Original Research Article

Clinical Profile of Sharp Syndrome: Is it rare in India?

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Abstract

Background: In 1972, Dr Sharp and colleagues described a new connective tissue disease, characterized by overlapping features of systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and polymyositis/ dermatomyositis (PM/DM) and by the presence of antibodies against the U1 small nuclear ribonucleoprotein autoantigen (U1 snRNP). This condition was termed mixed connective tissue disease (MCTD) and proposed as a distinct disease. Later, after observing the clinical evolution of MCTD patients, Sharp himself agreed that the original concept of MCTD had to be modified and that Internal organs were at risk for serious complications; patients were not always steroid responsive; prognosis was not always benign.

Materials and methods: Patients in the age group of 15-50 years diagnosed to have connective tissue diseases were included. 8 patients in the age group of 15-50 admitted in Medicine department were taken and they were evaluated for the clinical profile of sharp syndrome by thorough clinical examination, routine laboratory tests and special investigations depending on the clinical profile.

Results: 8 patients with connective tissue disease attending the medicine OPD were studied. Of these 8 patients were female patients. The median age of onset was 36 years, 8 patients met criteria by sharp and Alarcon-Segovia. The clinical features of patients at presentation are Raynaud's phenomena, Puffy fingers, esophagus dysmotility, skin rash, interstitial lung disease, arthritis, pulmonary hypertension, myositis, anemia.

Conclusion: SHARP syndrome is a rare condition, as evidenced by the small series of cases reported to date. Diagnosis is based on clinical and paraclinical criteria. The evolution can be interspersed with various complications that can affect the short, medium and long-term prognosis.

Key words

Sharp Syndrome, Systemic lupus erythematosus, Systemic sclerosis, Polymyositis, Dermatomyositis, Mixed connective tissue disease, Raynaud's Phenomena.

Introduction

Sharp's mixed connective tissue disease is rare, with an incidence rate that varies between 0.2 to 1.9/100,000 patients per year [1]. Originally described more than four decades ago, the concept of MCTD as a unique disease remains a subject of controversy up to the present time. The overlapping features of multiple CTDs, including SLE, inflammatory myositis, SSc, and rheumatoid arthritis with Anti-RNP antibodies were prevalent in, which helped to differentiate MCTD from other diseases like SLE [1].

MCTD patients were described as having a "milder" course of disease than patients with more typical SLE, namely a lower incidence of glomerulonephritis, less severe internal organ damage, and a more benign prognosis with favourable survival rates compared to other CTDs.

Joint Involvement

The spectrum of joint involvement in MCTD varies from a mild nonerosive and symmetric polyarthritis akin to what is observed in SLE to a more severe, erosive, and potentially destructive polyarthritis practically indistinguishable from RA.Polyarthralgia's and arthritis are common and often present early in the disease, affecting between 60% to 95% of patients with MCTD [2].

Skin Involvement

Raynaud's phenomenon is one of the most prevalent findings in MCTD patients, reported to occur in as many as 75% to 90% during the course of their disease Often, it is an early symptom for which a patient seeks medical attention or can be a sign picked up by a clinician evaluating the patient. It can even be present months or years before the onset of other clinical findings typical of MCTD [3].

Pulmonary Manifestations

Although considered a milder disease than other CTDs, MCTD nonetheless can cause serious and life-threatening organ damage, particularly with respect to the lungs. Overall, pulmonary involvement is seen in up to 85% of MCTD patients. Interstitial lung disease (ILD) accounts for the majority of pulmonary involvement and presents in a pattern similar to that seen in other CTDs such as SSc and inflammatory myositis [4].

Kidneys

Kidneys involved in 25% to 40% of patients. In many cases this involvement is mild, patients are often asymptomatic, and the prevalence of severe kidney disease is rare [3]. Membranous glomerulonephritis (GN) is the most common pathologic lesion observed and is often associated with immune complex deposition localized to the mesangium and/or subepithelial space [5].

Cardiovascular System

Cardiac involvement is common and can be detected in between 24% to 63% of MCTD patients according to one systematic review of the literature. The most common cardiac manifestation is pericarditis, which can affect between 30% to 43% of patients. Valvular heart disease is well reported, especially mitral valve prolapses [6].

Gastrointestinal Tract

Gastrointestinal complications of MCTD overlap prominently with those of SSc. Gastroesophageal reflux disease and dysphagia are by far most common complications, reported in as many as 77% and 61%, respectively, of patients with SSc, MCTD, and UCTD [7].

Muscle Involvement

Inflammatory myositis is a hallmark overlap feature and part of the original description of

MCTD [2]. Approximately 80% to 90% of patients with MCTD have muscle involvement of one type or another [3]. Myalgias are common, often without demonstrable weakness or abnormal creatine kinase (CK) levels, imaging, or electromyography (EMG) testing [8].

Aim and objectives

- To identify different clinical presentations of Mixed Connective Tissue Disorder
- To evaluate various hematological parameters of Mixed Connective Tissue Disorder

Materials and methods

Study subjects

Patients in the age group of 15-50 years diagnosed to have connective tissue diseases admitted in the Department of General Medicine in Malllareddy Institute of Medical Sciences, Suraram, Hyderabad.

Sample size and design

8 patients in the age group of 15-50 admitted in Medicine department were taken and they were evaluated for the clinical profile of sharp syndrome by thorough clinical examination, routine laboratory tests and special investigations depending on the clinical profile. This was a descriptive observational study a total of 24 patients were analyzed.

Study period

June 2020 - January 2022

Inclusion criteria

- Patients who met criteria by sharp and Alarcon-Segovia
- Patients who give consent.

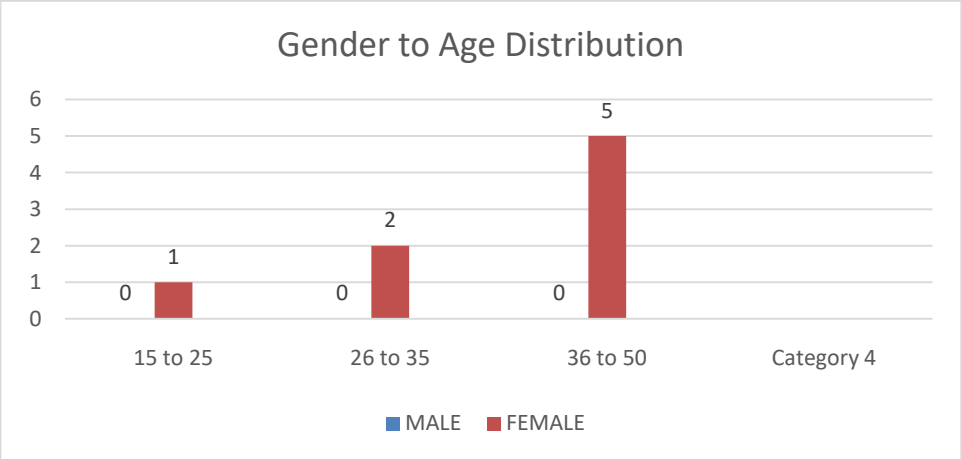
Exclusion criteria

- Patients less than 18 years.
- Pregnant and lactating women.
- Patients who do not give consent.
- Patients who do not met criteria by sharp and Alarcon-Segovia

Results

A total number of 8 cases were studied. The majority of patients were belonging to age group of 36-50 years (63%) followed by 25 to 35 years (25%) as per **Graph – 1** and **Pie Diagram – 1**.

Graph – 1: Age Distribution.

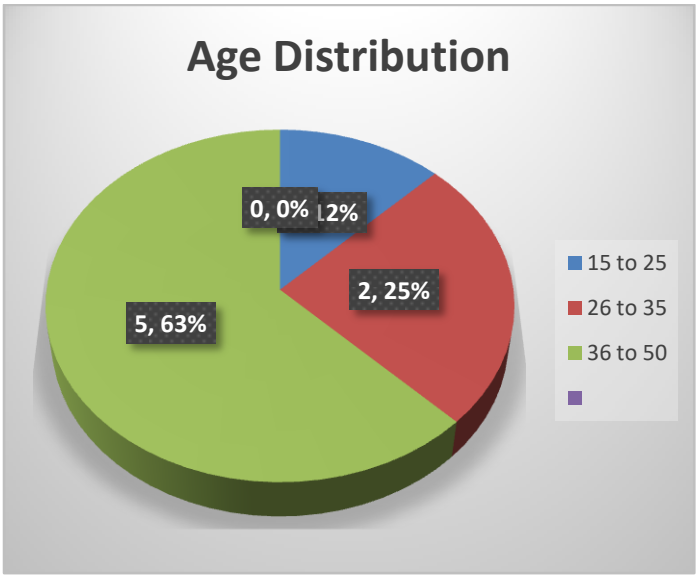


Prevalence of MCTD between sexes with between 5 to 10 times as many women affected as men but in our study Among 8 patients, MCTD seen in only females (**Graph – 1**).

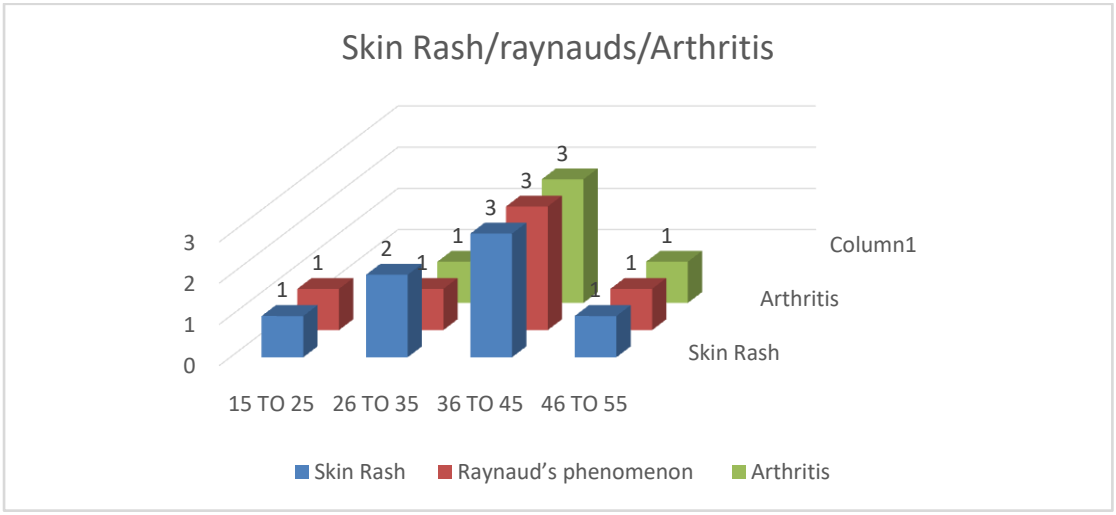
In our study, symptoms distribution was skin rash (21%), Raynaud's phenomenon (17%), Arthritis (17%), CVS (11%), CNS (3%) symptoms were most common clinical features and Most Common Age Group was 35 to 45 years (**Graph – 2**, **Pie Diagram - 2**).

The mean hemoglobin level was 9.3 g% and other hematological parameters Mean RDW was 43 and Mean ESR 50 mm/hr were seen in our study (**Table – 1**).

Pie Diagram – 1: Age distribution.



Graph – 2: Symptoms distribution.



Pie diagram – 2: Symptom distribution.

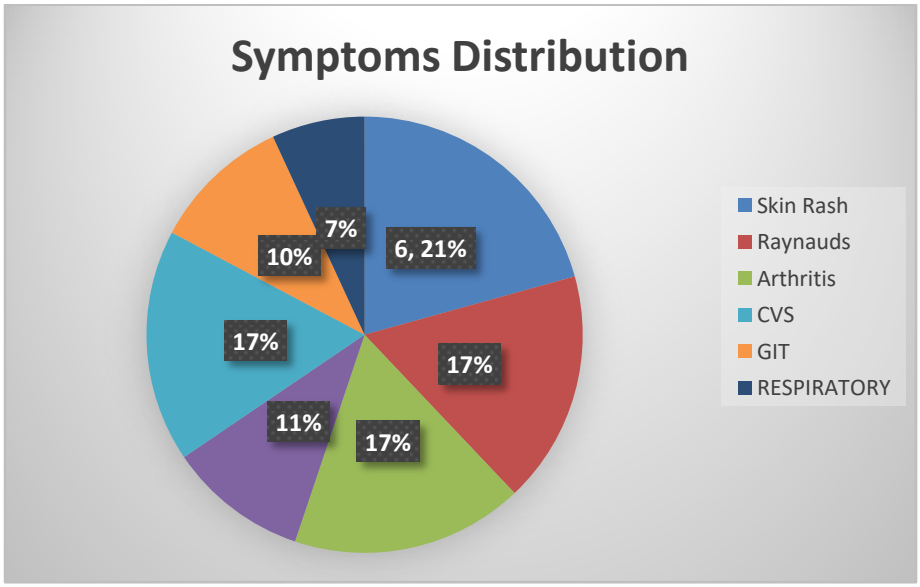
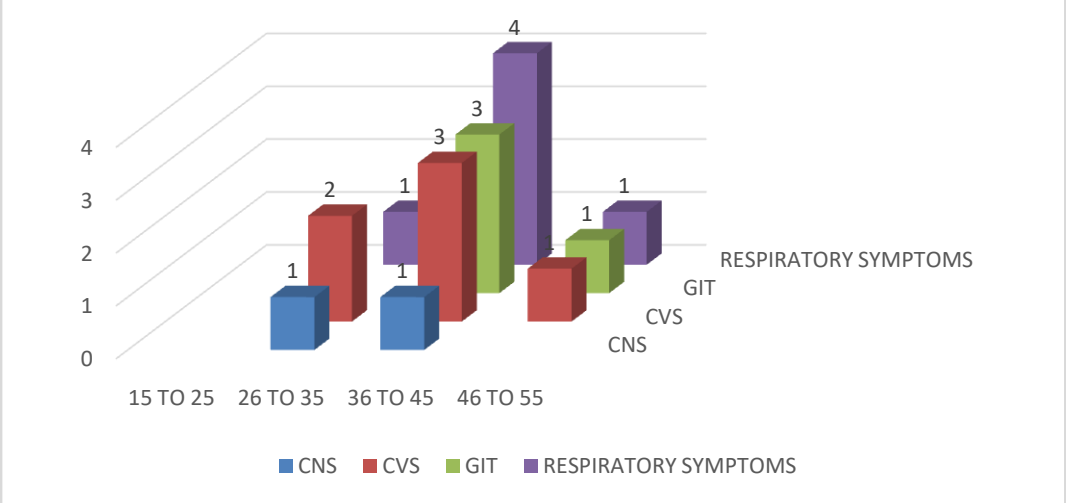


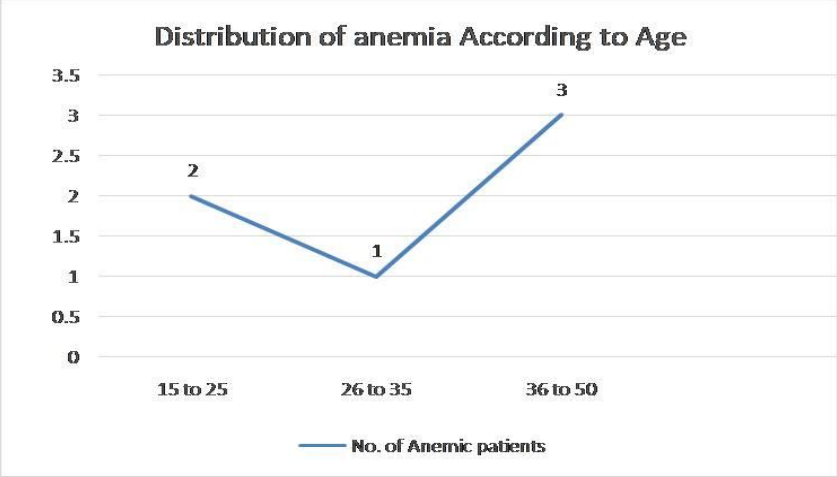
Table – 1: Hematological Parameters.

	N	Minimum	Maximum	Mean	Median	SD
Age	8	15	50	36	37	11.31
Hemoglobin (g/dl)	8	6.8	12	9.3	9.6	2.3
RDW	8	37.6	54.2	43	45	7.2
ESR (mm/hr)	8	50	102	50	53	28.7

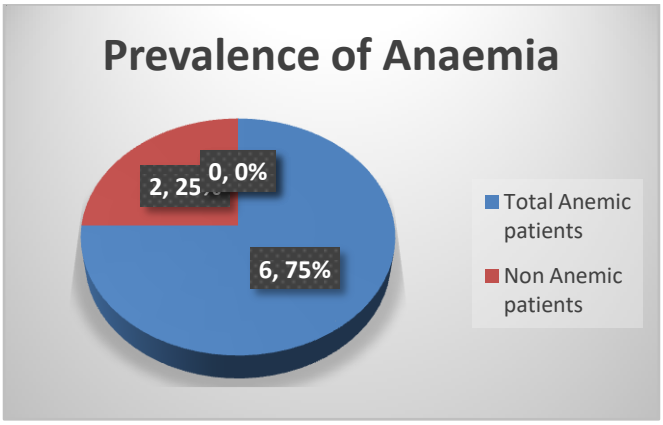
Graph – 3: CNS/CVS/GIT/Respiratory symptoms – Distribution to age.



Graph – 4: Age to hemoglobin distribution.



Graph – 5: Prevalence of Anemia in MCTD.



The total number of anemic patients were 6 out of 8 with minimum hemoglobin 6.8 g/dl and maximum hemoglobin was 12 g/dl with Mean 9.3, Median 9.6 and Standard Deviation was 2.3, Red Cell Distribution width was raised to 54.2 in patients with Pulmonary Arterial Hypertension (**Table - 1**).

CNS/CVS/GIT/Respiratory symptoms – Distribution to age was as per **Graph – 3**. Age to hemoglobin distribution was as per **Graph – 4**. Prevalence of Anemia in MCTD was as per **Graph – 5**. Hemoglobin levels did not show any significant correlation with Age and Severity of the Disease of the patients. But in some cases, there was significant reduction in hemoglobin in sever disease which causes more morbidity to the patients.

Discussion

A total number of 8 cases were studied. The majority of patients are belonging to age group of 36 to 50 years (63%) with female sex predilection (100%). Within the rheumatic diseases the diagnosis of well-established rheumatoid arthritis, progressive systemic sclerosis, dermatomyositis, and SLE is usually clearcut. However, the initial manifestations of general malaise, arthralgias, and vascular instability are deceptively similar; a definitive diagnosis usually depending upon a period of careful follow-up to detect a characteristic evolution of physical findings, laboratory tests, and radiological changes [2]. Alarcon-Segovia's criteria used for sharp syndrome diagnosis are as per **Table - 2**.

Table – 2: Alarcon-Segovia's criteria.

Alarcon-Segovia's criteria
A. Serological criteria
Anti-RNP antibodies with a hemagglutination titer of ≥1:1600
B. Clinical criteria
1. Swollen hands
2. Synovitis
3. Myositis*
4. Raynaud's phenomenon
5. Acrosclerosis
MCTD is present if:
Criterion A is accompanied by three or more clinical criteria - one of which must include synovitis or myositis.

Many patients can suffer severely with multiple organ involvement like hemorrhagic pericardial effusion, Liebman–Sacks endocarditis, Pulmonary arterial hypertension, Restrictive lung disease, lupus Nephritis and Polyserositis. Overall, PAH remained the leading cause of death in patients with MCTD. The prevalence of cardiovascular morbidity and mortality, malignancy, and thrombotic events increased during the disease course of MCTD. The presence of antiphospholipid antibodies raised the risk of mortality [9].

Conclusion

Sharp's mixed connective tissue disorder patients will initially present within distinct symptoms like joint pains, easy fatiguability, skin rash, swollen puffy fingers, small joint pains, difficulty in swallowing, photosensitivity and pain abdomen. These patients gradually end up with multiple organ involvement like Massive haemorrhagic pericardial effusion, Liebman–Sacks endocarditis, Pulmonary arterial hypertension, Severe restrictive lung disease, lupus Nephritis and Polyserositis. With prompt diagnosis and early treatment, we can reduce sever morbidity and mortality rates of the patients who are suffering with sharp's syndrome which is not rare in India.

References

1. Scagliusi P, Muratore M, Martiradonna A, Berlingerio G, Carrozzo M. La sindrome di Sharp. Studio clinico, immunologico e nosografico [Sharp's syndrome. Clinical, immunological and nosographic aspects]. Minerva Med., 1980 Dec 15; 71(50): 3655-63. Italian. PMID: 6161325.
2. Bennett RM, O'Connell DJ. The arthritis of mixed connective tissue disease. Ann Rheum Dis., 1978; 37(5): 397–403.
3. Mohan C, Putterman C. Genetics and pathogenesis of systemic lupus erythematosus and lupus nephritis. Nat Rev Nephrol., 2015; 11(6): 329–341.
4. Bodolay E, Szekanecz Z, Dévényi K, et al. Evaluation of interstitial lung disease in mixed connective tissue disease (MCTD). Rheumatol Oxf Engl., 2005; 44(5): 656–661.
5. Kitridou RC, Akmal M, Turkel SB, et al. Renal involvement in mixed connective tissue disease: a longitudinal clinicopathologic study. Semin Arthritis Rheum., 1986; 16(2): 135–145.
6. Ungprasert P, Wannarong T, Panichsillapakit T, et al. Cardiac involvement in mixed connective tissue disease: a systematic review. Int J Cardiol., 2014; 171(3): 326–330.
7. Weston S, Thumshirn M, Wiste J, et al. Clinical and upper gastrointestinal motility features in systemic sclerosis and related disorders. Am J Gastroenterol., 1998; 93(7): 1085–1089.
8. Vianna MAAG, Borges CTL, Borba EF, et al. Myositis in mixed connective tissue disease: a unique syndrome characterized by immunohistopathologic elements of both polymyositis and dermatomyositis. Arq Neuropsiquiatr, 2004; 62(4): 923–934.
9. Hajas A, Szodoray P, Nakken B, Gaal J, Zöld E, Laczik R, Demeter N, Nagy G, Szekanecz Z, Zeher M, Szegedi G, Bodolay E. Clinical course, prognosis, and causes of death in mixed connective tissue disease. J Rheumatol., 2013 Jul; 40(7): 1134-42. doi: 10.3899/jrheum.121272. Epub 2013 May 1. PMID: 23637328.
10. Abugroun A, Hallak O, Ahmed F, Gaznabi S. Massive Hemorrhagic Pericardial Effusion with Cardiac Tamponade as Initial Manifestation of Mixed Connective Tissue Disease. Cardiol Res., 2018 Feb; 9(1): 68-71. doi: 10.14740/cr654w. Epub 2018 Feb 11. PMID: 29479391; PMCID: PMC5819634.