Felty's syndrome preceding rheumatoid arthritis in a patient with a history of rheumatic fever: a case report

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ABSTRACT

Background: Felty's syndrome (FS), a rare condition affecting 1%-3% of patients with rheumatoid arthritis (RA). It typically arises after a prolonged course of RA. Although rheumatic fever (RF) and RA may share overlapping features, they are distinct entities; their co-occurrence in a patient is rare and considered coincidental.

Case presentation: A 27-year-old woman with childhood RF and mitral stenosis presented with low-grade fever and inflammatory arthritis. Three years earlier, she had developed pancytopenia and hepatosplenomegaly and was recently diagnosed with seropositive RA. Her earlier cytopenias and organomegaly were retrospectively attributed to FS, likely preceding RA onset. Treatment with corticosteroids and hydroxychloroquine led to significant improvement, and methotrexate was added for maintenance and relapse prevention.

Conclusion: Careful medical history and clinical examination, as well as thorough other investigations, should be performed to exclude other causes of neutropenia.

Keywords: Felty's syndrome, rheumatoid arthritis, rheumatic fever, hepatosplenomegaly, pancytopenia.

Type of Article: CASE REPORT **Specialty:** Rheumatology

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Background

Rheumatoid arthritis (RA) is a systemic disease that affects multiple systems, resulting in some patients with complications such as Felty's syndrome (FS) [1]. FS occurs in 1%-3% of patients with RA, characterized by destructive joint involvement, absolute neutrophil count of less than 1,500/mm^3, and splenomegaly [1,2]. Additional symptoms associated with FS include fever, anemia, mucosal and skin ulcers, respiratory tract infections, thrombocytopenia, and lymphadenopathy [2]. Both the humoral and cellular immune systems are involved in neutrophil activation and apoptosis in FS patients [1,3]. FS occurs after a long course of RA, although it may present simultaneously at the time of RA diagnosis or precede the RA diagnosis [1,3]. FS may be asymptomatic in 15%-40% of patients, but clinical syndromes are usually present with infections, especially dermal and pulmonary tracts [3].

Rheumatic fever (RF) is a temporary, acute condition triggered by strep throat infection, while RA is a chronic immune disease. While they share some overlapping symptoms, such as joint pain and fever [4]. Our case report presents a patient with a diagnosis of RA presented by FS as a first manifestation, with a previous medical history of RF.

Case Presentation

A 27-year-old female patient presented on March 2025, to University Hospital in Damascus, Syria, with a three-month history of arthralgia, swelling of the joints of the hands and knees, and persistent fatigue.

The patient had a history of RF diagnosed 10 years ago, which resulted in mitral valve stenosis. Over the past 3 years, she had persistent pancytopenia, hepatomegaly, and splenomegaly, without pain or swallowing of in the small joints of the hands or feet, along with negative antinuclear antibodies (ANA), anti-citrullinated peptide (CCP), and RF. In September 2024, laboratory investigations revealed no malignancy, hematologic disorders, or autoimmune disease. The patient had no nutritional deficiencies or toxin exposure. She was managed supportively with blood transfusions as needed.

Additionally, the patient had recurrent upper respiratory tract infections over the past 2 years, treated intermittently with azithromycin (500 mg every three days). At the time of admission, she was not receiving any regular medications. There was no significant family medical history.

Physical examination showed fever (38.1°C), arthritis in hands, wrists, and knees, in addition to hepatomegaly and splenomegaly.

Laboratory tests are shown in Table 1

ANA, antinuclear antibodies; Anti-CCP, anti-citrullinated peptide; ASLO, anti-streptolysin O titer; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MCV, mean count volume; RF, rheumatoid factor.

Viral serology tests for *Streptococcus pneumoniae*, Epstein-Barr virus, herpes simplex virus, and influenza A and B were negative. Blood and urine cultures were also negative.

A hand X-ray only demonstrated soft tissue swelling, without periarticular osteopenia or erosions.

Two-dimensional transthoracic echocardiography revealed thickened mitral valve cusps, left atrial enlargement, a normal or small left ventricle, and reduced mitral valve orifice size during diastole. The mitral valve area is between 1.5 and 2.5 cm^2, while the pressure half-time is *P*1/2*t* is less than 150 ms, which suggested mild stenosis (Figure 1).

Transesophageal echocardiography revealed commissural fusion, chordal shortening, leaflet thickening, reduced leaflet mobility, and the characteristic "hockey-stick" appearance of the anterior mitral valve leaflet, with no evidence of infective endocarditis.

Contrast-enhanced CT of the chest, abdomen, and pelvis confirmed hepatomegaly and splenomegaly, without portal vein dilatation or collateral vessels, and with normal liver morphology.

Liver biopsy revealed nonspecific inflammation and architectural changes suggestive of nodular regenerative hyperplasia.

Bone marrow biopsy showed normocellular marrow with focal spicules and trilineage hematopoiesis. There was no evidence of overt dysplasia. However, a left shift was observed, along with increased immature mononuclear cells and a marked reduction in mature neutrophils.

The patient was diagnosed with RA according to the ACR/EULAR Criteria 2010 [5], along with evidence of neutropenia and splenomegaly. Together, these factors allowed us to diagnose FS in early RA patients.

The patient was initiated on oral prednisolone at a dose of 30 mg daily, tapered by 5 mg each week, in addition to hydroxychloroquine 200 mg/day. One month later, she showed complete resolution of arthritis, normalization of the white blood cell count, and a significant reduction in erythrocyte sedimentation rate (ESR) at 22 mm/h and C-reactive protein (CRP) at 4.5 mg/dl. After a month, methotrexate was added at a dose of 7.5 mg/week, along with folic acid 5 mg/week. The patient was advised to continue regular follow-up every three months, under the treatment of 7.5 mg/week methotrexate, 5 mg/week folic acid, and 200 mg/day hydroxychloroquine, with close monitoring of blood counts and liver function tests.

Discussion

Group A Streptococcus pharyngitis can cause RF, which damages the skin, joints, heart, and central nervous system. The rheumatic heart disease commonly involves the

Table 1. *The laboratory tests.*

LABORATORY PARAMETERS	PATIENT'S VALUES	NORMAL RANGE
Leukocyte count, per µl	2.3×10^3	4-10×103
Hemoglobin, g/dl	8.1	12.3-15.3
MCV	92	80-100
Platelet count, per µl	98,000	150,000-450,000
ESR, mm/h	52	0-30
CRP, mg/l Lactic acid, mg/dl	23 2.5	<6 4.5-19.8
Creatinine, mg/dl	0.7	0.7-1.3
SGOT, g/dl	21	8-35
SGPT, g/dl	18	8-35
AIP, unit per liter ASLO, UI/ml RF Anti-CCP	294 186 120 391	64-306 <200 <20 <20
ANA HIV, copies/ml Hepatitis B anticore Hepatitis C	Negative Negative Negative (non-reactive) Negative (non-reactive)	- - - -

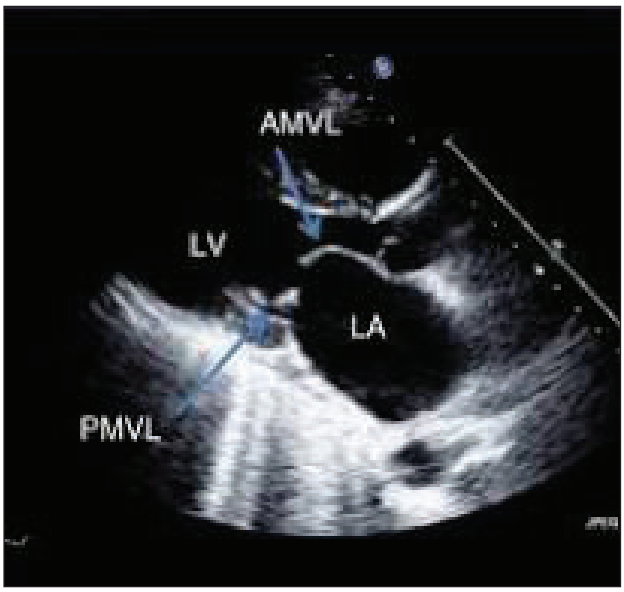

Figure 1. *Mitral stenosis findings in echography .*

mitral and/or aortic valves [6,7]. Our patient shows signs of chronic valvular damage.

FS occurs in women with long-standing RA. It is a clinical diagnosis that commonly includes hepatosplenomegaly and neutropenia. Splenomegaly and neutropenia present in 90% of FS patients as salient features, but some RA patients present with rheumatoid nodules, hepatosplenomegaly, lymphadenopathy, fever, weight loss, and others [1-3]. Our patient had fever, arthritis, hepatosplenomegaly without portal hypertension, and neutropenia. In this case, the diagnosis is clinically and laboratory substantiated. FS pathology is multifactorial, involving an autoimmune response that leads to neutropenia, splenomegaly, and RA. Autoantibodies targeting deiminated histones, neutrophil extracellular traps, and immune complexes, which promote neutrophil destruction. Splenomegaly contributes by sequestering and destroying neutrophils, while genetic factors like the HLA-DR4 allele are strongly associated with the condition [3,8]. HLA-DRB1*0401, IgG Anti-G-CSF, and autoantibodies binding to extracellular chromatin traps of neutrophils, leading to neutrophil sequestration [3].

The differential diagnosis for pancytopenia with splenomegaly includes hematologic disorders such as leukemia, myelodysplastic syndrome, or aplastic anemia, infections such as HIV, TB, malaria, or viral infections, liver cirrhosis, certain autoimmune diseases such as lupus, and genetic conditions such as Gaucher disease [1-4,7,8]. Systemic lupus erythematosus can be distinguished from FS by a prominence of lymphopenia rather than neutropenia, hemolytic anemia, nephritis, and central nervous system disease [9]. Large granular lymphocytic leukemia can be differentiated from FS by the findings of large granular lymphocytes cells on peripheral smear and bone marrow biopsy [10]. In our case, all causes of FS were excluded.

The management for FS is supportive and directed towards controlling the underlying RA while also improving the neutropenia to prevent life-threatening infections. Initial management of RA with neutropenia includes low-dose methotrexate with folic acid, glucocorticoids, rituximab, and splenectomy in persistent cases [2,3,10], as we treated our patient. The standard of care for the initial management of RA has been methotrexate is effective as monotherapy and in combination with other conventional, biologic, and targeted-synthetic therapies, for the last decades[1-3,5]. Initial treatment for RA focuses on early use of disease-modifying antirheumatic drugs to prevent joint damage. However, the question of the best treatment option for RA patients still remains unanswered. Common interventions include MTX or HCQ monotherapy, MTX-HCQ or MTX-SSZ dual therapy, and MTX-HCQ-SSZ triple therapy [11].

In this instance, the initial difficulty was confirming the FS diagnosis in the absence of any early indications of RA joint involvement. Starting methotrexate safely was the second difficulty. She was able to attain stable liver function and a normal complete cell count through careful blood test monitoring and follow-up.

Salih and Gunasekera [3] had described a case of a 73-year-old man whoinitially presented with pancytopenia and splenomegaly, without finding an underlying hematological cause. The diagnosis of FS was confirmed through the identification of rheumatoid factor and anti-citrullinated protein antibody, the exclusion of other differential diagnoses.

Acute RF and RA are often indistinguishable clinically, particularly at the onset [4]. They may both start acutely with an infection of the upper respiratory tract or with a moderately high temperature, chilliness, perspiration, transitory inflammatory involvement of joints, leukocytosis, and anemia. Furthermore, the spleen and lymph nodes may be enlarged in each. The sedimentation rate has been found to present an increase in both of them, but the positive titer of RF, and anti-CCP are only found in RA. There were no data concerning the coexistence of these two diseases together; it is a coincidental presence.

The novelty in our case is the young age of our patient, the previous history of RF, the presence of FS as an early manifestation of RA, and the safety of starting methotrexate. A young age of onset for FS and RA is “worthy” of clinical attention because FS typically occurs in adults over 50 years, with long-standing (over 10 years) RA. Its rare appearance in younger patients, especially in children, is an atypical presentation that can make correct diagnosis challenging and may suggest different underlying disease mechanisms or a need for an extensive workup to rule out other conditions. FS appearing at the onset of RA is rare in the medical literature because it is an extra-articular manifestation that typically develops after a long, usually more

than 10 years, aggressive course of established RA, not at its initial presentation.

Conclusion

RA is a chronic systemic disease. FS can rarely occur in the absence of clinical manifestations of RA. For that, careful medical history and clinical examination, as well as thorough other investigations, should be performed to exclude other causes of neutropenia and /or hepatosplenomegaly. A multidisciplinary specialists was pivotal in the safe diagnosis and treatment of our patient.

RF and RA are distinct conditions. While they share some overlapping symptoms, they are not related in terms of cause or long-term progression.

What's new?

Felty's syndromeFS is a rare complication of long-standing rheumatoid arthritis (RA), typically characterized by the triad of RA, neutropenia, and splenomegaly. It usually occurs in patients with established seropositive RA and is considered a late manifestation of the disease.

This case is unusual because Felty's syndromeFS appeared prior to the clinical onset of rheumatoid arthritisRA, which is extremely rare. Additionally, the patient had a remote history of rheumatic fever, raising a unique diagnostic challenge and potential overlap in autoimmune pathology. To the author's knowledge, such a presentation has not been previously reported in the literature.

List of abbreviations

ANA	antinuclear antibodies
CCP	citrullinated peptide
CRP	C-reactive protein
ESR	erythrocyte sedimentation rate
FS	Felty's syndrome
RA	Rheumatoid arthritis
RF	Rheumatic fever

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

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Consent for publication

Written informed consent was obtained from the patient.

Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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Timeline

2015	Diagnosis of rheumatic fever, which resulted in mitral valve stenosis
2021-2024	Persistent pancytopenia, hepatomegaly, and splenomegaly, extensive laboratory investigations ruled out malignancy and hematologic disorders, managed supportively with blood transfusions as needed
2023-2025	Recurrent upper respiratory tract infections, treated intermittently with azithromycin (500 mg every three days)
2025	Persistent arthralgia, swelling of the joints of the hands and knees, and persistent fatigue
March 2025	Diagnosis of rheumatoid arthritis presented by Felty's syndrome, initiated treatment with prednisolone and hydroxychloroquine
April 2025	Methotrexate and folic acid were added to the treatment regimen, and the patient showed complete resolution of arthritis symptoms and normalization of white blood cell count.

Summary of the case

1	Patient (gender, age)	27 years, female
2	Final diagnosis	Felty's syndrome
3	Symptoms	Arthralgia, swelling of the joints of the hands and knees
4	Medications	Prednisolone, hydroxychloroquine, methotrexate, folic acid
5	Clinical Procedure	None
6	Specialty	Rheumatology