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An observational study to determine clinical profile,immunological profile of MCTD patients and adverse events developed during the duration of treatment.

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Abstract :

Background: Mixed connective tissue disease (MCTD) is a rare autoimmune disease, characterized by the production of specific autoantibody anti-RNP, which presents with varied overlapping symptoms of different connective tissue disorders. The aim of this study is to identify the frequency and patterns of MCTD.

Objective :To demonstrate the clinical profile,immunological profile of MCTD patients and adverse events developed during the duration of treatment

Design :Prospective observational study

Setting : A large, academic, tertiary medical center

Methodology:All MCTD cases admitted in Sapthagiri Institute of Medical Sciences and Research Centre was included.Data was collectedthrough a prepared performa.Patients were followed up till death or discharge.

Results:All 10 cases of MCTD, U1RNP is positive.

8 of the 10 cases were treated aggressively with immunosuppressants.

Most common secondary infection was Pneumonia.

One patient developed Abdominal TB

One patient developed avascular necrosis of femur secondary to high dose steroids.

Interpretation and conclusion:It can be noted that even though the relapse rate was lower among patient treated aggressively the chance of developing secondary infection was very high

Hence it is important to monitor the cases which are treated with immunosuppressants, for early diagnosis and treatment of any adverse events.

Key words:MCTD,Pneumonia,avascular necrosis

INTRODUCTION

Mixed connective tissue disease (MCTD), also known as Sharp´s syndrome, was originally defined in 1972 as a connective tissue disorder characterized by the presence of high titers of a distinctive autoantibody, now called anti-U1 RNP. MCTD is an autoimmune condition with overlapping of at least two connective tissue diseases, including Systemic Lupus erythematosus (SLE), Scleroderma and Polymyositis (PM), and rheumatoid arthritis.[1] The distinctive overlap features commonly appear sequentially over time.[2]

MCTD occurs worldwide and in all races, with a peak incidence in adolescence and the 20s. About 80% of people who have the disease are women.[3] The cause of MCTD is unknown.[4] The natural history and outcome of MCTD patients are not well-characterized as preceding reports yielded inconsistent results. One study reported that more than 50% of patients with MCTD evolved to either SS or SLE, while a subsequent study found such evolution in only 13% of their cohort.[5,6]

There is very little information available regarding the prevalence and incidence of MCTD.[7] In a 2011 nationwide study in Norway, the prevalence of MCTD was 3.8 per 100,000 adults, with an incidence of 2.1 million per year. Frequently the first manifestations resemble early SLE, Systemic scleroderma, Polymyositis, or even Rheumatoid arthritis, with many patients appearing to have an undifferentiated connective tissue disease initially.[8] The early clinical features of MCTD are non-specific and may consist of general malaise, arthralgia, myalgia, and low-grade fever. Raynaud phenomenon may precede other manifestations by years. Swollen hands and puffy fingers are typical, skin findings include lupus or dermatomyositis-like rashes, and diffuse scleroderma-like skin changes may develop.[9]

MATERIALS AND METHODS:

Source of data:

All patients diagnosed with MCTD at the Sapthagiri Institute of Medical Sciences and Research Centre will be included.

A. Study design: Prospective Observational study

B. B. Study period: 18 months February 2021 to August 2022

C. Place of study: Research Facility of the Sapthagiri Institute ofMedical Sciences.

D. Sample Size : 10

E. INCLUSION CRITERIA :

- Those with MCTD who are admitted to the SIMS&RC.
- At least 18 years old
- People who are willing to provide informed consent

F. EXCLUSION CRITERIA:

- Immunocompromised patients

G. METHODOLOGY:

- Source of data :
- All MCTD cases diagnosed clinically with supportive investigation that presented to our institution over past 2 year were compiled and compared.

All patient included in this review were required to meet the criteria

1 .Serological criteria:Positive antibodies to U1 RNP antibodies in a titer >1:1600 dilution

2 .Clinical criteria(Alarcon-Segovia)

a) Swollen hands (puffy hands)
b) Synovitis
c) Myositis
d) Raynaud's phenomenon
e) Acrosclerosis

STATISTICAL ANALYSIS:

Using SPSS V.20 for analysis, the obtained data will be entered into Microsoft Excel. The result will be expressed in the form of descriptiveand inherently statistics.

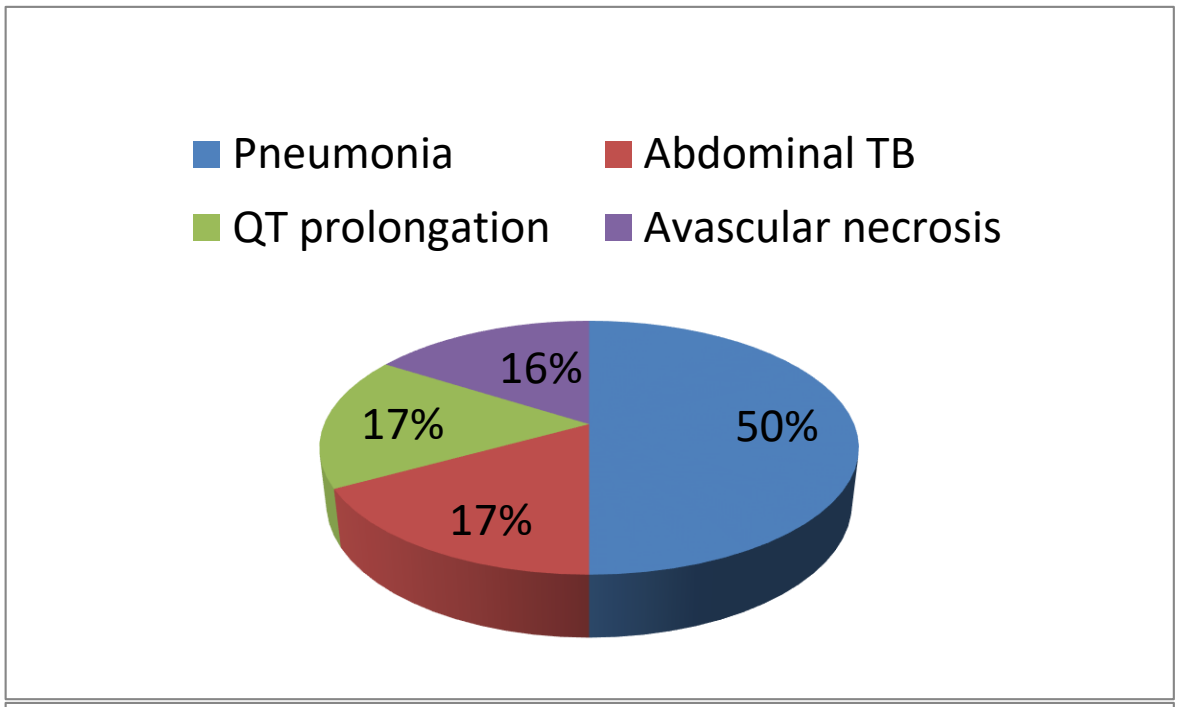
If $p < 0.05$, it is said to be statistically significant

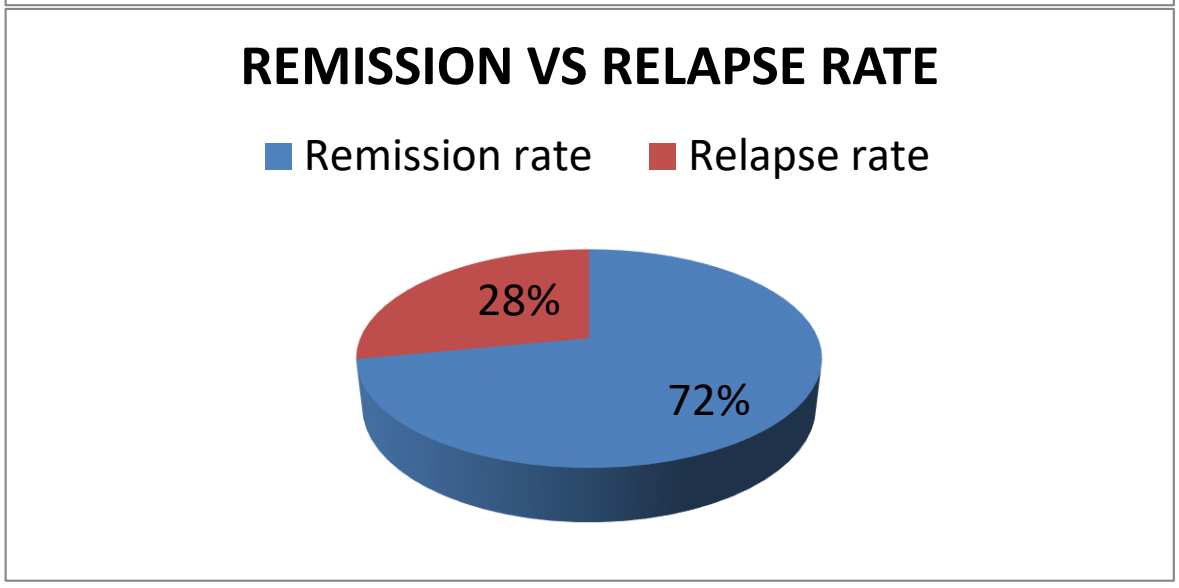
RESULTS:

Results

The majority of the patients (96.7%) were female and only 3.3% were male. The study shows that 30% were aged between 30–39 years, 26.6% were aged 40–49 years, 16.7% were aged 60 years and above, 16.7% were aged 18–29 years, and the remaining 10% were aged 30–39 years

Fatigue manifested as a constitutional symptom in all patients, fever in 63.3% and weight loss in 63.3%The most common cutaneous symptoms were erythematous rash in half of the patients, skin tightness in 23.3%, and sclerodactyly in 20%.





All 30 cases of MCTD, U1RNP is positive.

18 of the 30 cases were treated aggressively with immunosuppressants.

Most common secondary infection was Pneumonia.

One patient developed Abdominal TB

One patient developed avascular necrosis of femur secondary to high dose steroids.

One patient developed QT prolongation secondary to hydroxychloroquine.

Relapse rate was more in the patient treated with low dose steroids compared to aggressively treated patient.

One patient treated with low dose steroid developed ITP,which resolved after high dose pulse therapy

DISCUSSION:

MCTD is a rare disorder and presents with varied overlapping manifestations of different connective tissue disorders.[14] Many patients evolve into other connective tissue disorders with the passage of time. In this study, MCTD has been investigated in 30 Sudanese patients at Omdurman Military Hospital during the period from February 2019 to July 2019 in the rheumatology clinic patients, according to Alarcon-Segovia criteria.

The majority of the patients (96.7%) were females and only 3.3% were male. Thirty percent of all the patients aged were between 30–39 years with a mean age of 34.5 years. This is comparable to previous studies, for example a study in Karachi, Pakistan reported that among patients with MCTD 80% were females and 20% of patients were males. The mean age was 30.5 years.[15] A study in Gabon showed that seven patients with mixed connective tissue disease were women (100%), with an average age of 39.5 years.[16] The most common clinical presentation was arthralgia in all the patients, which were symmetrical in 90% of the patients, followed by arthritis in 63.3%, puffy fingers in 63.3%, and hand swelling in 60% as major musculoskeletal symptoms. A previous study by Amigues et al reported that about 60% of patients complain of arthralgia.[17] This is comparable to a study in the Philippines in which the chief complaint was most commonly joint pain, at 67%.[18,19]

CONCLUSION :

IT CAN BE NOTED THAT EVEN THOUGH THE RELAPSE RATE WAS LOWER AMONG PATIENT TREATED AGGRESSIVELY THE CHANCE OF DEVELOPING SECONDARY INFECTION WAS VERY HIGH

HENCE IT IS IMPORTANT TO MONITOR THE CASES WHICH ARE TREATED WITH IMMUNOSUPPRESSANTS, FOR EARLY DIAGNOSIS AND TREATMENT OF ANY ADVERSE EVENTS.

Disclosure

All authors declare no conflicts of interest in this work.

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