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Ankylosing spondylitis coexisting with *Clonorchis sinensis* infection: A case report

Tian-Xin Yi, Wei Liu, Wen-Fei Leng, Xiao-Chuan Wang, Liang Luo

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Abstract

BACKGROUND

Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory disease. The prevailing theory links AS onset to infections in susceptible individuals. Furthermore, infections may impair the immune responses. Numerous studies have investigated links between AS and various infections-bacterial, viral, fungal, and other microorganism infections. However, limited attention has been given to the association between AS and *Clonorchis sinensis* (*C. sinensis*) infection.

CASE SUMMARY

A 27-year-old male with a 10-yr history of AS presented to our hospital with inflammatory lower back pain as the primary manifestation. Ten years ago, the patient had achieved a stable condition after treatment with biological agents. However, he experienced a recurrence of lumbosacral pain with an unexplained cause 10 d before hospital admission. A lumbosacral magnetic resonance imaging (MRI) scan revealed bone marrow edema in the left sacroiliac joint, and laboratory indicators were elevated. Moreover, the presence of *C. sinensis* eggs was detected in the stool. The patient was prescribed praziquantel, resulting in the disappearance of *C. sinensis* eggs in subsequent routine stool tests and relief from lumbosacral pain. A follow-up MRI scan performed after 4 months revealed a reduction in bone marrow edema around the left sacroiliac joint.

CONCLUSION

C. sinensis infections could potentially trigger the exacerbation of AS. Clinicians should pay attention to investigating the presence of infections.

Key Words: Ankylosing spondylitis; *Clonorchis sinensis*; Parasites; Infection; Case report

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Core Tip: This study explored the link between *Clonorchis sinensis* (*C. sinensis*) infection and ankylosing spondylitis (AS). While previous research extensively explored the association between AS and various infections, the association with *C. sinensis* received limited attention. The findings highlight the potential role of parasitic infections, particularly *C. sinensis*, in affecting AS disease activity. This study provides valuable insights into the less-explored aspects of AS etiology, emphasizing the need for further investigation into parasitic infections to comprehend and manage AS.

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INTRODUCTION

Ankylosing spondylitis (AS) is a chronic inflammatory and rheumatic disease resulting from an imbalance between innate and acquired immune responses[1]. While it can affect any part of the spine, its primary symptoms are persistent back pain and stiffness in the lower back and pelvis. The prevalence of AS per 10000 individuals is 23.8 in Europe, 31.9 in North America, 16.7 in Asia, 10.2 in Latin America, and 7.4 in Africa[2]. Infections commonly occur in the first 3 months and may act as potential triggers for the first symptoms of AS, often manifesting as gastrointestinal, urinary tract, and respiratory infections of microbiological origin[3,4].

Clonorchis sinensis (*C. sinensis*) infection is a severe parasitic disease affecting millions globally, especially prevalent in China, South Korea, the Far East of Russia, and Vietnam, with an estimated 15 million cases[5]. Transmission occurs through the consumption of undercooked freshwater fish containing metacercariae. Adult *C. sinensis* parasites then establish themselves within the human hepatobiliary system[6]. *C. sinensis* infection triggers the activation of sphingosine 1-phosphate receptor 2, leading to the injury and fibrosis of the hepatobiliary[7]. Recent research in a rat model found that *C. sinensis* infection increases the risk of hepatocellular carcinoma by stimulating hepatic progenitor cell proliferation[8]. Complications of *C. sinensis* infection include cholestasis, cholangitis, biliary system fibrosis, and in severe cases, the development of cholangiocarcinoma[9]. Consequently, the primary preventive measure is to abstain from consuming raw or undercooked freshwater fish. Praziquantel is the recommended and effective treatment for this infection[10].

While there is existing literature on the coexistence of AS and parasitic infections, there is limited research specifically addressing the simultaneous presence of AS and *C. sinensis* infection. This case report details a rare scenario of AS coexisting with *C. sinensis* infection, underscoring the potential impact of *C. sinensis* infection on AS disease activity.

CASE PRESENTATION

Chief complaints

A 27-year-old male patient with persistent lumbosacral pain for more than 10 yr had a recurrence 10 d before a hospital visit.

History of present illness

The patient, in his late twenties, reported experiencing lumbosacral pain for more than 10 years. The pain intensified while sitting or at rest but improved in the mornings. Throughout this period, there were no signs of heel pain, eye inflammation, symmetrical swelling, pain in small joints, psoriasis, sausage fingers/toes, facial erythema, photosensitivity, oral ulcer, alopecia, frequent urination, or urgency. Consequently, he was admitted to the Rheumatology Department at the Traditional Chinese Medicine Hospital of Dianjiang, Chongqing. Examinations conducted indicated a positive response to human leukocyte antigen B27, and magnetic resonance imaging (MRI) scans revealed localized edema around the bilateral sacroiliac joint bone marrow. Upon confirmation of AS, rheumatologists recommended a tailored treatment regimen. Subsequently, the patient managed his condition with subcutaneous administration of recombinant human tumor necrosis factor (TNF)- α receptor II: Immunoglobulin G Fc fusion protein, leading to a reduction in lumbosacral pain. Lumbosacral pain recurred 10 d before the patient's hospital admission without a clear cause. Despite orally taking aceclofenac at a dosage of 100 mg twice daily, the pain persisted and was not alleviate.

History of past illness

He had no notable past medical history.

Personal and family history

No significant medical findings were identified in the patient's personal history or family background.

Physical examination

The physical examination confirmed tenderness and percussive pain in the left sacroiliac joint. The Schober test recorded a value of 5 cm, with a finger-to-ground distance of 30 cm, a measured pillow wall distance of 0 cm, and a chest expansion of 4 cm. The physiological curvature of the spine was within the normal range, and no tenderness was detected within the cervical, thoracic, and lumbar spinous processes, vertebral bodies, and paravertebral bodies.

Laboratory examinations

Elevated levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) indicated inflammation, while blood routine tests, liver and kidney functions, blood coagulation functions, and a routine urinalysis showed values within the normal range. Subsequent T-SPOT.TB and tumor marker tests were conducted to detect tuberculosis infection and prepare for the use of biological agents. The T-SPOT.TB result was negative, but alpha-fetoprotein levels were slightly elevated. However, routine stool examination revealed the presence of *C. sinensis* eggs (Figure 1).

Imaging examinations

The MRI scan of the sacroiliac joint displayed bone marrow edema in the left sacroiliac joint (Figure 2A and B). A subsequent colonoscopy indicated congestion in the descending colon, sigmoid colon, and rectum (Figure 3). No liver abnormalities were observed in the upper abdominal computed tomography.

FINAL DIAGNOSIS

Considering the patient's symptoms, physical examination, laboratory tests, and imaging results, the final diagnosis was AS coexisting with *C. sinensis* infection.

TREATMENT

Based on the patient's medical history, he had consumed uncooked freshwater fish the month before hospital admission. Therefore, praziquantel was administered orally at a dosage of 210 mg/kg/d, three times daily for 3 d.

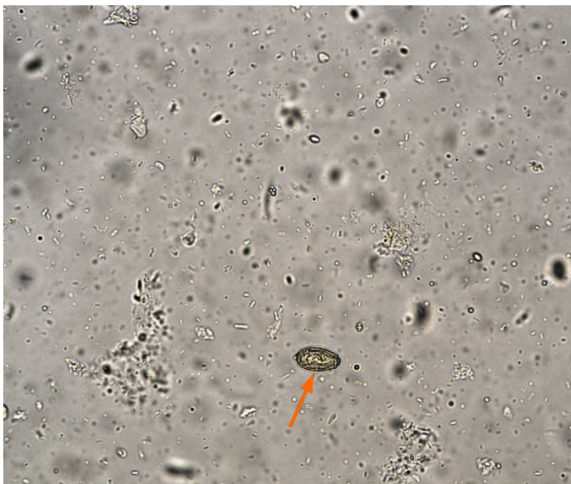
OUTCOME AND FOLLOW-UP

One week later, a post-treatment fecal examination showed no *C. sinensis* eggs, and both ESR and CRP levels were normal. Notably, the lumbosacral pain had also subsided, and no *C. sinensis* eggs were detected in the three subsequent follow-up visits. The MRI indicated a reduction in bone marrow edema around the left sacroiliac joint after 4 months (Figure 2C and D).

DISCUSSION

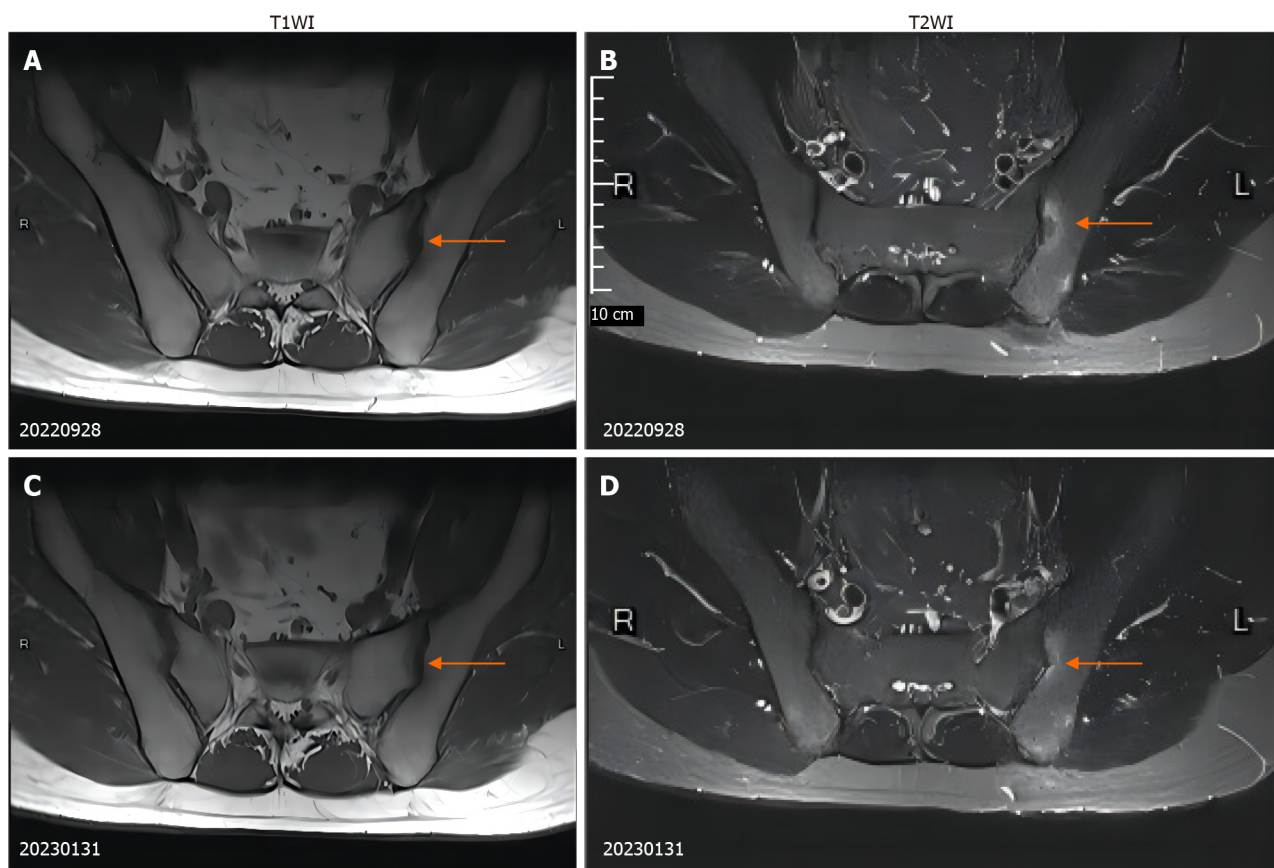
The prevalence of AS in China is currently 0.29%, showing an upward trend. Sex-based differences in prevalence have been observed, with males exhibiting a prevalence rate 2.8 times higher than that of females[11]. The patient was diagnosed with AS 10 years ago and achieved a stable health condition following treatment with biologicals. Before the onset of backache, the patient ate uncooked freshwater fish, and *C. sinensis* eggs were detected. Both laboratory and imaging tests revealed an active AS disease. Concurrently, lumbosacral pain symptoms notably improved after insecticidal treatment, and relevant laboratory findings demonstrated improvement. Thus, there is speculation about the potential association between disease activity and *C. sinensis* infection.

Recent reviews have suggested that AS might coexist with various parasitic infections. Some researchers have reported the occurrence of AS alongside mucosal leishmaniasis, *Strongyloides stercoralis*, and *Toxocara canis*[12-14]. A study emphasized the potential risk of latent infection reactivation in individuals undergoing immunosuppressive anti-TNF treatment[12]. Additionally, another study supported a notable link between *C. sinensis* infection and immune suppression, influenced by gender dynamics[15]. Notably, AS patients with parasitic infection may undergo treatment using non-steroidal anti-inflammatory agents. However, administering corticosteroids is contraindicated until insecticidal treatment has been initiated[13].



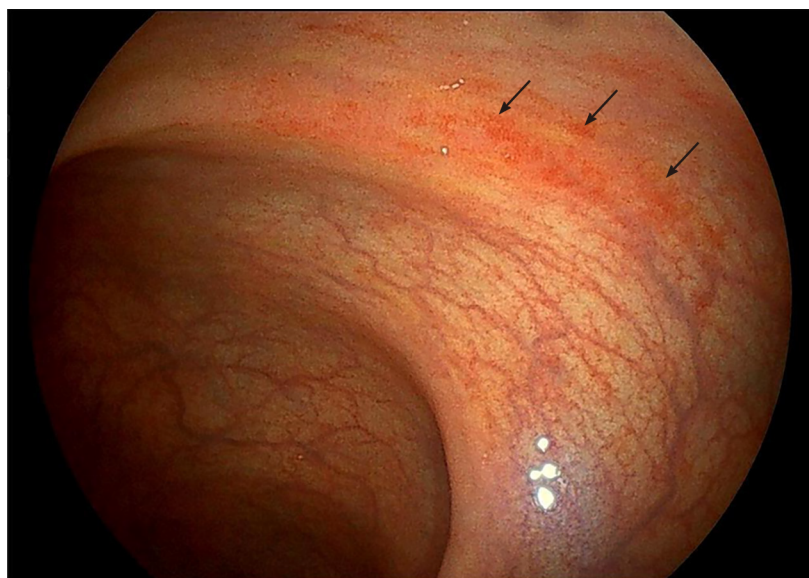
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Figure 1 Routine stool examination. On September 29, 2022, the presence of *Clonorchis sinensis* eggs (arrow) was confirmed through microscopic examination of stool samples during hospitalization.



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Figure 2 Magnetic resonance imaging of the sacroiliac joint. A: Axial T1-weighted magnetic resonance imaging (MRI) of the sacroiliac joint showing bone marrow edema in the left sacroiliac joint (September 28, 2022); B: T2-weighted MRI of the sacroiliac joint showing bone marrow edema in the left sacroiliac joint. The patient's condition at the time of admission indicates the presence of inflammation and edema in the left sacroiliac joint (September 28, 2022); C: Axial T1-weighted MRI of the sacroiliac joint showing a reduction in the area around the bone marrow edema in the left sacroiliac joint (January 31, 2023); D: T2-weighted MRI of the sacroiliac joint showing a reduction in the area around the bone marrow edema in the left sacroiliac joint. After treatment, follow-up at 4 months indicated a reduction in inflammation and edema of the sacroiliac joint (January 31, 2023).



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Figure 3 Colonoscopy image. On September 29, 2022, colonoscopy performed during hospitalization revealed scattered congestion in the descending colon, sigmoid colon, and rectum.

Microbial infections have shown a close correlation with autoimmune diseases, supported by evidence from clinical studies and animal experiments[16]. Earlier research indicated that *C. sinensis* might worsen arthritis progression, with this adverse effect potentially linked to changes in immune cell profiles and associated cytokine levels[17]. However, another study suggested that *C. sinensis*-induced protein could suppress new bone formation in a mouse model *in vivo* [18]. Notably, the role of *C. sinensis* infections in modulating arthritis symptoms is a multifaceted and complex phenomenon. Presently, it remains unclear whether there are differences in the pathogenic mechanisms of *C. sinensis* between humans and other animals. Hence, further research is crucial to explore this correlation.

This case report provided significant insights, an imbalance in the Th1/Th2 immune response might compromise the body's defense mechanisms against specific viral, bacterial, and parasitic pathogens, potentially heightening the risk of opportunistic infections[19]. Patients with rheumatic diseases are frequently treated with biologicals, such as anti-TNF, which increases susceptibility to opportunistic infections[20]. Therefore, rheumatologists must evaluate the patient's condition and manage the duration of biological treatment appropriately. Various microbial infections should be ruled out before initiating biologicals, particularly parasitic infections that might be overlooked due to improving environmental conditions. Early detection and treatment of these parasitic infections can significantly improve patient outcomes.

During the diagnosis of this case, some limitations were encountered. For instance, although colonoscopy suggested intestinal mucosal congestion, further pathological biopsies were not conducted. Given these limitations, advocating for continued monitoring of this patient through scheduled follow-up colonoscopy examinations is essential. If any signs of colonic abnormalities emerge during these assessments, then it is prudent to consider subsequent pathological biopsies for a more comprehensive evaluation.

CONCLUSION

Our findings suggest that *C. sinensis* infections could potentially trigger the exacerbation of AS. Clinicians should be mindful of the occurrence of *C. sinensis* infections, particularly in endemic areas when evaluating patients with rheumatic diseases. Despite providing significant insights, further studies are necessary to elucidate the mechanisms underlying the association between AS and *C. sinensis* infections.

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FOOTNOTES

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