Case Report

RESPIRATORY MANIFESTATIONS OF MIXED CONNECTIVE TISSUE DISEASE IMITATING COVID-19

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ABSTRACT

Mixed Connective Tissue Disease (MCTD) is an autoimmune disorder showing features of a combination of primary lupus, scleroderma, and polymyositis. Sjogren syndrome is observed in some people with this uncommon disease. The patient does not show symptoms of the separate diseases in early phase, instead, they tend to show up gradually for several years, which can complicate the diagnostic procedure. The characteristic feature of MCTD is the antisemite antibodies and antibodies against U1-ribonucleoprotein (RNP) complex. Clinically numbness of toes and fingers, myopathy, Raynaud's syndrome, swollen hands, rash, arthritis, polymyositis and interstitial lung disease are observed. The patient presented with fever, shortness of breath and dry cough and was treated along the lines of coronavirus disease. His pulmonary features resembled those of post COVID fibrosis, hence the disease was overlooked due to this pandemic.

Key Words: COVID-19, Mixed Connective Tissue Disease, Fever

doi: https://doi.org/10.51127/JAMDCV4I3CR01

How to cite this:
Khan H, Piracha MI, Zaheer S, Shujaat K. Respiratory manifestations of mixed connective tissue disease imitating covid-19. JAMDC. 2022;4(3): 145-148
doi: https://doi.org/10.51127/JAMDCV4I3CR01

INTRODUCTION

Mixed connective tissue disease (MCTD) was well-defined in 1972 for the first time as an Autoimmune Disease Syndrome. MTCD is called overlap disease because it shows shared features of Polymyositis, Systemic Sclerosis, Systemic Lupus Erythematosus (SLE), and its related disease with the presence of antibodies against RNA sensitive extractable nuclear antigen.[1] In MTCD autoantibodies appeared against ENA, now known as RNP.[2] MCTD is diagnosed by the manifestation of anti-smith and anti-ribonucleotide antibodies and it is the first rheumatic disease confirmed by a serologic test.

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Clinically it shows fatigue, muscle pain, joint pain, low-grade fever, a high frequency of Raynaud's syndrome, systemic sclerosis, systemic lupus erythematosus and dermatomyositis/polymyositis.[3] For the past 30 years, there has been an ongoing discussion to consider MCTD a 'distinct clinical entity.[4]

MCTD is known to occur around the world. This disease shows high female occurrence, with male to female ratio of 1:16. This disease affects every age group with a range of 4 - 80 years but 35 is the mean age of occurrence.[5] T-cell & B cell response is also seen in patients with decreased immunity. Distinguishing lesions observed in the organs are severe obliterative vascular lesions with minimal inflammatory infiltrates. Early phases of the MCTD comprise the majority of patients complaining of Raynaud's phenomenon, myalgias, arthralgias and easy fatigability. Fevers of unidentified reasons are the main systemic feature of MCTD.[6] Malar rash and erythematous rash are the most common skin changes seen in 75%-

100% of patients. Arthritis is observed in an average of 60% of patients. 30%-50% of patients show signs of myalgias and myositis. The GIT symptoms vary from diarrhea, heartburn, dysphagia and malabsorption. In upper GIT, motility dysfunction is a crucial problem[7] commonly, lungs and pleura can be involved. Pleurisy, pleural effusion, pulmonary arterial hypertension and diffuse parenchymal lung disease are characteristic features.[8] In MTCD heart, it shows abnormal ECG findings which involve all layers of the heart.[9] Neurological symptoms are minimal, which present as trigeminal neuralgia, aseptic meningitis, demyelination, transverse myelitis and peripheral neuropathy. Renal disease is absent, which is a hallmark of MCTD. The characteristic high values of anti-RNP antibodies can guard the advancement of diffuse proliferative glomerulonephritis. Some patients can present with diffuse glomerulonephritis or renal crisis of scleroderma.[10]

CASE REPORT

A 39-year-old male came to the emergency with a high-grade fever of 101°F, shortness of breath, and dry cough. His oxygen saturation was 70 percent, BP was 50/30 mmHg, heart rate 120/min, and respiratory rate 48 bpm. He was a suspected case of pulmonary embolism so Pulmonary Angiogram CT was done to rule out it. After admission to ICU, he was started on dual cardiac support with norepinephrine and dobutamine with normal saline. The oxygen saturation was improved to 90 percent with oxygen support and vitals were improved with blood pressure 90/60 mmHg, heart rate 100 bpm and respiratory rate 36 bpm. The patient was stable and depending on his laboratory results. He was diagnosed with a case of post-covid fibrosis, especially based on similar events of symptoms he had in November 2020 and July 2021. Labs showed Hb 7.6 g/dl, CRP 150 mg/L, TLC 26 cells/mm^3. His PCR for COVID was negative. On a previous visit, he was suspected as a case of having post-COVID fibrosis and bronchopneumonia. He also had co-morbid skin involvement with generalized severe acne all over the body and was diagnosed with seborrheic dermatitis. ACE, C3 and C4 levels were not significant. He was started on a broad-spectrum antibiotic and I/V steroids. But due to poor response, the patient was referred to a rheumatologist for detailed history. Screening for ANA levels was done which were positive. Antibodies were significantly raised against anti-smith and ribonucleic acid. A recent CT scan was compared with the previous one and showed interval progression in subpleural, mediastinal, hilar, axillary and upper abdominal lymphadenopathy and dilated air-filled esophagus leading to suspicion of mixed connective tissue disorder/overlap syndrome. The patient was stabilized and shifted to the room. He was discharged on oral medications Deltacortil and hydroxychloroquine. He was advised to follow up after 2 weeks.

DISCUSSION

Diagnosis of mixed connective tissue disease is based on clinical features and lab values along with the CT scan findings.

Serological criteria: Positive Anti RNP antibody. Anemia, leukopenia, raised ESR, positive Coomb's test, hypergammaglobulinemia (100%) and positive rheumatoid factor in patients (50-70%) are the laboratory findings.[11] Raised titers of antinuclear antibodies are observed in all patients with a non-uniformed speckled pattern. Hemagglutination test which detects Anti U1RNP antibodies are the distinguishing feature of MCTD. In some patients' antibodies appeared against hnRNP-A2, fibrillin-1 and nucleosomes. No antibodies were detected against RNA polymerases.[12] Management of MTCD patients is based on the specific remedies for the alike problems observed in SLE, scleroderma or polymyositis. In contrast scleroderma-like features show decreased response to therapy. Calcium channel blockers are used for PAH, NSAIDs are used to treat pain and immunosuppressive agents (steroid and methotrexate) are specifically used in patients of severe arthritis, serositis

which involves pleura, pericardium and pulmonary hypertension. There is a good prognosis seen in patients with MCTD because of a lower incidence of kidney disease and neurologic problems. The marked morbidity rate is observed in patients of MTCD because of numerous factors i.e. recurrent musculoskeletal pain, fibromyalgia and acid reflux disease. According to different studies, in MTCD, the mortality rate in the age group of 10 to 12 years ranges from 16% to 28%. Patients show poor prognosis having principal signs of scleroderma and polymyositis. Progressive pulmonary arterial hypertension and cardiac complications associated with it are the major cause of death.[13]

CONCLUSION

The present case report gives the importance of mixed connective tissue disorder to be in the differential diagnosis of any patient presenting with an overlap-features of SLE and scleroderma. Due to the pandemic, these symptoms and CT scan findings mimic those of COVID therefore, a proper history and examination are the key to the proper diagnosis and prompt treatment.

AUTHOR'S CONTRIBUTION

HK: Manuscript writing
MIP: Review manuscript
SZ: Data collection
KS: Review

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