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OPIS PRZYPADKU
CASE REPORT

Overlap of rheumatoid arthritis flare and *Yersinia*-induced reactive arthritis: A clinical case and literature review

Nakładanie się zaostrzenia reumatoidalnego zapalenia stawów i reaktywnego zapalenia stawów wywołanego przez *Yersinia* – opis przypadku i przegląd literatury

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ABSTRACT

Yersiniosis is a zoonotic bacterial disease caused by *Yersinia enterocolitica* (*Y. enterocolitica*) and *Yersinia pseudotuberculosis*, which can lead to the development of extraintestinal inflammatory complications, including reactive arthritis. In patients with rheumatoid arthritis (RA), *Yersinia* infection may mimic a disease flare or coexist with an exacerbation, thereby posing a significant diagnostic challenge. This study presents the case of a 61-year-old woman with seronegative RA in long-term clinical remission, who was hospitalized due to an abrupt worsening of joint symptoms, high fever, and gastrointestinal complaints. Laboratory tests revealed extremely elevated levels of inflammatory markers, including C-reactive protein, ferritin, and D-dimers, as well as neutrophilia with concomitant lymphopenia and significantly elevated titers of anti-*Y. enterocolitica* IgM, IgA, and IgG antibodies. Imaging studies revealed enlarged mesenteric lymph nodes, further supporting the infectious etiology. A comprehensive clinical and laboratory assessment indicated the coexistence of two parallel pathophysiological processes – an autoimmune exacerbation of RA and *Yersinia*-associated reactive arthritis. Initiation of the antibiotic therapy in combination with anti-inflammatory and immunomodulatory treatment resulted in significant clinical improvement and gradual normalization of laboratory parameters. This case highlights the importance of considering bacterial infections, particularly those caused by *Y. enterocolitica*, in the differential diagnosis of RA flares, especially when systemic inflammatory activity is disproportionately high relative to articular manifestations. Early diagnosis and initiation of etiological treatment can prevent disease progression and irreversible joint damage.

KEYWORDS

rheumatoid arthritis, infection, *Yersinia*, *Yersinia enterocolitica*

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STRESZCZENIE

Jersinioza jest zoonotyczną chorobą bakteryjną, wywoływaną przez *Yersinia enterocolitica* (*Y. enterocolitica*) oraz *Yersinia pseudotuberculosis*, która może prowadzić do rozwoju pozajelitowych powikłań zapalnych, w tym reaktywnego zapalenia stawów. U pacjentów z reumatoidalnym zapaleniem stawów (*rheumatoid arthritis* – RA) zakażenie *Yersinia* może naśladować rzut choroby lub współistnieć z jej zaostrzeniem, stanowiąc istotne wyzwanie diagnostyczne. W pracy przedstawiono przypadek 61-letniej pacjentki z seronegatywnym RA, pozostającej w długotrwałej remisji klinicznej, hospitalizowanej z powodu gwałtownego nasilenia dolegliwości stawowych, wysokiej gorączki oraz objawów ze strony przewodu pokarmowego. Badania laboratoryjne wykazały ekstremalnie podwyższone wskaźniki stanu zapalnego, w tym białka C-reaktywnego, ferrytyny i D-dimerów, a także neutrofilię z limfopenią oraz bardzo wysokie miana przeciwciał IgM, IgA i IgG przeciwko *Y. enterocolitica*. Badania obrazowe ujawniły powiększone węzły chłonne krezkowe, co dodatkowo przemawiało za tłem infekcyjnym. Całościowa analiza kliniczno-laboratoryjna wskazywała na nakładanie się dwóch równoległych procesów patofizjologicznych – autoimmunologicznego zaostrzenia RA oraz reaktywnego zapalenia stawów związanego z jersiniozą. Antybiotykoterapia w połączeniu z leczeniem przeciwzapalnym i immunomodulującym wpłynęła na istotną poprawę stanu klinicznego pacjentki oraz stopniową normalizację parametrów laboratoryjnych. Opisany przypadek podkreśla konieczność uwzględniania zakażeń bakteryjnych, zwłaszcza *Y. enterocolitica*, w diagnostyce różnicowej zaostrzeń RA, szczególnie w sytuacjach, gdy aktywność zapalna jest niewspółmiernie wysoka w stosunku do obrazu zmian w stawach. Wczesne rozpoznanie i wdrożenie leczenia przyczynowego mogą zapobiec progresji choroby oraz trwałym uszkodzeniom stawów.

SŁOWA KLUCZOWE

reumatoidalne zapalenie stawów, infekcja, *Yersinia*, *Yersinia enterocolitica*

INTRODUCTION

Yersiniosis is a rare zoonotic bacterial disease caused by two enteropathogenic Gram-negative bacilli of the *Yersinia* genus: *Yersinia enterocolitica* (*Y. enterocolitica*) and *Yersinia pseudotuberculosis* (*Y. pseudotuberculosis*). The reservoirs of these bacteria, which are related to *Salmonella* species, are pigs and other wild and domestic animals [1,2]. Infection in humans usually occur via the fecal-oral route, most often through contaminated food. Yersiniosis usually manifests as enteritis or enterocolitis with acute, self-limiting diarrhea (most commonly associated with *Y. enterocolitica*). It may also present as mesenteric lymphadenitis and inflammation of the terminal ileum (usually caused by *Y. pseudotuberculosis*), mimicking acute appendicitis [3,4,5]. Diarrhea is less common in infections caused by *Y. pseudotuberculosis* than by *Y. enterocolitica*. The least common manifestations are sepsis and metastatic abscesses. A hallmark of *Yersinia* infections is the presence of extraintestinal symptoms, such as reactive arthritis and erythema nodosum [4,6]. In the described case, the patient's *Yersinia* infection manifested as an exacerbation of rheumatoid arthritis (RA).

CASE REPORT

History and physical examination

A 61-year-old female patient, who was diagnosed with seronegative RA in 2021, presented with increasing neck pain accompanied by restricted mobility (numeric rating scale [NRS] 6–7/10), headache, and swelling of the knees and feet. Her medical history also revealed a 3-week period of abdominal pain, a sensation of abdominal fullness, and fever reaching up to 39.2°C. Outpatient laboratory testing showed a significantly elevated serum C-reactive protein (CRP) concentration >236.7 mg/L (reference range: <5 mg/L).

In the medical history, the patient reported concomitant thyroid nodules. She was the non-smoker and had been receiving long-term pharmacological treatment with methotrexate at a dose of 20 mg per week, folic acid, meloxicam, diclofenac, esomeprazole, as well as ibuprofen and paracetamol in the days prior to admission. The patient denied any known allergies; however, she reported recurrent mild urticaria. At the time of admission to the internal medicine ward, patient was conscious and retained logical contact. Physical examination revealed painful limitation of cervical spine mobility, as well as involvement of the hand, knee, and ankle joints. The patient's gait was unsteady, characterized by short, surfing steps. Edema and tenderness were observed in the thenar eminence, distal interphalangeal joints of both hands, both knees, and the right ankle and midfoot. Ulnar deviation of the fingers was also present. The distal interphalangeal joints and right midfoot were erythematous. The initial severity of symptoms was high, with a Disease Activity Score 28 (DAS28 CRP) of 7.74.

Laboratory tests

The laboratory test summarize key biochemical and hematological parameters measured in the diagnostic process. The detailed findings are presented in Table I.

Table I. Laboratory test results

Parameter	Result	Reference range
CRP – initial	227.0 mg/L	<5 mg/L
CRP – follow-up	97.3 mg/L	
Leukocytes (WBC)	9.76 × 10³/µL	4.0–10.0 × 10³/µL
Neutrophils	7.86 × 10³/µL	2.0–7.5 × 10³/µL
Lymphocytes	0.87 × 10³/µL	1.0–4.0 × 10³/µL
Monocytes	0.93 × 10³/µL	0.2–0.8 × 10³/µL
RBC	3.55 × 10⁶/µL	4.2–5.4 × 10⁶/µL
PLT	515 × 10³/µL	150–450 × 10³/µL
ESR	78 mm/h	<20 mm/h
Total protein	5.79 g/dL	6.4–8.3 g/dL
HDL cholesterol	35 mg/dL	≥50 mg/dL
D-dimer	5074.99 ng/mL	<550 ng/mL (FEU)
Ferritin	733 ng/mL	13–150 ng/mL
Total IgE	847 ng/mL	<240–360 ng/mL
ANA – PCNA antibodies	1.20	Negative: <1.0
Yersinia IgM	4.5	Positive: >1.1
Yersinia IgA	29.3	Positive: >1.1
Yersinia IgG	8.2	Positive: >1.1

CRP – C-reactive protein; WBC – white blood cells; RBC – red blood cells; PLT – platelets; ESR – erythrocyte sedimentation rate; HDL – high-density lipoprotein; FEU – fibrinogen equivalent units; ANA – anti-nuclear antibodies; PCNA – proliferating cell nuclear antigen; IgM – immunoglobulin M; IgA – immunoglobulin A; IgG – immunoglobulin G

Diagnostic imaging

A contrast-enhanced computed tomography (CT) of the abdomen and pelvis revealed several mildly enlarged mesenteric lymph nodes present in the right lower abdomen, with a maximum diameter of 7 mm. A comparative anteroposterior radiography of the upper limbs showed degenerative changes in the left first carpometacarpal joint, as well as narrowing of the distal interphalangeal joint spaces II–V bilaterally, particularly affecting the second and third fingers, more pronounced on the right side. These findings are suggestive of an early erosive form of osteoarthritis (erosive osteoarthritis) (Figure 1). A non-contrast spiral chest CT, performed with high-resolution reconstruction (HRCT), demonstrated pleural adhesions and thickening in the lung apices, subtle fibrotic-atelectatic changes in the basal regions of both lungs and in segment 8 of the left lung along the oblique interlobar fissure. Additionally, single nonspecific pulmonary micronodules were present bilaterally. A non-contrast CT of the paranasal sinuses demonstrated slight protrusion of the carotid canals into the posterior parts of the sphenoid sinus, as well as exudative changes in several air cells of the left mastoid process, ccompanied by a reduction in its volume and marked sclerotic thickening of its inferolateral bony walls, most likely representing chronic changes.

Treatment

Immediately upon admission to the Department of Internal Medicine, empirical antibiotic therapy with a third-generation cephalosporin (cefotaxime) was initiated, following the collection of blood and urine samples for microbiological testing. Later, cefotaxime was replaced with levofloxacin (500 mg/day for 10 days) – due to negative cultures, the patient's medical history, and suspected *Yersinia* infection.

Administration of nonsteroidal anti-inflammatory drugs (diclofenac and meloxicam) was continued and systemic corticosteroid therapy was initiated, starting with oral prednisone, followed by intravenous methylprednisolone pulse therapy (250 mg, 125 mg, and 125 mg on three consecutive days). The methotrexate dose was temporarily increased to 25 mg per week. Inflammatory markers, including CRP, showed a gradual decline. Furthermore, a significant improvement in the patient's clinical condition was observed, along with resolution of peripheral joint complaints and overall improvement in general condition, with disease activity decreasing to a low level (DAS28 CRP score 2.75 following the antibacterial treatment).

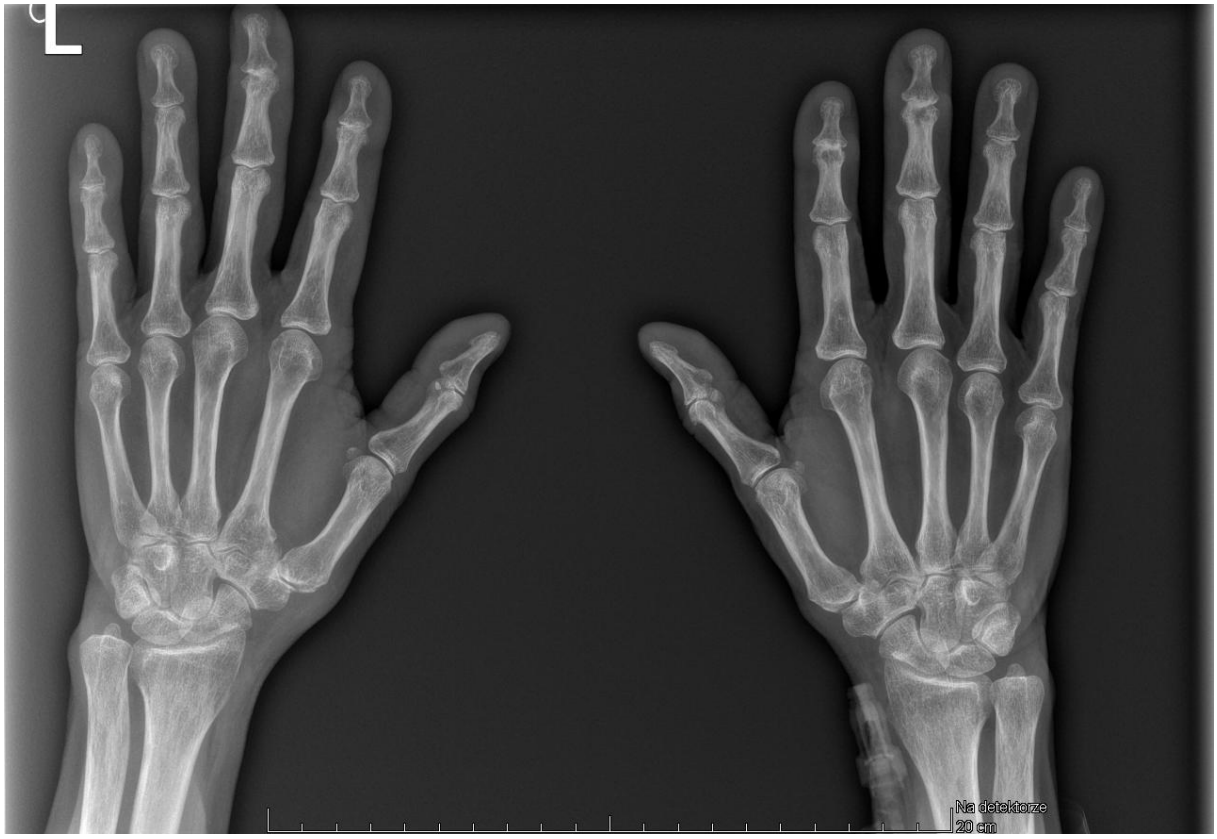

Fig. 1. Hands X-ray showing degenerative changes characteristic for early stage of rheumatoid athritis

DISCUSSION

In this case, we did not attempt to reassess or challenge the prior diagnosis of seronegative arthritis, as it had been established four years earlier and had demonstrated a sustained and convincing therapeutic response to methotrexate and nonsteroidal anti-inflammatory drugs. The patient remained in long-term clinical remission under disease-modifying therapy, which confirms the accuracy of the original diagnosis. Therefore, in this report, we focus mostly on the newly developed reactive arthritis.

Although the presented case exhibited clinical features typically associated with a flare of RA – including persistent, chronic pain in the hands and feet, marked morning stiffness, and a documented history of autoimmune disease with prior response to immunomodulatory therapy – the overall clinical picture could not be fully explained by a classic RA exacerbation. While such manifestations might initially suggest a relapse of disease, the concomitant presence of findings indicative of an active infectious process argues against this interpretation [7,8].

Conversely, several clinical and laboratory parameters strongly supported a reactive, *Yersinia*-associated arthritis. These included a dynamic and pronounced increase in acute-phase reactants, significantly elevated titers of anti-*Yersinia* antibodies (IgM/IgA/IgG), and a hematological profile atypical for isolated RA, characterized by neutrophil predominance and lymphopenia. Importantly, the degree of systemic inflammatory activity observed in biochemical assays was disproportionate to the severity of articular involvement alone, a pattern more commonly described in reactive or infection-related arthritis [2,4,5,9].

In summary, a comprehensive clinical and laboratory evaluation indicates that the disease presentation did not correspond to a typical RA flare. Extremely elevated inflammatory markers (CRP, ferritin, D-dimers), neutrophilia with concomitant lymphopenia, and positive IgM/IgA/IgG serology against *Y. entecolitica* suggested an infection-driven inflammatory process disproportionate to rheumatoid disease activity [10,11]. Ultimately, the clinical course supported the coexistence of two parallel pathophysiological processes: an autoimmune component related to RA, manifested by chronic and progressively worsening joint symptoms, and an infectious component associated with yersiniosis, responsible for excessive immune activation and a pronounced acute-phase response. Clinical improvement following antibiotic therapy in combination with anti-inflammatory treatment further substantiated the involvement of the infection in the disease process, while not excluding a concomitant RA flare. This observation supports a clinical model of overlapping autoimmune and infection-driven inflammatory mechanisms.

CONCLUSIONS

In patients with RA, *Yersinia* infection requires prompt diagnosis and immediate initiation of anti-inflammatory therapy to prevent erosive joint changes. This approach aims not only to cure the infection and alleviate its associated symptoms but also to limit the progression of RA and prevent further joint destruction characteristic for this disease.

Use of AI tools statement

AI tools (ChatGPT) were used to support the assessment and correction of the text for clarity and grammar.

Authors' contribution

Study design – O. Połeć, A. Guzowska, E. Pękala, A. Stanek

Data collection – E. Pękala

Manuscript preparation – O. Połeć, A. Guzowska, E. Pękala, A. Stanek

Literature research – O. Połeć, A. Guzowska

Final approval of the version to be published – O. Połeć, A. Guzowska, E. Pękala, A. Stanek

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