over an hour, joint swelling, and restricted mobility, without any accompanying systemic features such as fever, weight loss, or rash. There was no history of trauma or prior articular disease. Two years prior to this presentation, she had been evaluated by a hepatologist for elevated liver enzymes and nonspecific fatigue, which led to a liver biopsy confirming a diagnosis of Autoimmune Hepatitis Type 1 (AIH-1). The biopsy demonstrated interface hepatitis with plasma cell-rich portal infiltrates and bridging fibrosis. At that time, her antinuclear antibody (ANA) was positive at a titter of 1:160 with a homogeneous pattern, and her serum immunoglobulin G (IgG) was elevated. She was started on a long-term immunosuppressive regimen, consisting of: prednisolone 5 mg/day, azathioprine 50 mg/day, hydroxychloroquine 200 mg/day and calcium + vitamin D + bisphosphonate supplement.

During current evaluation for arthritis, her anti-cyclic citrullinated peptide (anti-CCP) level was found to be highly elevated >25000 U/mL, surpassing the analytical range of the assay. In addition, rheumatoid factor (RF) was positive, and both erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were markedly elevated, further supporting a diagnosis of active inflammatory arthritis. Results of clinical and lab investigations conducted are summarized in [Table 1].

Table 1: Summary of the Current Laboratory Findings

Parameter	Result	Reference Range
Anti-CCP	>25000 U/mL	Negative: <20 U/ml, Positive: >60 U/ml
Rheumatoid Factor (RF)	26.7 IU/ml	<20 IU/mL
ANA	98.6 U/ml	Negative: <20 U/ml, Positive: >60 U/ml
ESR	47 mm/hr	<20 mm/hr
CRP	5.4 mg/L	<5 mg/L
Alkaline Phosphatase (ALP)	193 IU/L	42-98 IU/L
Aspartate Transaminase (AST)	14 IU/L	<31 IU/L
Alanine Transaminase (ALT)	8 IU/L	<34 IU/L
Total Bilirubin	0.8 mg/dl	0.3-1.0 mg/dl

Given the classic articular involvement, serologic positivity for anti-CCP and RF, and elevated inflammatory markers, a diagnosis of rheumatoid arthritis (RA) was established. The coexisting diagnosis of AIH-1, supported by prior liver histology and ANA positivity, established this case as a rare example of RA overlapping with autoimmune liver disease. The patient's immunosuppressive regimen was adjusted to manage the severity hepatic disease in addition to controlling the RA. She was counselled for close monitoring of liver function during disease-modifying anti-rheumatic drug (DMARD) therapy as these are associated with hepatotoxicity leading to elevated liver enzymes, fibrosis, cirrhosis. She was advised regular follow-up with rheumatology and gastroenterology dept.

Discussion

The overlap of rheumatoid arthritis (RA) with autoimmune hepatitis type 1 (AIH-1) presents a diagnostic and immunological complexity that remains underrecognized. In this case, the patient developed RA in the context of previously confirmed AIH-1, demonstrated by symmetrical inflammatory polyarthritis, high anti-cyclic citrullinated peptide (anti-CCP) titres (>25000 U/mL), even after the dilution of 1:10, 1:20 and

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up to 1:50 and RF positivity, fulfilling ACR/EULAR criteria for RA. While hepatic arthropathy is a known extrahepatic manifestation of autoimmune liver disease, it is typically non-erosive, affects large joints, and lacks specific serologic markers like anti-CCP.[7,8] The present case adds to a limited pool of literature describing a true immunopathologic overlap of RA and AIH.

Anti-CCP antibodies are highly specific for RA, with sensitivity estimates ranging from 67%–80% and specificity above 95%.[9] In hepatic disorders, RF may be elevated due to chronic immune activation; however, anti-CCP rarely occurs outside of RA and is not typically associated with AIH or viral hepatitis.[4,6] A prospective study by Koga and colleagues evaluated anti-CCP in patients with AIH, PBC, and chronic HCV, finding minimal to no high-titre anti-CCP positivity in non-RA liver disease patients—supporting its discriminatory role.[6] In the present case, the initial result of anti-CCP titre was above the linearity of the analyser i.e., >500 U/mL. (Roche e411). Such a high level is well above diagnostic thresholds, and consistent with true RA rather than hepatic-related arthropathy. We performed further dilution of 1:10, 1:20 and 1:50 to rule out the 'Hook effect' or prozone phenomenon associated with immunoassay technique. However, the testing for the presence of heterophile antibodies was not performed as the patient refused for the same.

Additionally, the utility of anti-CCP in preclinical RA states has been validated. GR et al. (2022) showed anti-CCP positivity in 20.9% of asymptomatic first-degree relatives (AFDRs) of RA patients, indicating its utility in identifying autoimmunity before emergence of clinical arthritis. Similarly, few studies have demonstrated anti-CCP as a predictive marker appearing years before joint involvement, particularly in genetically predisposed individual. [10,11] The pathophysiological overlap may involve the shared epitope hypothesis, which implicates certain HLA-DRB1 alleles in both RA and AIH. [12,13] Shared alleles like *HLA-DRB1*04 have been linked to antigen presentation abnormalities and enhanced citrulline peptide reactivity, driving T-cell activation and chronic inflammation. [14-16] This genetic predisposition, coupled with a common cytokine milieu (e.g., elevated TNF-α, IL-6), may explain concurrent autoimmune manifestations in liver and joint tissues. [17]

Furthermore, certain environmental triggers, such as viral infections or dysbiosis, may facilitate epitope spreading and molecular mimicry, contributing to autoimmune overlaps.[18] While AIH may initially mask early RA symptoms due to overlapping use of immunosuppressants like azathioprine or steroids, elevated anti-CCP levels as seen here should prompt independent rheumatologic evaluation.[19] An interesting case of Wilson's disease with RA was reported by Haridas and Haridas (2023), illustrating how hepatic comorbidities can obscure rheumatologic diagnoses.[20] However, their patient's liver disease was metabolic in origin and lacked autoimmune serology, distinguishing it from the autoimmune–autoimmune overlap in our patient. The comparison of overlap syndromes involving liver disease and RA is summarized in [Table 2].

This case invites further inquiry into the immunological intersections between autoimmune liver disease and systemic rheumatoid disease conditions. The presence of high anti-CCP antibodies in an AIH-1 patient presenting with articular symptoms suggests that true RA may develop or remain latent in patients with autoimmune hepatic conditions, particularly in those with shared genetic or serologic susceptibilities. Future research should focus on:

- Prospective screening protocols for RA-specific autoantibodies in patients with AIH and unexplained joint symptoms,
- Immunogenetic profiling to identify shared pathways or risk alleles,
- And longitudinal studies to establish causality, frequency, and therapeutic implications of such Overlap syndrome.

Recognition of these rare but consequential associations is essential for early diagnosis, appropriate immunomodulatory treatment, better patient care and long-term outcomes.

Table 2: Comparison of Overlap Syndromes Involving Liver Disease and RA. Summary of Selected Case Reports

Feature	Present Case (AIH + RA)	Haridas et al. (2023) – WD + RA [20]	Koga et al. (2008) – AIH cohort [6]
Hepatic disorder	Autoimmune Hepatitis Type 1	Wilson's Disease (genetic copper overload)	AIH (non-RA liver disease cohort)
RA diagnosis confirmed?	Yes (Anti-CCP >500, RF+, ESR/CRP↑, clinical features)	Yes (Anti-CCP+, RF+, articular symptoms)	No (no joint features consistent with RA)
Anti-CCP status	Extremely elevated >25000 U/mL	Moderately elevated	Mostly negative or low-level titres (<20 U/mL)
Rheumatologic presentation	Small symmetrical joint involvement	Similar (hands, wrists, knees)	Not described
Immunological overlap	ANA+, biopsy-confirmed AIH	Negative autoimmune markers	ANA+ in some cases, but no joint disease
Novelty	First documented AIH + RA with anti-CCP >25000	First documented Wilson's Disease + RA case	First comprehensive anti-CCP screening in liver disease

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Conclusion

This case highlights the rare but clinically significant overlap between autoimmune hepatitis type 1 (AIH-1) and rheumatoid arthritis (RA), confirmed through the presence of symmetrical inflammatory arthritis, rheumatoid factor, and markedly elevated anti-CCP antibody levels (>25000 U/mL). While musculoskeletal symptoms can be seen in hepatic disorders, anti-CCP positivity at high titres remains a specific marker for RA and should prompt further rheumatologic evaluation. Clinicians must remain vigilant when AIH patients present with persistent or atypical joint complaints. Even if the diagnosis of AIH precedes the onset of rheumatologic symptoms, the emergence of articular involvement in conjunction with anti-CCP and RF seropositivity should raise suspicion for true RA rather than hepatic arthropathy. This case underscores the importance of early interdisciplinary collaboration between hepatology and rheumatology. Timely recognition and tailored immunosuppressive strategies can mitigate disease progression and improve outcomes. Further longitudinal studies are warranted to explore the frequency and implications of such autoimmune overlaps and to guide screening strategies in AIH patients presenting with joint symptoms.

- **Consent to participate**: Informed consent was obtained from the participant included in the study.
- **Consent to publish:** The participant has consented to the submission of the case report to the journal.

Reference

1. Kroot E-JJA, De Jong BAW, Van Leeuwen MA, et al. The prognostic value of anti–cyclic citrullinated peptide antibody in patients with recent-onset rheumatoid arthritis. Arthritis & Rheumatism 43 (2000): 1831-5.
2. Lee DM, Schur PH. Clinical utility of the anti-CCP assay in patients with rheumatic diseases. Annals of the Rheumatic Diseases 62 (2003): 870-4.
3. Manns MP, Lohse AW, Vergani D. Autoimmune hepatitis – Update 2015. Journal of Hepatology 62 (2015): S100-S11.
4. Bombardieri M, Alessandri C, Labbadia G, et al. Role of anti-cyclic citrullinated peptide antibodies in discriminating patients with rheumatoid arthritis from patients with chronic hepatitis C infection-associated polyarticular involvement. Arthritis Research & Therapy 6 (2004): R137-R41.
5. Fusconi M, Vannini A, Dall'aglio AC, et al. Anti-cyclic citrullinated peptide antibodies in type 1 autoimmune hepatitis. Alimentary Pharmacology & Therapeutics 22 (2005): 951-5.
6. Koga T, Migita K, Miyashita T, et al. Determination of anti-cyclic citrullinated peptide antibodies in the sera of patients with liver diseases. Clinical and Experimental Rheumatology 26 (2008): 121-4.
7. Boyer F, Guazzelli É, Pouliquen O. Unifying suspension and granular rheology. Physical review letters 107 (2011): 188301
8. Efe C, Kav T, Aydin C, et al. Low serum vitamin D levels are associated with severe histological features and poor response to therapy in patients with autoimmune hepatitis. Digestive diseases and sciences 59 (2014): 3035-42.
9. van der Linden MPM, van der Woude D, Ioan-Facsinay A, et al. Value of anti–modified citrullinated vimentin and third-generation anti–cyclic citrullinated peptide compared with second-generation anti–cyclic citrullinated peptide and rheumatoid factor in predicting disease outcome in undifferentiated arthritis and rheumatoid arthritis. Arthritis & Rheumatism 60 (2009): 2232-41.
10. Gr P, Dihingia P, Jha AK, et al. Rheumatoid Arthritis Co-relation with Anti-CCP Antibodies with special reference to its Prevalence in Asymptomatic First-Degree Relatives. Mediterranean Journal of Rheumatology 33 (2022): 42-7.
11. Nielen MMJ, van Schaardenburg D, Reesink HW, et al. Specific autoantibodies precede the symptoms of rheumatoid arthritis: A study of serial measurements in blood donors. Arthritis & Rheumatism 50 (2004): 380-6.
12. Kolfenbach JR, Deane KD, Derber LA, et al. A prospective approach to investigating the natural history of preclinical rheumatoid arthritis (RA) using first-degree relatives of probands with RA. Arthritis Care & Research 61 (2009): 1735-42.
13. Raychaudhuri S, Sandor C, Stahl EA, et al. Five amino acids in three HLA proteins explain most of the association between MHC and seropositive rheumatoid arthritis. Nature Genetics 44 (2012): 291-6.
14. Lettre G, Rioux JD. Autoimmune diseases: insights from genome-wide association studies. Human Molecular Genetics 17 (2008): R116-R21.
15. Yang F, Zhou L, Shen Y, et al. Metabolic heterogeneity caused by HLA-DRB1*04:05 and protective effect of inosine on autoimmune hepatitis. Frontiers in Immunology 13 (2022): 1-15.
16. Oka S, Furukawa H, Yasunami M, et al. HLA-DRB1 and DQB1 alleles in Japanese type 1 autoimmune hepatitis: The predisposing role of the DR4/DR8 heterozygous genotype. PLOS ONE 12 (2017): e0187325.
17. Tan EM, Smolen JS. Historical observations contributing insights on etiopathogenesis of rheumatoid arthritis

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DOI:10.26502/fjhs.375

and role of rheumatoid factor. Journal of Experimental Medicine 213 (2016): 1937-50.

18. Siebert S, Tsoukas A, Robertson J, et al. Cytokines as Therapeutic Targets in Rheumatoid Arthritis and Other Inflammatory Diseases. Pharmacological Reviews 67 (2015): 280-309.

19. Rosenblum MD, Remedios KA, Abbas AK. Mechanisms of human autoimmunity. The Journal of Clinical Investigation 125 (2015): 2228-33.

20. Haridas V, Haridas K. Wilson's disease with anti-CCP positive rheumatoid arthritis: A rare co-existence. Internet Journal of Rheumatology and Clinical Immunology 11 (2023): 01-3.

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