

Felty's Syndrome with Nodular Regenerative Hyperplasia of Liver and Portal Hypertension

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Case report

A 32 year old female presented with easy fatigability and breathlessness on exertion of 1 year duration. She also gave history of multiple joint pain and swelling with prolonged early morning stiffness. She complained of diffuse abdominal pain with early satiety and recurrent episodes of fever. She is a known case of hypothyroid on thyroxin supplementation. On examination she was very pale, febrile with multiple furuncles over her labial region with active polyarthritis (involving both small and large joints of upper and lower limbs). On evaluation her Haemoglobin was 4.8 g/dl, total leukocyte counts of 1700 cells/cu.mm (neutrophils–21%) and platelets 75,000 cells/cu.mm. Her previous investigations showed a gradual decline in counts of all three lineages. Peripheral smear was suggestive of haemolytic anaemia. Her liver function tests were normal except for mild elevation in indirect bilirubin. She had raised Lactate dehydrogenase (LDH) levels with normal renal function and urine examination. Her erythrocyte sedimentation rate (ESR) was 103 mm/hr and C- reactive protein (CRP) of 22.2 mg/dl. She tested positive for Rheumatoid factor (1:640 titre by latex agglutination) and also strongly positive for Anti CCP (cyclic citrulinated peptide) (5.6 by ELISA). All other immunological workup including antinuclear antibody were negative. Bone marrow examination was done which was suggestive of reactive marrow with myeloid hyperplasia and no evidence of malignancy. Her Ultrasonography of abdomen was done, which showed hepatosplenomegaly with an enlarged portal vein (diameter of 16 mm). Computed tomography of abdomen confirmed the same, with enlarged nodular liver and a massive spleen of 21 cm. Her upper GI scopy was normal with no varices. Patient was not willing for a liver biopsy. Her X rays of hand and foot were normal except for soft tissue swelling and juxtaarticular osteoporosis. So a diagnosis of Seropositive Rheumatoid arthritis (RA) with Felty's syndrome was made. The points to ponder in this case are the presence of portal hypertension, hypersplenism, nodular liver enlargement and relatively short duration of joint symptoms with no joint erosions or deformity.

The patient was initially treated with antibiotics, blood transfusion, G-CSF (Granulocyte – colony stimulating factor) injections followed by steroids (20 mg/day initially and tapered gradually), 400 mg of hydroxychloroquine and 1 g of sulfasalazine. With treatment the patient improved symptomatically (decreased joint

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pain and swelling) and after 6 months of treatment her blood counts improved with a Haemoglobin of 10 g/dl, total counts of 5600 cells/cu.mm and platelets of 106,000 cells/cu.mm. Her spleen size reduced to 17 cm, portal vein size became normal with reduction in nodularity of liver after 8 months of treatment with above drugs.

Discussion

Felty's syndrome is one of the rare extra articular manifestations of rheumatoid arthritis described as early as 1924 [1]. But it is rarely seen these days due to early initiation of treatment for rheumatoid arthritis. It comprises the classical triad of joint symptoms (RA) with neutropenia and splenomegaly. Usually it is found in patients with long standing rheumatoid arthritis with joint erosions, deformities and rheumatoid nodules. They usually have HLA DR4 positivity with high titers of rheumatoid factor [2]. But our patient had relatively short duration of disease with no erosions, deformities or rheumatoid nodules. Felty's syndrome as the presenting manifestation of Rheumatoid arthritis has been rarely reported in literature [2]. Our patient though had joint symptoms previously, she presented only because of worsening of symptoms due to severe anemia. These patients can have commonly skin, soft tissue and upper and lower respiratory tract infections. Our patient had recurrent episodes of fever with soft tissue infections (**Figure 1**).

Liver involvement in Felty's syndrome is quite rare but can have an

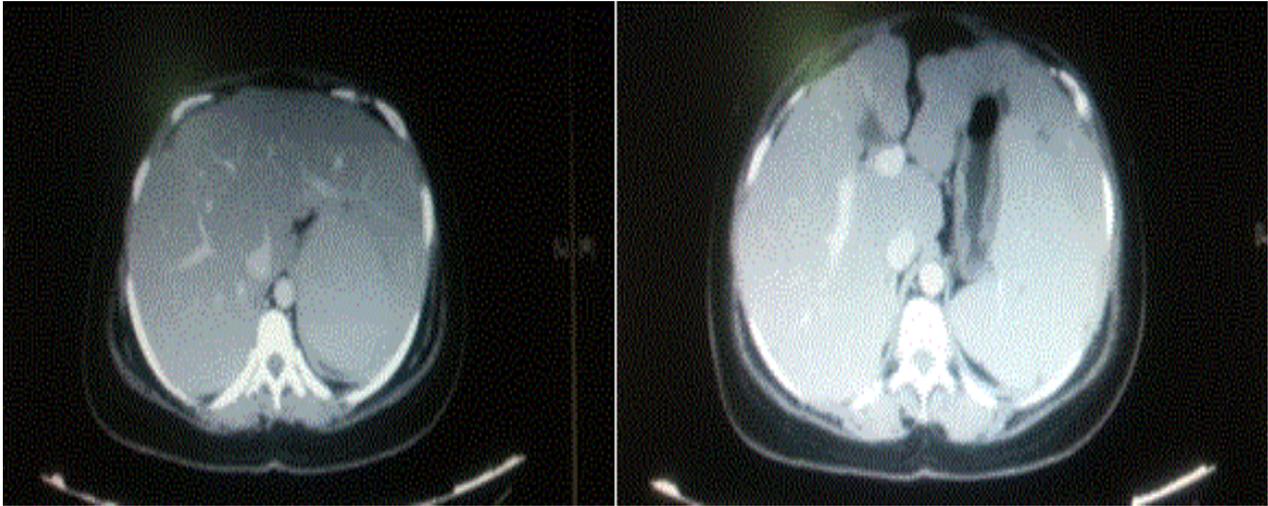


Figure 1 Abdominal CT shows massive liver and splenic enlargement.

enlarged liver due to 'Nodular regenerative hyperplasia'. In 1953, Ranstrom first described an entity called as 'Miliary hepatocellular adenomatosis' which is now termed as 'nodular regenerative hyperplasia' (NRH). It comprises of portal hypertension, liver cell hyperplasia, secondary nodules with minimal or absent fibrosis [4]. In our patient, there was nodular enlargement of liver in both Ultrasound and computed tomography of abdomen. Ideally liver biopsy should be done but a diagnosis of nodular regenerative hyperplasia was assumed, as our patient had a clinical picture of rheumatoid arthritis with massive splenomegaly, pancytopenia, portal hypertension and with other potential causes being ruled out. NRH can also be associated with other rheumatological disorders like systemic lupus erythematosus, scleroderma, polyarteritis nodosa, antiphospholipid antibody syndrome etc. [3]. Several possible reasons were proposed, like regenerative nodules pressing on intrahepatic blood vessels, obliterative portal venopathy, vasculitis, immune complex deposition etc. [5].

Splenomegaly can be found in 5–10% of RA patients. The causes vary from non-specific hyperplasia of spleen (common) to amyloidosis and rarely Felty's syndrome [6]. Development of portal hypertension in Felty's syndrome is rare and having a variceal bleeding is even more rare [7]. Usually the varices due to portal hypertension in Felty's syndrome get decompressed after

splenectomy unlike varices in cirrhotic patients. The other major difference is, patients with a variceal bleed in Felty's syndrome don't develop hepatic encephalopathy [5].

There is not much of evidence for management of Felty's syndrome as its incidence is very rare. All the synthetic disease modifying agents like methotrexate, leflunomide, sulfasalazine and hydroxychloroquine has been tried with good response. Among biological agents, there are reports on rituximab being effective in Felty's syndrome [8]. Our patient had pancytopenia due to hypersplenism and hence initially she was treated with tapering dose of steroids, antibiotics and with G-CSF and blood transfusion. Once her haemoglobin and counts improved, she was started on hydroxychloroquine, sulfasalazine and after 6 months of treatment her blood counts improved and joint symptoms were controlled.

Conclusion

In conclusion, Felty's syndrome need not always be a long term complication and can occur early without joint erosions or deformity. Rarer features like Nodular regenerative hyperplasia leading to portal hypertension and hypersplenism responds to disease modifying agents and patients respond well to treatment.

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