# UNDIFFERENTIATEFD CONNECTIVE TISSUE DISORDER PRESENTING AS TUBERCULAR MONOARTHRITIS AND MEMBRANOUS NEPHROPATHY:

# A CASE REPORT


## ABSTRACT

**Background:**
The Term undifferentiated connective tissue disease is used to define conditions characterised by the presence of signs and symptoms suggestive of a systemic autoimmune disease that does not satisfy the classification criteria for defined connective tissue diseases (CTD) such as systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), rheumatoid arthritis (RA) and others[1].

The most characteristic symptoms of UCTD are represented by arthritis and arthralgias, Raynaud's phenomenon and leukopenia, while neurological and renal involvement are rare. Only one-third of the UCTDs evolves into full-blown CTD within the initial years (3-5). Here we are presenting a case of a 36-year female presenting with mono arthritis, proteinuria and severe anaemia who was diagnosed to have undifferentiated connective tissue disorder with tubercular mono arthritis of knee joint and membranous nephropathy. The patient was given anti-tubercular drugs , corticosteroids, hydroxychloroquine and PRBC transfusions. The patient was discharged and showed significant improvement on subsequent follow-ups. This case report provides insight into the various presentations of connective tissue disorder and also its multi-system involvement. Also sometimes these disorders cant be classified by a criterion clinically or based on laboratory investigations into one single connective tissue disease.




**Introduction**

Autoimmune diseases are complex and in general, relatively rare. Characteristic signs, symptoms, and autoantibodies define specific connective tissue diseases. Some patients meet criteria for more than one defined connective tissue disease (CTD), while others have several symptoms characteristic of autoimmune diseases yet cannot be definitively classified [8,9]. Tuberculosis is a common disease worldwide. However, it now is clear that tuberculosis can affect the kidney more insidiously. We describe a case of lumbar tuberculosis associated with simultaneous membranous nephropathy and interstitial nephritis, in which recovery of renal function occurred after treatment with steroids in addition to antituberculosis agents [10].

## 1. AIMS

This case report provides insight into the various presentations of connective tissue disorder and also its multi-system involvement.

## 2. CASE PRESENTATION

A 36-year female patient not a known case of any co morbidities, a housewife presented with complaints of weight loss for 2 months and right-sided knee joint swelling for one month. The patient was relatively asymptomatic before 2 months then the patient developed a complaint of weight loss. It was gradual in onset and progression. It was associated with easy fatigability and generalized weakness. The patient was unable to carry out daily activities. The patient developed a complaint of swelling over the right knee joint. It was gradual in onset and progressive. The patient was unable to bear weight on that limb. It was associated with swelling and tenderness and reduced range of motion of that joint. There was no history of fever, chest pain, breathlessness, multiple joint pains, joint stiffness or swelling of any other joints. The patient had no significant past history. The patient was 2 Para. Both full-term normal vaginal deliveries. The patient had a complaint of oligomenorrhea. LMP was 24/5/2021. No significant personal history. On admission, the patient was conscious, cooperative and well oriented to time place and person. Her temperature was afebrile. Pulse was 110 beats per minute. the blood pressure was 100/60 mmofhg. On general examination pallor was present and mild grade I pedal oedema was present . Following investigations were done

Table 1 : pathological standard

| | |
|---|---|
| Hemoglobin | 5.2 mg/dl |
| Total counts | 10900 cells per cu mm |
| Platelets | 2.71 lac per cu mm |
| ESR | 21 mm/hour |
| S. Creatinine | 1.5 mg/dl |
| total bilirubin | 0.3 |
| Serum sodium | 139 mmol/L |
| Serum potassium | 3.9 mmol/L |
| Serum Total protein | 7 g/dl |
| Albumin | 2 |

Based on the findings in above investigations, patient was further investigated for anaemia and renal impairment. The patient was found to have microcytic hypochromic anaemia but iron profile was within normal limits. Further USG abdomen was done wherein the kidney size was normal with preserved cortico- medullary differentiation. Also in view of proteinuria 24 hour, urinary protein was sent. Also suspecting an autoimmune condition ANA profile was sent. The 24-hour urinary protein was 1700 mg. ANA was positive at 1:40 dilution with the nuclear pattern . Based on above findings further ANA profile and complement 3 and complement 4 were sent. C3,C4 were within normal ranges so were cholesterol and triglycerides. All of these findings indicated Nephritic syndrome. ANA profile was positive for anti SSA , anti SSB and anti-Ro antibodies . Ultrasonography of right knee indicated an echoic collection with few internal septa and no internal vascularity noted in the suprapatellar pouch approx 7*3.4 in size extending from the knee suggestive of moderate joint effusion in the right knee. After orthopaedic consultation, joint fluid was drained and sent for examination. The fluid was turbid pale yellow in colour with ph of 7 , sugar 50, protein 1.0, ADA 29 and LDH 569. Total cell count of synovial fluid were 13000 out of which 95% were polymorphs ,5% lymphocytes . No organism was seen on gram , ZN and KOH

stains nor any organism was detected in culture. Fluid was sent for CBNAAT under NTEP to rule out Koch.

During the course of treatment , seven pints of packed cell volume was transfused. After attaining hb of 10.6, a renal biopsy was done to find out the definite pathology in kidneys and to rule out lupus nephritis . The renal biopsy was suggestive of membranous nephropathy. Meanwhile the CBNAAT for synovial fluid came positive for mycobacterium tuberculosis, sensitive to rifampicin and isoniazid . The patient was given anti-tubercular drugs according to the NTEP regime and along with that she was given corticosteroids and hydroxychloroquine . After few months of treatment the patient didn't achieve remission and hence was started on azathioprine. Patient is currently on azathioprine .

## 3. DISCUSSION

A considerable proportion of individuals have clinical and serological features that are suggestive of a systemic autoimmune disorder, but cannot be diagnosed as having a defined connective tissue disease. These diseases have been variably defined as incomplete systemic lupus erythematosus, latent lupus, early undifferentiated connective tissue diseases, and undifferentiated connective tissue diseases (UCTD). It is the fact that the majority of patients (80–99%) are female, with a mean age at disease onset ranging from 32 to 44 years [7].Literature data show clearly that 30% of patients with an undifferentiated onset will develop a defined CTD over the follow-up. Most commonly patients develop systemic lupus erythematosus (SLE), Although an evolution to other CTDs such as systemic sclerosis (SSc), Sjogren's syndrome (SS), mixed connective tissue disease (MCTD), systemic vasculitis, polydermatomyositis (PM/DM), rheumatoid arthritis (RA).[9]

As patient didn't have any rash / oral ulcers / pericarditis / pleuritis /psychosis and nor anti sm and anti ds DNA were present hence SLE was less likely. Also, the patient didn't have any complaints of dry eye or dry mouth nor any positive oral or ocular signs, so the possibility of sjogrens was less likely. As the disorder didn't fit into a single criterion , it was classified as early undifferentiated connective tissue disorder.

Diagnosis of SLE is based on clinical findings and laboratory findings after all other differential diagnoses are excluded. The diagnosis can be refined with a detailed medical history, physical examination, SLE-specific laboratory tests, and regular follow-up. The American College of Rheumatology (ACR) defined in 1997 or the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria described in 2012 are often used by clinicians due to the lack of specific diagnostic criteria.[5,6] As these criteria are insufficient in some cases, some other diagnostic criteria have been proposed in the literature. According to these criteria, if the patient has non-specific organ involvement for SLE (e.g., optic neuritis), and fulfils two or three criteria of ACR or SLICC (four criteria for the definite diagnosis should be positive), the patient is diagnosed with probable SLE.[7] Although this case did not fully meet the SLE criteria, she fulfilled three criteria according to SLICC: non-scarring alopecia, peripheral sensorial neuropathy, and ANA positivity. These findings were compatible with the probable SLE described in the literature. In addition, the literature data suggest that a patient having signs and symptoms suggestive of a connective tissue disease (CTD) without fulfilling the criteria of any defined CTD and having ANA positivity can be defined as having a UCTD. If the disease duration is less than three years, patients can be defined as having an early UCTD. A longer follow-up would allow the correct classification of at least some false-negative patients.

Classification criteria of the SS have been updated for years and the most recent 2016

ACR and European League Against Rheumatism (EULAR) criteria have been established.Primary SS is not associated with other diseases, while secondary SS may be associated with other rheumatic diseases. In this case, although there was no supportive finding in the salivary gland biopsy, Schirmer's test resultswas negative. As the patient could not fulfil the primary SS classification criteria fully, she was diagnosed with secondary SS.

**4. CONCLUSION**

Inflammatory rheumatic diseases can be seen together, and diseases may overlap with each other. This case highlights the importance of detailed medical history and ultrasonographic assessment in addition to laboratory testing in rheumatic diseases. Based on our experience, we suggest that methotrexate may be useful when UCTD and axSpA are seen together.

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