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Case Report

Seronegative spondyloarthropathy (reactive arthritis) fourteen days following E. coli UTI: Case report

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Abstract

Reactive arthritis (ReA) is a post-infectious autoimmune condition classified as a seronegative spondyloarthritis (SpA). The current case report presents a 30-year-old female returned for follow-up visits after an acute onset of back pain that progressed to joint swelling and tenderness in both knees, and excruciating pain in her heels and the bottom of her feet four weeks ago. Two weeks prior to the onset of symptoms, the patient was treated for a urinary tract infection (UTI). Due to the symptoms and the inability to ambulate caused by feet pain, the patient was required to admit to a hospital for further evaluation. This case report depicts a unique presentation of ReA following UTI, and the discussion section aiding healthcare professionals in the diagnosis and management of ReA and patient education on ReA and disease course.

Introduction

Reactive arthritis (ReA), previously termed Reiter syndrome, is an autoimmune seronegative spondyloarthritis (SpA) that may develop several days to weeks following a bacterial gastrointestinal or urogenital infection. A more uncommon presentation of ReA is following an *Escherichia coli* urinary tract infection (UTI). Since there are no specific diagnostic laboratory tests for ReA, the diagnosis is based on patient history and physical examinations. ReA is associated with HLA-B27 (50-80%) and its subtypes, a class I major histocompatibility complex. HLA-B27 also has a strong association in other SpA conditions such as ankylosing spondylitis, anterior uveitis, psoriatic arthritis, and inflammatory bowel disease (IBD) associated arthritis. Clinical features include acute onset oligoarthritis or polyarthritis, conjunctivitis or iritis, and dermatologic manifestations following diarrheal or urogenital infection. In this case report, we describe a 30-year-old female who developed ReA two weeks afterward an UTI condition.

Case Report

A 30-year-old Hispanic female returned to the clinic, after one month, for a follow up visit after being admitted to the hospital with back pain, joint swelling, tenderness in knees, and pain in heels bilaterally. The symptoms started as lower back pain initially and progressively migrated towards her knees and heels experiencing joint swelling and tenderness in knees bilaterally and excruciating pain in her heels, hindering her ability to ambulate. The patient was transported to the emergency room with a wheelchair and was admitted for further examinations. She stated that she has never experienced these symptoms prior in her life. During the admission, her labs showed Hgb 10.5, mean corpuscular volume (MCV) 78, red blood cell distribution width (RDW) 27.8, white blood cell (WBC) 13.4, erythrocyte sedimentation rate (ESR) 105, rheumatoid factor 20, C-reactive protein (CRP) 19.6, antibody-positive for anti-scl 70, negative for anti-DsDNA, and negative for Erythrocyte sedimentation rate (ESR) and anti-CCP (cyclic citrullinated peptide) and ANA AB with reflex titer (Table 1). Her symptoms were managed with IV steroids and 2 units of blood transfusion, then she was discharged on prednisone 10 mg PO twice daily and ferrous sulfate 325 mg once a day. Eleven days following admission, repeated labs showed ESR 5 and CRP 0.4. During her most recent visit, 4 weeks after her intial episode the patient feels well and denies any pain or swelling or difficulty of ambulating. On the other hand, she complains of dry peeling skin on her knees and ankles. The patient denies any changes in her fingertips when exposed to cold or hot temperatures, oral ulcers, or rash. Pt also denies any history of recent travel. She has received both doses of her COVD-19 vaccination. The patient has not any significant past medical history, other than a UTI two weeks prior to the onset of her symptoms and was treated with cephalexin and completed

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Table 1. Patient's during admission on 04/26/2021

Laboratory findings	
Immunology labs	
Sedimentation rate	105 mm/h
CRP	19.6 mg/d
Rheumatoid factor, quant	20 IU/mL
Uric acid	5.2 mg/dL
Anti-CCP	Negative
ANTI-dsDNA	Negative
ANA AB with reflex titer	Negative
Anti-scl 70	Positive
CBC w/Auto diff with platelets	
WBC	(H) 13.4 K/UL
RBC	4.68 M/UL
Hemoglobin	(L) 10.5 G/DL
Hematocrit	36.5 %
MCV	(L) 78 fL
MCH	(L) 22.4 PG
MCHC	(L) 28.8 G/DL
RDW	(H) 27.8 %
Neutrophils	(H) 82.3 %
Lymphocytes	(L) 12.7 %
Monocytes	(L) 2.5 %
Eosinophils	0.8 % %
Basophils	0.0 %
Myelocytes	(H) 1.7 %
Platelet count	329 K/UL
Absolute neutrophils	(H) 11.03 K/UL
Metabolic panel	
Creatinine	0.52 mg/dL
eGFR	149 mL/min 1.73
BUN	13 mg/dL
B/C ratio	25
Glucose	(H) 116 mg/dL
Sodium	140 mEq/L
Potassium	4.0 mEq/L
Chloride	102 mEq/L
Carbon dioxide	26 mEq/L
Protein total	7.3 mg/dL
Albumin	(L) 3.4 g/dL
Globulin	(H) 3.9 g/dL
A/G ratio	(L) 0.9
Calcium level	8.8 mg/dL
ALT (SGPT)	18 U/L
AST (SGOT)	16 U/L
ALP	79 U/L
TSH	(H) 4.95

CRP: C-reactive protein; Anti-CCP: Anti cyclic citrullinated peptide antibodies; ANA AB: antinuclear antibody; Anti-dsDNA: Anti-double-stranded DNA; Anti-scl 70: Anti-Topoisomerase I; WBC: White blood cell, MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; TSH: thyroid stimulating hormone; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; eGFR: estimated glomerular filtration rate; BUN, blood urea nitrogen.

the course of her treatment (Table 2). She has a family history of rheumatoid arthritis (RA) and Systemic lupus erythematosus (SLE) in her sister, psoriasis in her mother, and SLE in her cousin. She lives a sedentary lifestyle and describes herself as not taking care of her health as she should. She is employed and works at a nail salon. The patient has no known drug allergies. She does not smoke or use illicit drugs but does drink wine occasionally. Now, she is completing treatment with the medications she was discharged with, prednisone and ferrous sulfate. Upon physical examination, the patient appears well and she is in no apparent distress. She has not tenderness to palpation of her knees or ankles. Visible dry peeling skin was noticed on her knees and ankles bilaterally. A diagnosis of peripheral spondyloarthropathy is suspected and the patient was further managed with sulfasalazine 1 g twice daily. Her prednisone was changed from 10 mg PO twice daily to 10 mg once a day. During the patient's two-week follow up her symptoms had drastically improved and repeated ESR and CRP examinations showed significant improvements, fitting the reference range.

Discussion

ReA is a post-infectious autoimmune condition, which manifests following exposure to infectious agents[1] such as *Yersinia, Salmonella, Shigella, Campylobacter, Clostridium difficile* causing gastrointestinal illness, and *Chlamydia trachomatis* causing urogenital infection.[1] Even though it is rare, but there are ReA cases reported to be occurred following a UTI condition caused by *E.coli*.[1-3] Other bacterial agents affecting the urinary or genital tract which has been reported as the cause of ReA are *Ureaplasma urealyticum, Enterococcus faecalis, Mycoplasma genitalium, Neisseria gonorrhoeae,* and *Gardnerella vaginalis*.[1,4,5] ReA is classified as SpA alongside other autoimmune ailments such as ankylosing spondylitis, anterior uveitis, psoriatic arthritis, and IBD associated arthritis due to their associations with HLA-B27. While HLA-B27 is reported to be 60-80% prevalent in subjects with ReA[4,5] but it does not mean that the absence of this factor excludes suspicions of ReA. Moreover, HLA-B27 should not be employed as a specific diagnostic marker.[4] Since ReA is a clinical complaint, it is essential to obtain a full history of any previous symptoms or illness, days to weeks prior to the onset of ReA.[4] The common clinical features of ReA are triad of urethritis, arthritis, and conjunctivitis, but most subjects do not present with the classic trio, as in this case conjunctivitis, iritis, or other ocular abnormalities were not diagnose.[4] Other notable manifestations that may occur are sacroiliitis (lower back pain), enthesitis (pain in heels or bottom of the feet), and dactylitis (painful finger swelling). The data on epidemiology and incidence of ReA is diverse globally, some of these diversities are certain regions may have different diagnostic criteria, differences in clinical presentation of disease, the absence of disease biomarkers,

Table 2. Patient's laboratory findings during the preceding episode of UTI on 04/15/2021

Laboratory Findings	
Urinalysis	
Urine turbidity	Slight
Urine color	Yellow
UA pH	6.0
Urine specific gravity	1.012
Urine blood	(A) Moderate
Urine ketones	Negative
Urine protein	Negative
Urine urobilinogen	(H) 4.0
Urine leukocyte esterase	(A) Small
Urine WBC/HPF	2
Urine bacteria	(A) Moderate
Urine squamous Epithelial/LPF	Occasional
Urine mucus	Few
Chemistry panel	
Creatinine	0.52 mg/dL
eGFR	128 mL/min 1.73
BUN	9 mg/dL
B/C ratio	17
Glucose	91 mg/dL
Protein total	(H) 8.8 mg/dL
Albumin	(L) 3.1 g/dL
Globulin	(H) 5.7 g/dL
A/G ratio	(L) 0.6
Calcium level	(L) 8.4 mg/dL
ALT (SGPT)	15 U/L
AST (SGOT)	10 U/L
ALP	75 U/L
CRP	(H) 31.6
CBC with platelets	
WBC	7.0 K/UL
RBC	(L) 4.17 M/UL
Hemoglobin	(L) 7.3 g/dL
Hematocrit	(L) 26.1 %
MCV	(L) 62.5 fL
MCHC	(L) 28.2 g/dL
RDW	(H) 21.8 %
MPV	8.5 fL
Platelet	294 K/UL
Segmented neutrophils	64.5 K/UL
Lymphocytes	27.1 K/UL

CRP: C-reactive protein; A WBC: White blood cell, MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RDW: Red cell distribution width; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; eGFR: estimated glomerular filtration rate; BUN, blood urea nitrogen; HPF, high-power-field. LPF: lower power field

diverse possibility of exposure to infectious agents in different parts of the world, and differences in hereditary predisposition.[5] ReA is reported to occur at an incidence of 0.6 to 27 per 100 000 and is more notably known to occur in adult males in their 20's and 30's.[4,5] With a low incidence rate, ReA is a rare occurrence, making this case notably unique as it occurred in a female aged 30 following an *E. coli* confirmed UTI fourteen days prior to her ReA symptom onset, which is not a classic presentation.[4] The disease course may be limited to several weeks, but it is not unusual for the extra-articular disease to persist for prolonged periods.[6] Treatment is considered on a case-by-case basis as the post-infectious autoimmune condition varies depending on the patient, e.g. some of the patients may experience a self-limiting disease course, while other may need a treatment procedure.[4] The aim of the treatment will be to provide symptomatic relief and prevent further complexities. During the acute phase, primary treatment with Non-steroidal anti-inflammatory drugs (NSAIDs) should be initiated.[4] For patients suffering from enthesitis and/or oligoarthritis, as was seen in this case, local or intra-articular glucocorticoids can be utilized.[4,5] However, the addition of systemic glucocorticoids for severe cases of ReA polyarthritis is recommended, but there are some reports showing its contraindication.[4,5] About the case reported in this study, the patient was managed with sulphasalazine, as disease-modifying antirheumatic drugs (DMARDs) can be given in the acute state and for chronic disease courses.[4,5] The choice to initiate sulphasalazine was due to the involvement of peripheral manifestations in our patient and its indication and efficacy in such presentation.[5] Additional DMARDS; hydroxychloroquine, methotrexate, and azathioprine may be prescribed for patients suffering more chronic arthritis unresponsive to NSAIDs.[4]

Conclusion

In conclusion, we have reported a unique case of UTI provoked seronegative spondyloarthritis (Reactive arthritis) in a 30-year-old female prompting an ER visit due to acute onset back pain, joint swelling and tenderness of both knees, and excruciating pain in her heels and the bottom of her feet fourteen days following an *E. coli* confirmed UTI. Although commonly seen following a bacterial diarrheal illness and urogenital infection, lower back pain and migratory joint pain following a UTI should prompt clinical suspicion for ReA.

Author Contributions
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Conflict of Interest
The authors declare no competing interests.

Informed Consent
Written informed consent was obtained from the patient.

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