

Hand-Foot and Mouth Disease and Reactive Arthritis: An Unusual Paediatric Case

Tas Tugba¹, Baltaci Neslihan¹, Yilmaz A. Esra¹, Yuksel C. Nuket¹ and Eminoglu Sancar²

ABSTRACT

Reactive arthritis is defined as arthritis that occurs during or after an extraarticular infection. It is mostly difficult to determine the causative agent that causes inflammation in the joints. Initially, *salmonella*, *shigella*, *chlamydia* and *yersinia* were considered to be pathogenic agents. But recently, in addition to demonstrated viral and bacterial agents, there are also other cases of reactive arthritis after vaccinations with Rubella and Influenza. Herein a 3-year old boy is reported with reactive arthritis of left knee that developed shortly after hand-foot and mouth disease. This report represents the first detailed description of a paediatric case in literature with reactive arthritis following hand-foot and mouth disease.

Key Words: Arthritis. Reactive arthritis. Hand-foot and mouth disease.

INTRODUCTION

Reactive arthritis is defined as a form of arthritis that develops during or after an extra-articular infection. The cause of the inflammatory response in joints cannot usually be determined. Common symptoms of arthritis are: limitation of movement, warmth, redness, pain, and swelling of joint. Previously, only bacterial gastrointestinal or genitourinary tract infections with causative agents of *salmonella*, *shigella*, *chlamydia* and *yersinia* etc. were thought to be involved in the etiology of reactive arthritis.¹ But now different etiologic agents of different extra-articular infections, other than gastrointestinal or urinary tract infections, have been demonstrated as giving rise to reactive arthritis. A majority of postinfectious arthritis may also occur during or after extra-articular viral infections with rubella, parvovirus B19, and hepatitis B. There are also reported cases of reactive arthritis after immunisation with rubella and influenza vaccines.^{2,3}

Herein we report a case of reactive arthritis associated with a recent history of hand-foot and mouth disease.

CASE REPORT

A 3-year boy was presented to our emergency department with complaints of restlessness and constant crying, especially at nights for 3 days. On physical examination, vital signs were normal. The patient's all growth parameters were normal, too. There were rare recovering cutaneous eruptions on palms and

soles, with simultaneous mucocutaneous vesiculo-ulcerative lesions in oropharynx and on soft palate. During examination, the patient had a painful facial expression and was unable to stand on his left leg for a long time. His lower extremity examination revealed swelling, redness, tenderness, and warmth with palpation on left knee. The circumferential measurements of the left and right knee in similar positions of extension were 16.5 cm and 15 cm, respectively. We assessed the left knee for synovial effusion by eliciting the bulge sign and performing ballottement. The remaining physical examination was normal. At that time, the values of the white blood cell, hemoglobin (Hb), hematocrit (Hct), and platelets (PH) were in normal ranges for his age (WBC : 12,500/mm³, Hg: 12 g/dL; Hct: 36.2%, Plt: 46,000/uL). Remaining blood counts, liver and kidney parameters were in normal ranges. The diagnostic laboratory tests for rheumatologic diseases like erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), anti-nuclear antibodies (ANA), anti-streptolysin O titer (ASO), rheumatoid factor (RF), were also in normal ranges or negative [ASO: 104 IU/mL (0-200 IU/ml), CRP: 3,4 mg/l (0-5 mg/L), ESR: 35 mm/hr (0-19 mm/hr), RF: 6,2 U/mL (0-14 U/mL)]. With these clinical and laboratory findings and recent history of a viral infection, diagnosis of reactive arthritis was made. He was treated with ibuprofen (40 mg/kg/d). After one week, he was symptom-free with normal physical examination.

DISCUSSION

The reactive arthritis is a type of arthritis with acute onset and nonsuppurative in nature. The causative agent cannot be isolated from the synovial fluid. We did not perform a synovial fluid analysis. In other words, it is a type of aseptic arthritis seen during or after an extra-articular infection. The mechanism of inflammation in joints is quite complex and not fully understood.^{2,4,5}

Department of Paediatric¹ / Paediatric Cardiology², Faculty of Medicine, Turgut Ozal University, Ankara, Turkey.

Correspondence: Dr. Ayse Esra Yilmaz, Assistant Professor, Department of Paediatric, Faculty of Medicine, Turgut Ozal University, Ankara, Turkey.

E-mail: aysesra@yahoo.com

Received: July 08, 2015; Accepted: February 18, 2016.

Some suggest that infection triggered cell-mediated immune response plays the major role in the etiology. According to this theory, the structural similarity of the histocompatibility antigen (HLA) B27 and certain bacterial antigens may cause immune response. On the other hand, it has been reported in some studies that humoral immunity may also play a role in the development of reactive arthritis. In a study, investigators found high titers of persistent IgM and IgG antibodies against the infectious agents in a group of patients who had reactive arthritis, while the remaining of the patients infected with same infectious agents had neither arthritis nor remarkable levels of IgM and IgG antibodies against that agent.^{2,6}

Although reactive arthritis may occur after viral infections, it has been thought that articular manifestations may be the result of a real viral intra-articular infection rather than representing post-infectious response. Likewise, antigen-antibody (Ag-Ab) type immune complexes were isolated from synovial fluid in hepatitis B and adenovirus infections and have been reported as possible factors in the pathogenesis of reactive arthritis.^{6,7} Diagnosis is established on the basis of a history of recently acquired extra-articular infection, positive cultures and microbiological investigations or only symptoms of rash and diarrhea, which may be sufficient. Use of non-steroidal anti-inflammatory drugs in first step, often in high dose, is usually of benefit for relief of arthritis and pain.^{2,8,9} Interval between infection and reactive arthritis is usually 2 - 4 weeks.¹⁰ According to literature, the causative agent is not isolated in 50% of cases, and 25% of cases have a history of asymptomatic infection.^{3,9} Hand-foot and mouth disease is characterised by fever, mucocutaneous vesiculo-ulcerative lesions in oropharynx and cutaneous eruptions on palms and soles in infants and children. Coxsackie virus A6 and Enterovirus 71 have been reported as the most common pathogens that cause hand-foot and mouth disease.^{10,11} This is the first reported paediatric case with reactive arthritis developing after hand-foot and mouth disease. An adult patient has been reported earlier with refractory fever, hand-foot and mouth disease, and systemic arthritis. They demonstrated Coxsackie virus A 16 as causative agent.⁴ Most of authors suggest that reactive arthritis is a kind of aseptic arthritis and can be seen during or after an extra-articular infection. In this case, we did not

demonstrate Coxsackie virus but the diagnosis of arthritis was made immediately after hand-foot and mouth disease. Lack of increase in acute phase reactants suggests that it might have been reactive arthritis associated with viral infection. Thus, we excluded bacterial and rheumatologic causes. It is not possible to suggest that arthritis is a complication of hand-foot and mouth disease with only one paediatric case. However, clinical flares of reactive arthritis, after viral infections, occur rarely; indicating that host factors and other environmental factors play important roles. In this report, we aimed to enhance the awareness of the clinicians to consider a recently acquired hand-foot and mouth disease, which also may cause epidemics, in the differential diagnosis of reactive arthritis.

REFERENCES

1. Rosner BM WD, Höhle M. Clinical aspects and self-reported symptoms of sequelae of yersinia enterocolitica infections in a population-based study. *BMC Infect Dis* 2013; **13**:236.
2. Hannu T. Reactive arthritis. *Best Pract Res Clin Rheumatol* 2011; **25**:347.
3. Townes JM. Reactive arthritis after enteric infections in the United States: The problem of definition. *Clin Infect Dis* 2010; **50**:247-54.
4. Masami Toya YE. Letter: An adult case of severe hand-foot-mouth disease accompanying persistent fever and systemic arthritis. *Dermatol Online J* 2012; **18**:14.
5. Hannu T IR, Granfors K. Reactive arthritis or post-infectious arthritis? *Best Pract Res Clin Rheumatol* 2006; **20**:419-33.
6. Cox CJ, Gaston JS. Investigation of infectious agents associated with arthritis by reverse transcription PCR of bacterial rRNA. *Arthritis Res Ther* 2003; **5**:1-8.
7. Moore TL. Specific viruses that cause arthritis. Uptodate. <http://www.uptodate.com/contents/specific-viruses-that-causearthritis2011>.
8. Ravinder GK. Reactive arthritis in children. *JK Sci* 2007; **9**:109-10.
9. Bruck NGM, Pessler F. Transient oligoarthritis of the lower extremity following influenza B virus infection: Case report. *Pediatr Rheumatol* 2010; **8**:4.
10. Bruck NGM, Pessler F. Transient Oligoarthritis of the lower extremity following influenza B virus infection: Case report. *Pediatr Rheumatol* 2010; **8**:4.
11. Beh Poay Ling FAJ. Detection and characterization of viruses causing hand, foot and mouth disease from children in Seri Kembangan, Malaysia. *Trop Biomed* 2014; **31**:654-62.

