Subacute Cutaneous Lupus Erythematosus in a Patient with Mixed Connective Tissue Disease

Nauman Ismat Butt

Department of Medicine and Allied, Azra Naheed Medical College, Superior University, Lahore, Pakistan

ABSTRACT

Mixed Connective Tissue Disease (MCTD) is an overlap syndrome of mild severity and good outcome. This disease consists of clinical features overlapping between Systemic Lupus erythematosus (SLE), scleroderma, rheumatoid arthritis, and polymyositis, in the presence of specific anti-RNP antibodies. We report a case of a 20-year girl who presented with a 3-month history of joint pains involving the small joints of her hands along with morning stiffness, skin thickening of hands, Raynaud's phenomena, and recurrent photosensitive skin rashes. On examination, she had a maculopapular rash over her face, neck, and arms with skin tightening, acrosclerosis, and Raynaud's phenomena of both hands along with clinical synovitis. She had positive anti-RNP antibodies, positive ANA and RA Factor with normal serum C3 and serum C4 with negative anti-DsDNA, anti-Ro, anti-La, anti-CCP, and anti-phospholipid antibodies. She was diagnosed as MCTD with subacute cutaneous lupus erythematosus (SCLE) and started on hydroxychloroquine and oral prednisolone. At 6 months follow-up, she was in remission and tolerating hydroxychloroquine without any adverse effects.

Key Words: *Mixed connective tissue disease, Anti-RNP antibodies, Subacute cutaneous lupus erythematosus, Skin biopsy*.

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INTRODUCTION

Mixed Connective Tissue Disease (MCTD) was first described in 1972 by Sharp *et al*.[1] as an overlap syndrome of mild severity and good outcome. This disease consists of clinical features overlapping between systemic lupus erythematosus (SLE), scleroderma, rheumatoid arthritis (RA), and dermatomyositis; therefore, it is termed as 'mixed'.[1] The prevalence and incidence of MCTD were reported to be 2.98 per 100,000 and 0.39 per 100,000 in a population-based study in 2022 in Manhattan, USA.[2] The mean age at diagnosis was 37.9 years with a female-to-male ratio of 3.3:1.[3] The 5-year, 10-year, and 15-year survival rates of MCTD were reported as 98%, 96%, and 88%, respectively.[4] The clinical features of MCTD may include swollen puffy fingers, sclerodactyly, acrosclerosis, oesophageal dysfunction, myositis, joint pains with or without synovitis, and the presence of anti-RNP antibodies.[5] MCTD was the first overlap syndrome for which association with specific auto-antibodies was established. In addition to the presence of anti-RNP antibodies, patients with MCTD have a higher incidence of Raynaud's phenomena and pulmonary arterial hypertension.[6] However, renal involvement is less severe and patients have a good overall outcome.

Correspondence to: Dr. Nauman Ismat Butt, Department of Medicine and Allied, Azra Naheed Medical College, Superior University, Lahore, Pakistan
E-mail: nauman_ib@yahoo.com

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Herein, we report a case of a 20-year girl who presented with a 3-month history of joint pains involving the small joints of her hands along with morning stiffness, skin thickening of hands, Raynaud's phenomena, and recurrent photosensitive skin rashes. She was diagnosed as MCTD with subacute cutaneous lupus erythematosus (SCLE) and started on hydroxychloroquine and oral prednisolone.

CASE REPORT

A 20-year girl presented with a 3-month history of bilateral symmetrical joint pains involving the small joints of hands along with morning stiffness lasting more than 60 minutes. She also reported skin thickening of hands and Raynaud's phenomena, especially on exposure to cold and in winters. There was a 2-year history of recurrent skin rashes, and currently, she was having erythematous rash over her face, neck, arms, and hands for the last 2 months along with photosensitivity over sun-exposed areas without any obvious skin scaling or peeling. She had consulted various general practitioners and dermatologists and had been prescribed various topical steroids which resulted in improvement of the rash. However, the rash recurred when she stopped applying the topical medicines. On exploration, there was history of recurrent painless oral ulcers and low-grade intermittent fever. However, there was no history of genital ulcers, alopecia, urinary complaints, altered bowel habits, body weakness or neuro-psychiatric complaints. She was unmarried and a student. She did not smoke or use illicit drugs. There was no family history of psoriasis, scabies or skin disorders.

On physical examination, she was vitally stable with a temperature of 100.0° F. There was wide-spread symmetric, non-scarring, photosensitive maculopapular rash over sun-exposed areas including the whole face involving naso-labial folds, neck, arms, and hands. There was evidence of skin tightening, acrosclerosis, and Raynaud's phenomena of both hands without any signs of calcinosis, digital ulcers, ischemia, or gangrene. Musculoskeletal examination revealed mild tenderness and swelling at a few metacarpophalangeal and proximal interphalangeal joints bilaterally without any limitation of movements. Other joints were normal. There was no focal sensory, motor or cerebellar neurological deficit with power of 5/5 in all four limbs. Cardiovascular and respiratory examinations were normal.

On investigation, a complete blood count revealed a mild normochromic normocytic anaemia with haemoglobin of 10.1 g/dl with normal total leukocyte count and platelet counts. Erythrocyte Sedimentation Rate (ESR) was raised at 55 mm/hour with normal C-Reactive Protein (CRP). Urinalysis, liver function tests, and renal function tests were normal. Blood and urine cultures were negative. Serologies for syphilis (TPHA), hepatitis B, hepatitis C, and human immunodeficiency virus (HIV) were negative. Her echocardiography for pulmonary hypertension screening and abdomino-pelvic ultrasound were normal. Chest X-ray and pulmonary function tests were normal. An excisional skin biopsy was performed which showed epidermis with mild basal cell vacuolization, hyperkeratosis, mild follicular plugging, focal melanin incontinence, and mild perivascular lymphocytic inflammation. An autoimmune profile was done which showed positive anti-RNP antibodies, positive anti-nuclear antibodies (ANA) and RA factor with normal serum C3 and serum C4 and negative anti-dsDNA, anti-Ro, anti-La, anti-CCP, and anti-phospholipid antibodies. Her serum creatine phosphokinase (CPK) and serum aldolase were normal.

She was diagnosed as having MCTD with SCLE and started on hydroxychloroquine, 300mg (5 mg/kg body weight) per day. Due to synovitis and skin rash, she was given a short course of oral prednisolone, starting from 30 mg (0.5 mg/kg body weight) per day with tapering and stopping in 4 weeks. In addition, she was prescribed topical steroids, sunblock SPF 60, oral omerprazole, iron, calcium, and vitamin D supplements. She showed marked improvement after initiation of therapy with resolution of rash and synovitis within 4 weeks. At 6 months follow-up, she was in remission and tolerating hydroxychloroquine without any adverse effects.

DISCUSSION

MCTD generally has a favourable outcome.[4] However, the presence of renal disease, thrombotic events, and cardiovascular complications can lead to substantial morbidity and mortality in these patients.[6] More than 90% of patients with MCTD have joint pains while synovitis may be seen in up to 60%.[3] Myalgia and myositis may be seen in up to 70%.[3] Pulmonary symptoms may be seen in up to 75% of patients with MCTD and interstitial lung disease (ILD) may be seen in almost half the patients.[3] Pulmonary artery hypertension is the most common cause of death followed by ILD, infections, and cardiovascular disease.[6] Therefore, it is of pertinent importance that MCTD be diagnosed timely and early treatment be initiated to prevent complications. With a sensitivity of 69.4% and specificity of 99.4%, the Alacron-Segovia criteria is commonly used for diagnosing MCTD.[5] Requirement for diagnosis of MCTD is $\geq$3 clinical criteria (oedema of hands, synovitis, myositis, Raynaud's phenomenon or sclerodactyly/acrosclerosis) in the presence of anti-RNP antibodies.[5] Based on these criteria, our patient had a score of 3; namely, synovitis, Raynaud's phenomena, and acrosclerosis in the presence of positive anti-RNP antibodies.

The most common skin manifestation in MCTD is Raynaud's phenomena seen in up to 90% of the patients.[3] Other common cutaneous manifestations include acrosclerosis, sclerodactyly, digital infarcts and nail fold vascular changes. Skin rashes resembling lupus or dermatomyositis can also be present.[7] However, truncal scleroderma is rare in MCTD. Very rarely cutaneous mucinosis and sub-cutaneous lupus erythematosus may be seen in patients of MCTD.[8] Management of MCTD is complex and variability in clinical practice exists as the treatment is dictated by disease severity and organ system involvement. There are no definite guidelines for the treatment of MCTD and therefore recommendations from guidelines of SLE, RA, scleroderma, and dermatomyositis are often utilised in the management of MCTD.

Corticosteroids are often used as first-line agents because of their rapid onset of action and powerful anti-inflammatory actions.[9] The dose and duration of steroids depend on the disease severity and organ involvement. Hydroxychloroquine is especially useful to treat fatigue, mucocutaneous and musculoskeletal manifestations in MCTD and to prevent disease flares.[9,10] Hydroxychloroquine is safe during all trimesters of pregnancy and also improves long-term survival by protecting against irreversible organ damage, thrombosis, and bone mass loss.[10] Even with long-term hydroxychloroquine use, retinal toxicity is rare but should be monitored with ocular coherence tomography (OCT).[10] Other agents that may be used in MCTD include simple analgesics (paracetamol and NSAIDs) for pain relief, conventional DMARDs (methotrexate, azathioprine, mycophenolate, cyclophosphamide) and biological DMARDs (rituximab) with increasing disease severity and involvement of major organ systems especially pulmonary system.[11,12] Lung transplantation may be reserved for refractory cases. It is important to monitor for pulmonary disease with regular chest radiographs, yearly pulmonary function estimations including DLCO and yearly echocardiography for systolic mean pulmonary artery pressure to look for pulmonary hypertension.[3] Early diagnosis and treatment of pulmonary complications can lead to reduction in morbidity and mortality. SCLE can occur very rarely in patients with MCTD and is usually characterised by annular or maculopapular lesions, photosensitivity and the presence of anti-Ro and anti-La antibodies.[8] Our patient had maculopapular photosensitive skin rash with negative anti-Ro and anti-La antibiodies. However, the skin biopsy findings were

characteristic of SCLE, thus aiding the diagnosis. Our patient had predominant mucocutaneous involvement and mild synovitis without any major organ system involvement. She responded well to treatment with hydroxychloroquine and a short course of oral prednisolone. At 6 months of follow-up, her disease was in remission with hydroxychloroquine and she did not suffer any adverse effects.

In conclusion, this case highlights the difficulties and delays faced in the diagnosis of rheumatic diseases such as SCLE and MCTD especially when the disease activity is mild and the patient has non-specific complaints. The occurrence of SCLE in MCTD is a rare presentation. It is necessary that the treating physician keep rheumatic diseases such as SCLE and MCTD in the differentials when managing such patients so that timely referrals to dermatologists and rheumatologists can be made. Early diagnosis and prompt treatment may lead to a reduction in morbidity and mortality in such patients.

PATIENT'S CONSENT:
Written informed consent was obtained from the patient.

COMPETING INTEREST:
The author declared no competing interest.

AUTHOR'S CONTRIBUTION:
NIB: Conception, data collection, literature review, and manuscript writing.

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