Case Report

# Ataxia-telangiectasia With Acute Rheumatic Fever: A Case Report

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## ABSTRACT

**Background:** Ataxia-telangiectasia is a multi-organ disease. It is due to a mutation of the Exon No. 5 ataxia telangiectasia mutated gene (*c.381delA: p.v128fls*). Complications including recurrent infections, progressive cerebellar ataxia, and varying degrees of humoral and cellular immunodeficiency arise.

**Case Presentation:** We report a 7-year-old girl patient with A-T who developed acute rheumatic fever.

**Conclusion**: Rheumatoid disorders and or infectious diseases such as acute rheumatic fever could be observed in A-T patient.

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## Background

After antibody deficiencies, well-defined syndromes with immunodeficiency are the most common primary immunodeficiency in north Iran [1, 2]. Ataxia-telangiectasia (A-T) is an autosomal recessive, multi-organ disease caused by a mutation of the Exon No.5 ataxia telangiectasia mutated (*ATM*) gene (*c.381delA: p.v128fls*) [3]. The symptoms include progressive cerebellar ataxia, dysarthria, oculomotor apraxia, chorea/dystonia, oculocutaneous telangiectasia, and immunodeficiency. Ataxia is demonstrated when the child is walking [4, 5]. *ATM* mutation causes combined immunodeficiency with immune dysregulation, which causes susceptibility to lymphoid malignancies and sensibility to ionizing radiation [6]. ATM kinase performs a vital function within lymphocytes in acquiring immune competencies, which depends on its DNA double-strand repair function. Disturbed B and T cell homeostasis and failure of immune surveillance impede the improvement of autoimmune and autoinflammatory disorders, organ-precise pathology, and lymphocyte proliferation in A-T-affected children [6]. Immunodeficiency in A-T patients is associated with susceptibility to infection [7]. Acute rheumatic fever is an immune reaction to throat infection with *Streptococcus pyogenes* [8]. The illness is characterized by varying degrees of joint and heart inflammation, typically manifesting as polyarthritis and valvular regurgitation [8]. Diagnosing acute rheumatic fever depends on laboratory and clinical findings based on the Jones criteria [8]. In this article, we report a 7-year-old girl with A-T who presented with polyarthritis and the final diagnosis of acute rheumatic fever. To our knowledge, the concurrence of A-T and acute rheumatic fever has not been reported before.

## Case Presentation

Our patient was a 7-year-old girl with a previous diagnosis of A-T. She was presented with telangiectasia in the sclera and skin, ataxia, and mutation of Exon No.5 ataxia-telangiectasia mutated (*ATM*) gene (*c.381delA: p.v128fls*) at 1 year old. She experienced fever, pain, and swelling of her right ankle 3 days before hospital admission. She is the only child in the distant-consanguineous healthy family. The medical history revealed several hospitalizations due to infection in different parts of her body: Cervical lymphadenitis two months ago and plural empyema last year. She also experienced two episodes of febrile convulsion at 12 and 15 months old. She had a common cold about 2 weeks ago. On physical examination, her temperature was 38.3°C axillary, blood pressure was 99/60 mm Hg, pulse rate was 110 beats per minute, and respiratory rate was 32 per minute. Diffuse hyperpigmented plaques were seen on her face and upper and lower extremities. Conjunctival pallor, scleral telangiectasia, and periorbital edema were notable on examination. Other abnormal findings were purulent post-nasal drip and multiple submandibular and cervical lymphadenopathies. Effusion, erythema, and tenderness of the right ankle were considerable. Other joints were normal. Laboratory tests showed anemia, a significant increase in erythrocyte sedimentation rate, and C-reactive protein (CRP), 120 mm/h and 73 mg/dL, respectively. Laboratory findings on the admission day are presented in Table 1. The patient had a history of allergy to vancomycin, so treatment with intravenous ceftazidime and clindamycin started. The patient was still febrile on the second day of admission, and arthritis was noted on her left wrist and elbow joints. Ultrasonography of the right ankle showed edema around the tibiotalar tendon. Other ultrasonography findings were moderate effusion in the left elbow with multiple lymph nodes (maximum size 5 mm) and mild effusion in the left wrist. In addition, the liver and spleen span were 114 and 111 mm (both greater than normal values) on ultrasound. An echocardiogram was performed, and mild to moderate mitral regurgitation (MR) was detected. Electrocardiogram (ECG) was normal. Investigation for infectious agents, such as Epstein-Bar virus (EBV) and Cytomegalovirus (CMV), were negative. ANA (antinuclear antibody) and ASO (antistreptolysin O) were negative too. Based on the patient's history, her physical examination, paraclinical measures, and lab tests, the diagnosis of acute rheumatic fever (ARF) was made despite negative ASO (normal range: <200 IU/mL). Therefore, the patient was treated with high-dose oral aminosalicylic acid (30 mg/kg/d) and Penicillin benzathine 600000 IU every 4 weeks. The fever and arthritis subsided dramatically during the next 2 days, and the patient was discharged. In the follow-up appointment, 7 days after discharge, ASO titer had risen significantly (500 Todds). Aspirin was tapered gradually during the next month. The patient has had no cardiac or joint complaints or complications during three years of follow-up.

## Discussion

We reported a 7-year-old girl with A-T with polyarthritis and the final diagnosis of acute rheumatic fever. We encounter serious challenges in diagnosing acute rheumatic fever in a patient with immune deficiency, fever,

**Table 1.** Laboratory results during hospitalization of the patient

| Variables | 1st Day | 4th Day | 8th Day |
|---|---|---|---|
| WBC ($10^3$/μL) | 8.1 | 5.03 | 5.54 |
| RBC ($10^6$/μL) | 3.19 | 3.10 | 3.22 |
| HGB (g/dL) | 8.8 | 8.6 | 9.1 |
| HCT (g/dL) | 25.7 | 25.4 | 27.9 |
| PLT (platelets) | 190 | 184 | 516 |
| ESR, 1 h (mm/hr) | 120 | 137 | 135 |
| CRP (mg/dL) | 73 | 65 | 13 |
| Urea (mmol/L) | - | 20 | 29 |
| Creatinine (mg/dL) | - | 0.5 | 0.5 |
| AST (IU/L) | 31 | 26 | 118 |
| ALT (IU/L) | 20 | 18 | 62 |
| ALP (IU/L) | 254 | - | 272 |
| PT (seconds) | 15.5 | - | - |
| PTT (seconds) | 32 | - | |
| INR | 1.4 | - | - |
| ASO | <200 | <200 | 200 |

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Abbreviations: WBC: White blood cell; RBC: Red blood cell; HGB: Hemoglobin; HCT: Hematocrit; PLT: Platelets; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; AST: Aspartate transaminase; ALT: Alanine transaminase; ALP: Alkaline phosphatase; PT: Prothrombin time; PTT: Partial thromboplastin time; INR: International normalized ratio; ASO: Antistreptolysin O.

polyarthritis, and lack of evidence for recent streptococcal infection. A-T is an autosomal recessive, multisystem disorder caused by mutations in the A-T mutated gene, a serine/threonine kinase that activates over two dozen proteins involved in DNA damage response and cell cycle regulation [9]. The immunologic deficiencies range substantially from person to person. The most frequent defects of humoral immunity encompass dwindled or absent serum and salivary IgA, serum IgE, and impaired antibody responses to many bacterial and viral antigens [9]. The patients may experience infections of different sites; otitis media reported in 46% of patients, sinusitis in 27%, bronchitis in 19%, and pneumonia in 15% [9]. The pathogenesis of acute rheumatic fever remains partly understood. Evidence supports the view that acute rheumatic fever results from a response to pharyngeal infection with group A Streptococcus in genetically predisposed individuals; this is mediated via molecular mimicry [8]. Although little genetic and epidemiological evidence exists for skin infection because of the occasion that ends in acute rheumatic fever, pharyngeal infection is considered the cause in maximum cases [8]. Acute rheumatic fever (ARF) can be misdiagnosed as osteomyelitis or septic arthritis [10]. Typically, signs of ARF develop 2 to 3 weeks from infection onset and might persist long after the infection has cleared. The migratory polyarthritis visible in ARF is frequently the primary symptom of ARF and takes place in 35% to 66% of patients [11]. The arthritis of ARF prefers large joints and typically affects the lower extremities first. The ankles, knees, elbows, and wrists are commonly affected [11]. Many patients with ARF may present at a time of monoarticular involvement. Thus, clinicians must have a high suspicion of arthralgia migration and investigate this thoroughly with a detailed history and exam [11]. Diagnosing the arthritis of ARF is challenging, given its migratory nature and non-specific clinical presentation [11]. The ASO antibody is either absent or present in very low concentrations in sufferers who do not have a current streptococcal infection. Antibodies are produced after about 1 week to a month

after the preliminary strep infection. ASO titers peak at about 4 to 6 weeks after the infection. Antibodies taper off afterward. However, they might also be at detectible degrees for numerous months after the strep contamination has resolved [12]. If the test is negative or if ASO is found in very low concentrations, then the affected person probably no longer has a strep infection, particularly if a titer taken 10 to 14 days later is likewise negative or minimal [12]. Antistreptolysin O titer is a blood test to check for antibodies towards streptolysin O, a substance produced through institution A streptococcus bacteria. Antibodies are proteins our bodies produce after they come in contact with dangerous substances, which include bacteria [12]. As seen in this patient, arthritis on presentation closely mimics septic arthritis, as it was warm, tender to touch, monoarticular, and the patient was febrile [11, 13]. Because of background immunodeficiency in our patient, when polyarthritis developed, we could not exclude septic arthritis. Still, close physical examination, poor response to antibiotics, and typical findings on echocardiography led to the diagnosis of acute rheumatic fever without laboratory evidence of previous streptococcal infection. Although eventually, rising titers of ASO were found.

## Conclusions

Rheumatoid disorders and infectious diseases such as acute rheumatic fever could be observed in A-T patients. Therefore, although we should consider other causes of poly arthritis, we must also consider ARF in an immunodeficient patient such as A-T.

## Ethical Considerations

### Compliance with ethical guidelines

Written informed consent was obtained from the patient to publish this case report and accompanying images.

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### Authors contributions

First operator on the case, planning and executing the procedure and deciding on the hardware and technique used: Mohammad Reza Khosravi; Contribution to procedure and manuscript preparation: Ghazal Abbasi, Leila Shahbaznejad, Javad Ghaffari, and Abbas Dabghzade;

### Conflicts of interest

The authors declared conflict of interest.

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