LETTER TO THE EDITOR

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RHEUMATOID FACTOR: WHAT GOOD FOR PEDIATRIC RHEUMATOLOGY?

Mustafa Çakan[1], Merve İşeri Nepesov[2]

[1]University of Health Sciences Turkey, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Clinic of Pediatric Rheumatology, İstanbul, Turkey

[2]University of Health Sciences Turkey, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Clinic of Pediatric Infectious Diseases, İstanbul, Turkey

To editor:

Rheumatoid factor (RF) is an immunoglobulin M molecule directed against the fragment crystallizable portion of immunoglobulin G. It is mainly found in patients with rheumatoid arthritis, with approximately 80-90% of patients with rheumatoid arthritis testing positive for RF (1,2). Juvenile idiopathic arthritis (JIA) is the most common type of chronic arthritis in childhood. It is a diagnosis of exclusion, in which other causes of arthritis should be excluded, and arthritis should be present for at least 6 weeks. JIA has seven subtypes, and RF-positive polyarticular JIA comprises only 5% of children with JIA (3,4). RF positivity can also be found in other rheumatic diseases, such as Sjögren disease, systemic sclerosis, mixed connective tissue disease, cryoglobulinemia, and granulomatosis with polyangiitis. Additionally, RF may be present in infectious diseases like hepatitis B, hepatitis C, Epstein-Barr virus, and subacute bacterial endocarditis. Moreover, around 3-8% of healthy children may test positive for RF, especially after infection (1,2).

In pediatric rheumatology, no single diagnostic test is available for any disease. Laboratory tests are used to support the clinical diagnosis given to a patient after history taking and physical examination (1,2,5). Herein, we present 4 cases that were referred to pediatric rheumatology due to RF positivity with the provisional diagnosis of RF-positive polyarticular JIA and discuss the outcomes of the children. A summary of the cases is presented in Table 1.

A 15-year-old boy was referred to our pediatric rheumatology department for right knee pain with RF positivity [RF 138 IU/mL (normal: 0-14)]. The child had right knee pain for 2 weeks. He had febrile diarrhea for 7 days and had been taking antibiotics for 10 days a week before the symptoms started. The family did not report any rash, joint swelling, or fever during the visit. The child did not have arthritis in any joint but exhibited point tenderness in the superior medial part of the proximal tibia. Acute phase reactants were elevated [C-reactive protein (CRP): 88 mg/L (normal 0-5)], erythrocyte sedimentation rate (ESR): 65 mm/hr (normal: 0-15)]. The clinical picture was compatible with subacute osteomyelitis, and an orthopedic consultation was made. An X-ray of the right knee was normal, and magnetic resonance imaging revealed diffuse medullary edema (hyperintense on T2, hypointense on T1) in the upper two-thirds of the tibia with involvement of adjacent soft tissue. The child underwent surgery, and *Staphylococcus aureus* was isolated from the pus. He received antibiotic treatment for a month and was discharged without sequelae.

A 13-year-old girl was referred to pediatric rheumatology for joint pain in the hands for 2 months and RF positivity (RF: 52 IU/mL). She described pain in her hands and fingers with morning stiffness. Physical examination revealed arthritis in the bilateral wrists, elbows, 2nd and 3rd metacarpophalangeal and proximal

Address for Correspondence: Mustafa Çakan, University of Health Sciences Turkey, Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Clinic of Pediatric Rheumatology, İstanbul, Turkey
E-mail: mustafacakan@hotmail.com **ORCID ID:** orcid.org/0000-0002-1034-6406
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Table 1. Demographics, laboratory features, and outcomes of the cases

	Age	Gender	Main complaint	Laboratory results	Referral diagnosis	Final diagnosis	Outcome
Case 1	15	M	Right knee pain for 2 weeks	RF: 138 IU/mL CRP: 88 mg/L ESR: 65 mm/hr	JIA	Subacute osteomyelitis	Complete healing with surgery and antibiotics
Case 2	13	F	Joint pain for 2 months	RF: 52 IU/mL CRP: 23 mg/L ESR: 42 mm/hr	JIA	JIA	Remission with methotrexate and prednisolone
Case 3	10	M	Recurring artralgia, swelling, and redness in the ankle joints for 2 years	RF: 25 IU/mL CRP 1.2 mg/L ESR: 8 mm/hr	JIA	FMF	Remission with colchicine treatment
Case 4	13	F	Joint pains for 2 years	RF: 36 IU/mL CRP: 0.6 mg/L ESR: 5 mm/hr	JIA	BJHS	Remission with physical therapy

M: Male, F: Female, RF: Rheumatoid factor, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, JIA: Juvenile idiopathic arthritis, FMF: Familial Mediterranean fever, BJHS: Benign joint hypermobility syndrome

interphalangeal joints. Acute phase reactants were elevated (CRP: 23.6 mg/L, ESR: 42 mm/hr). The clinical picture was compatible with RF-positive polyarticular JIA, and methotrexate (15 mg/m^2/week, sc) and prednisolone (1 mg/kg/day, po) were started. Prednisolone was administered for 6 weeks and was discontinued with gradual tapering. By the 3rd month of treatment, she had resolution of arthritis in all joints.

A 10-year-old boy was referred to pediatric rheumatology due to pain and swelling in the ankle joints and a positive RF test (RF: 25 IU/mL). He did not have arthritis in any joints at the time of referral. There was medical history of joint pain and swelling in the ankles over the past 2 years. The swellings, occurring on either the right or left ankle, were lasting for 5-7 days and recurring every 2-3 months, accompanied by redness around the ankle in some episodes. He had elevated CRP (40-60 mg/L) and ESR (35-65 mm/hr) levels during the arthritis attack. The clinical features were compatible with arthritis and erysipelas-like erythema attacks of familial Mediterranean fever. The family denied any prior episodes of recurrent fever and abdominal pain. *MEFV* gene analysis showed a homozygous M694V mutation, and colchicine treatment was started. The child has been taking colchicine for 3 years and has only experienced one episode of arthritis without any accompanying fever or abdominal pain.

A 14-year-old girl was referred to pediatric rheumatology due to joint pain and a positive RF test result (RF: 36 IU/mL). She had been experiencing joint pain for 2 years, without reporting any joint swelling or morning stiffness, but noted that the pain was more pronounced after exercise. On examination, she did not have arthritis but joint hypermobility. The clinical picture was compatible with benign joint hypermobility syndrome, and she was referred to the physical therapy unit. At the 6th month of follow-up, the RF test was negative.

As demonstrated in the present case series, pediatric rheumatologists do not rely solely on laboratory results for diagnosis. Laboratory tests should be ordered and interpreted in combination with patient history and physical examination findings.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.Ç., M.İ.N., Concept: M.Ç., M.İ.N., Design: M.Ç., M.İ.N., Data Collection or Processing: M.Ç., M.İ.N., Analysis or Interpretation: M.Ç., M.İ.N., Literature Search: M.Ç., M.İ.N., Writing: M.Ç.

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