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Profile of Sharp Syndrome in Thiès: A Preliminary Study in Two Internal Medicine Departments

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Abstract

Introduction: Sharp syndrome is a rare autoimmune disease characterized by the presence of autoantibodies targeting the U1 ribonucleoprotein (U1RNP), with significant clinical polymorphism that may include features of systemic sclerosis, systemic lupus erythematosus, inflammatory myopathies, and rheumatoid arthritis. Several classification criteria can be used for diagnosis, including those of Sharp, Alarcon-Segovia, Kasukawa, and Kahn. The clinical picture is characterized by cutaneous and mucosal, joint, and muscular involvement and may be complicated by pulmonary arterial hypertension or diffuse interstitial lung disease. The objectives of this study were to determine the prevalence and to describe the clinical, paraclinical, evolutionary, and therapeutic aspects of Sharp syndrome. **Methods:** This was a retrospective, descriptive, analytical longitudinal study conducted from January 2014 to January 2024 in two internal medicine departments: the Regional Hospital Center of Thiès and the Mame Abdou Aziz SY Dabakh Hospital in Tivaouane. The study included patients with a confirmed diagnosis of mixed connective tissue disease. **Results:** The prevalence was 0.70%, with a female predominance. The mean age was 35.8 years. Regarding sociodemographic characteristics, 80% of the patients were married, two had a university education, two were housewives, and three lived in peri-urban areas. All three cases came from the Amadou Sakhir Ndiéguene Regional Hospital Center in Thiès. One patient had type 2 diabetes. Three patients were nulligravida, and one was using oral contraception. General health deterioration was observed in 80% of cases. Clinically, 80% pre-

sented with inflammatory-type arthralgia involving both small and large peripheral joints. Raynaud's phenomenon and "puffy fingers" were found in 60% of patients. One patient had myalgia localized to the lower limbs. Pulmonary involvement included two cases of interstitial lung disease with pulmonary fibrosis. No cases of pulmonary arterial hypertension were recorded. Cardiac involvement consisted of one patient with a left anterior fascicular block on ECG. Gastrointestinal manifestations included epigastric pain suggestive of ulcer in 60% of cases. Biologically, an inflammatory syndrome was present in two patients. Immunologically, all patients tested positive for antinuclear antibodies and anti-U1RNP antibodies, with titers greater than 241. All patients were treated with corticosteroids and hydroxychloroquine. The mean follow-up duration was 4.4 years. **Conclusion:** Sharp syndrome had a low prevalence in our study, with articular involvement being the most common clinical manifestation. Interstitial lung disease was the most frequent complication, and all patients were treated with corticosteroids and antimalarial agents. A multicenter national study is warranted to gain a more comprehensive understanding of this rare disease.

Keywords

Autoimmune Disease, Sharp Syndrome, Thiès

1. Introduction

Sharp syndrome is a rare autoimmune disease characterized by the expression of autoantibodies targeting the U1 ribonucleoprotein (U1RNP). This entity was first described in 1972 by Sharp and is associated with significant clinical polymorphism [1].

It also presents overlapping clinical features with systemic sclerosis, systemic lupus erythematosus, and inflammatory myopathies [2].

The pathogenesis remains unclear, although several hypotheses have been proposed [3].

It is a rare condition with an annual incidence of 1.9 per 100,000 inhabitants, based on studies conducted over a 20-year period from 1985 to 2014 [4].

Several classification criteria can be used for diagnosis, including those proposed by Sharp, Alarcón-Segovia, Kasukawa, and Kahn [5].

The clinical presentation is primarily marked by mucocutaneous, articular, and muscular involvement, and may be complicated by pulmonary arterial hypertension or interstitial lung disease [5].

Therapeutic strategies depend on the clinical presentation and complications observed, with corticosteroids and immunosuppressants being the most commonly used treatments.

In Senegal, internal medicine was officially recognized as a specialty in 2004 [6]. Since then, scientific research has highlighted the presence of autoimmune diseases in previously unsuspected proportions and has demonstrated the critical role of internal medicine in improving healthcare delivery, including during the

COVID-19 pandemic [7].

It is in this context that we aimed to study the clinical features of Sharp syndrome in the Thiès region.

The objective of our study was therefore to determine the prevalence and describe the clinical, paraclinical, evolutionary, and therapeutic aspects of Sharp syndrome. To the best of our knowledge, this is the first study of its kind, compiling cases from two centers: the Internal Medicine Departments of El Hadji Ahmadou Sakhir Ndiéguene Regional Hospital in Thiès and the Mame Abdou Aziz SY Dabakh Public Health Establishment in Tivaouane. The study period extended from January 2014 to January 2024.

2. Personal Work

2.1. Study Objectives

2.1.1. Main Objective

To describe the epidemiological, diagnostic, and management characteristics of Sharp syndrome.

2.1.2. Specific Objectives

- To determine the prevalence of mixed connective tissue diseases (MCTD) relative to other diagnosed autoimmune diseases over a 10-year period.
- To describe the clinical, biological, immunological, and radiological manifestations of Sharp syndrome.
- To investigate the complications and their correlation with disease duration.
- To evaluate the management of Sharp syndrome.

2.2. Patients and Methodology

2.2.1. Study Setting

The study was conducted in two internal medicine departments at the Regional Hospital Center of Thiès and the Mame Abdou Aziz SY Dabakh Hospital in Tivaouane.

2.2.2. Study Type and Duration

This is a retrospective, descriptive, and analytical longitudinal study covering the period from January 2014 to January 2024.

2.2.3. Study Population

- Inclusion Criteria: Any patient diagnosed with mixed connective tissue disease (MCTD) based on recognized classification criteria and who had regular follow-up at the chosen sites.
- Exclusion Criteria: Incomplete records and patients lost to follow-up.

2.2.4. Parameters and Aspects Studied

The various characteristics and aspects studied in the patients include:

- Sociodemographic characteristics of the patients;
- Medical history and background;

- Clinical, paraclinical, and diagnostic features;
- Therapeutic aspects;
- Evolutionary and prognostic aspects.

2.2.5. Data Collection and Processing

We reviewed five (5) medical records of patients potentially eligible for the study out of 709 records of patients with autoimmune diseases. A data entry application was developed using the Epi-Info software.

3. Results

3.1. Prevalence Description

Out of 709 patients with autoimmune diseases, five met the diagnostic criteria for mixed connective tissue disease, resulting in a prevalence of 0.70% (n = 5).

3.2. Sociodemographic Characteristics

3.2.1. Gender

All five cases were women.

3.2.2. Age

The average age was 35.8 years, with a range from 24 to 52 years.

3.2.3. Other Characteristics

- 80% of the patients were married;
- Two patients had a university education;
- 40% of the cases were housewives;
- Three patients lived in a suburban area, representing 60% of the cases;
- The diagnosis was made at the Thiès Regional Hospital Center for three patients.

3.3. Medical History and Background

One patient had type 2 diabetes at the time of diagnosis. No family history of autoimmune diseases was found.

3.4. Gynecological and Obstetric History

- Three women were nulligravida;
- One woman was on oral contraception.

3.5. Clinical Aspects

3.5.1. General Signs

- The average blood pressure was 115/82 mm Hg, with extremes of 93/60 mm Hg and 141/102 mm Hg.
- The average pulse was 91.75 beats per minute.
- The average weight was 57.4 kg, with extremes of 44 kg and 75 kg.
- Four patients had weight loss.
- 60% of the cases presented with physical asthenia and fever.

3.5.2. Joint Involvement

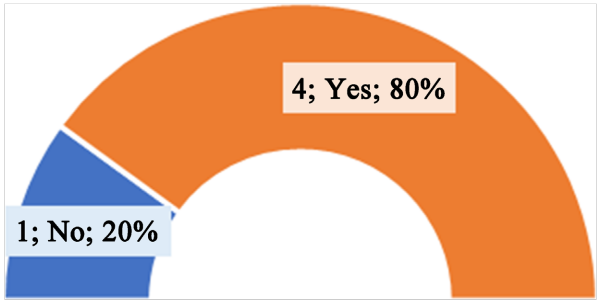

Figure 1. Distribution according to the presence of arthralgia.

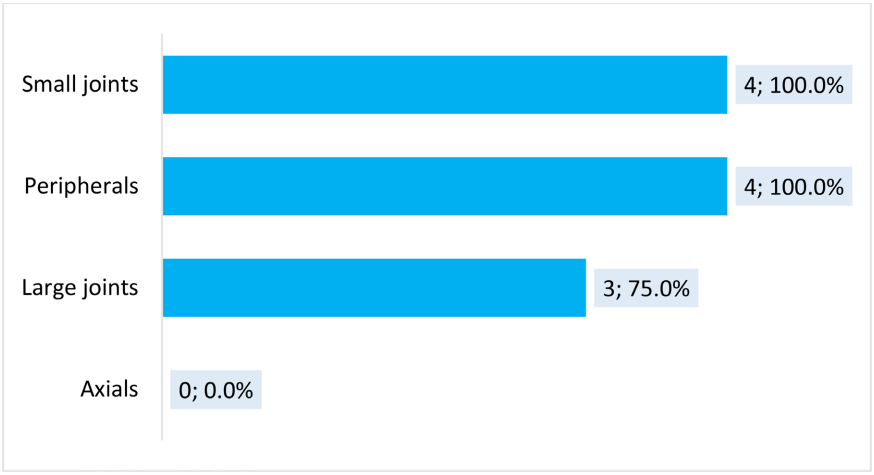

Figure 2. Distribution of joint involvement by site.

80% of patients had peripheral inflammatory arthralgias, predominantly in the small joints. One case of "buttonhole" joint deformity of the 3rd left finger was noted.

3.5.3. Muscular Involvement

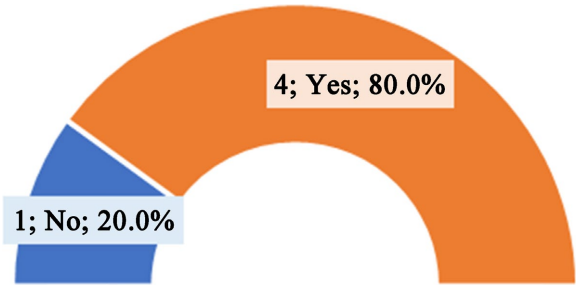

Figure 3. Distribution according to the presence of myalgia.

One patient presented with myalgia in the lower limbs.

3.5.4. Mucocutaneous Involvement

Three patients exhibited Raynaud's phenomenon and "sausage fingers." 40% of

the cases had sclerodactyly with skin thinning.

Other mucocutaneous findings included one case of oral ulcers and one case of pruritus with scratching lesions.

3.5.5. Pulmonary Involvement

- Three patients were asymptomatic.
- One case of right basal pulmonary condensation syndrome was observed.

3.5.6. Cardiac Involvement

One patient presented with an anterior hemiblock on ECG.

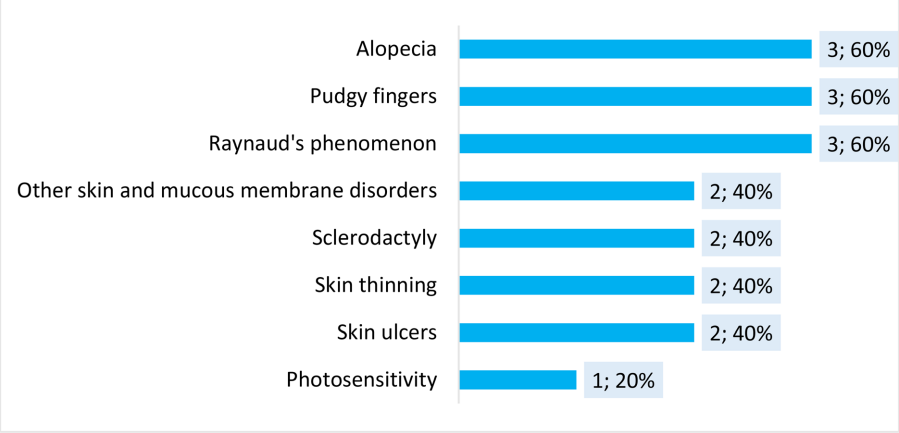

Figure 4. Distribution according to mucocutaneous involvement.

3.5.7. Digestive Involvement

Three patients had digestive issues: two with epigastralgia suggestive of ulcers, and one with gastroesophageal reflux.

Summary of disorders

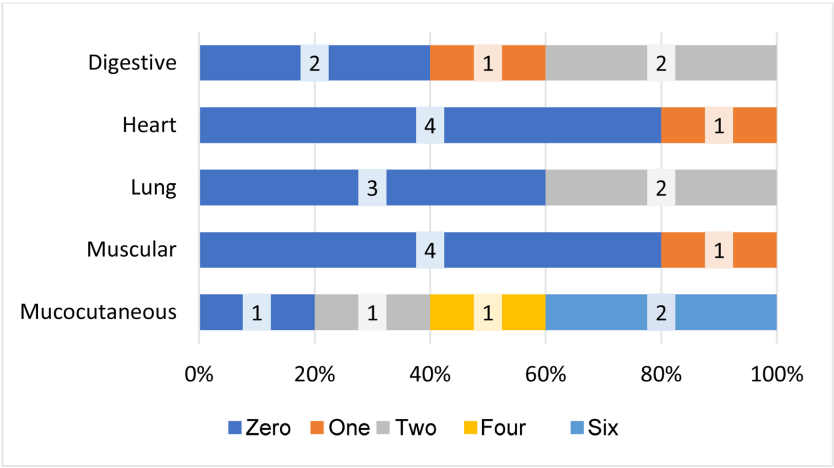

Figure 5. Number of cases by clinical presentation.

80% of patients had mucocutaneous and joint disorders.

Two patients had no complications.

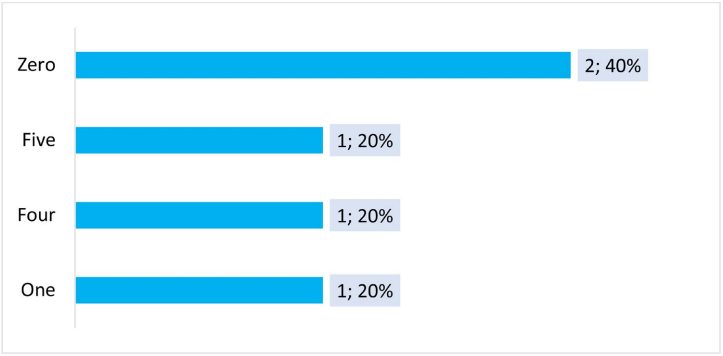

Figure 6. Distribution by number of complications.

3.6. Paraclinical Aspects

3.6.1. Laboratory Tests

The mean white blood cell count was 7910/ul with a mean neutrophil count of 4256/ul and a mean lymphocyte count of 2313/ul.

The mean haemoglobin level was 11.4 g/dl and the mean platelet count was 296250/ul.

Mean creatinemia was 7.7 mg/l.

There was one case of polyclonal hypergammaglobulinaemia on serum protein electrophoresis.

Two patients had a biological inflammatory syndrome.

3.6.2. Immunology

Anti-nuclear antibodies were positive in all patients with a mottled appearance. Anti-U1RNP antibodies were positive in all cases at levels above 241. Anti-SSA/Ro antibodies were positive in 40% of cases and anti-native DNA antibodies in 20% of cases.

3.6.3. Imaging and Endoscopy

The chest X-ray showed a bilateral interstitial syndrome in one case. 40% of patients had a chest CT scan with diffuse interstitial lung disease. Upper Gastrointestinal endoscopy was normal in 60% of cases.

3.7. Diagnostic Criteria Used

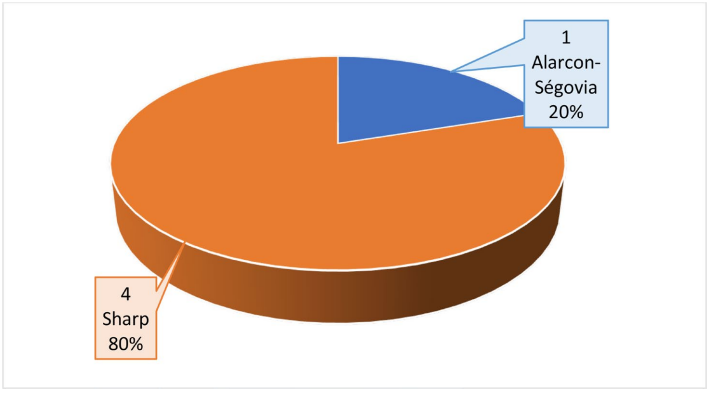

Figure 7. Distribution of individuals according to diagnostic criteria used.

Sharp's diagnostic criteria were used in 80% of cases.

3.8. Therapeutic Aspects

Corticosteroid therapy, hydroxychloroquine and proton pump inhibitors were used in all patients.

3.9. Duration of Follow-Up

The mean follow-up duration for the patients was 4.4 years, ranging from 1 to 9 years.

Over the course of the disease, two patients developed pulmonary complications in the form of interstitial lung disease; one patient presented with a cardiac complication characterized by a left anterior fascicular block on ECG; and two patients experienced gastrointestinal complications, including epigastric pain and heartburn

3.10. Correlation of Follow-Up with Complications

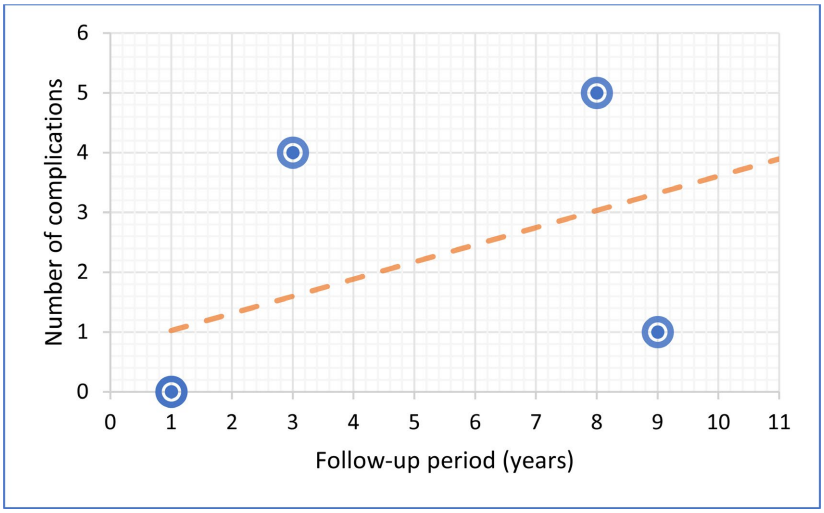

Figure 8. Scatter plot of follow-up time and number of complications.

The Spearman correlation coefficient (Rho) between the number of complications and the duration of follow-up was estimated at 0.7, suggesting that a longer follow-up period is associated with a greater number of complications. However, given the relatively small sample size, the result is not statistically significant (p-value = 20%).

4. Discussion

Mixed connective tissue disease (MCTD), also known as Sharp's syndrome, belongs to a group of disorders characterized by wide clinical and paraclinical heterogeneity, ranging from single-organ involvement to systemic disease.

The prevalence of MCTD was 0.70% over a ten-year period in our study. This low prevalence is consistent with findings from Algeria, with six cases over six

years [8], and from Gabon, with seven cases over five years [9]. In Senegal, a multicenter study on autoimmune diseases conducted from 2005 to 2015 identified six cases out of 726 patients, corresponding to a hospital-based prevalence of 0.82%. These findings support the notion that MCTD remains a rare entity. However, in Norway, a larger cohort was reported with 147 cases over a three-year period, based on a multicenter study involving 16 public hospitals [10]. This highlights the importance of conducting multicenter or nationwide studies to better understand the epidemiology of this condition.

In our series, all cases involved female patients. Female predominance has been consistently observed in African studies [8] [9] [11], as well as in cohorts from the United States (84%) [4] and Italy (91%) [12]. This gender imbalance suggests a potential hormonal influence on the etiology of MCTD.

The mean age of patients in our study was 35.8 years (range: 24 - 52 years), similar to findings from Norway (37.9 years) [10] and Gabon (39.5 years) [9]. However, our population was younger than that of the Norwegian (48.1 years) [10] and Algerian (50 years) cohorts [8]. Although MCTD most frequently begins in the third decade of life, it can occur at any age [13].

Clinically, 80% of patients experienced weight loss, 60% had fever, and 60% reported physical fatigue. Sharp *et al.* originally described fever in 32% of patients [14], while the Moroccan series reported fever in 25% of patients, with constitutional symptoms observed in 54% [11]. Despite the higher prevalence of these symptoms in our study, they are often nonspecific initial signs of autoimmune disease, including MCTD [15].

Articular involvement was prominent, with 80% of patients experiencing inflammatory arthralgia of small joints, particularly affecting the proximal interphalangeal joints and wrists, and 75% reporting involvement of large joints (**Figure 1**, **Figure 2** and **Figure 5**): This non-deforming inflammatory polyarthralgia has been reported in other studies—93.3% in Tunisia [16], 86% in the United States [4], and 86.7% in Gabon [9]. Thus, joint manifestations are among the most frequent features of MCTD. One patient presented with a boutonnière deformity of the third digit on the left hand. Such deformities are rare in MCTD compared to rheumatoid arthritis and may indicate disease progression toward a more defined connective tissue disorder, necessitating careful monitoring.

Regarding cutaneous and mucosal involvement (**Figure 4** and **Figure 5**), 60% of patients had Raynaud's phenomenon and puffy fingers. These features are commonly reported with varying prevalence—Raynaud's phenomenon in 50.3% to 93.2%, and puffy fingers in 53% to 72% of cases at diagnosis [12].

Other nonspecific cutaneous manifestations included sclerodactyly and skin thinning, observed in 40% of patients. Similar rates were noted in the Moroccan cohort (42%) [11], while lower frequencies were found in Italian studies (29.2% and 14%, respectively, according to Ungprasert *et al.*) [12]. These differences may reflect the influence of environmental and genetic factors on the clinical presentation of MCTD across populations.

Muscle involvement was present in one patient (20%), manifesting as myalgia in the lower limbs without motor deficit or muscle weakness (**Figures 3-5**). This prevalence is consistent with findings from Moroccan, American, and Italian studies, which reported frequencies of 32% [11], 24% [4], and 27.9% [12], respectively. However, in the Gabonese study, muscle involvement was among the most common manifestations, affecting 85.7% of patients [9].

Among the evaluated complications (**Figure 6**), two patients exhibited pulmonary involvement. Cough and dyspnea were present in 40% of cases, with one patient displaying a pulmonary consolidation syndrome. Thoracic CT scans revealed diffuse interstitial lung disease (ILD) with pulmonary fibrosis in 40% of patients. In comparison, ILD was reported in 18% of cases in the United States and in 14% of cases in a Tunisian cohort, both lower than the frequency observed in our series. ILD is considered one of the most prevalent complications, followed by pulmonary arterial hypertension (PAH). Although PAH was not observed in our series, it remains a significant cause of mortality [11].

In terms of cardiovascular involvement, all patients were asymptomatic. One patient presented with a left anterior fascicular block on electrocardiogram, while transthoracic echocardiography findings were unremarkable. No pericardial or myocardial involvement was identified. Pericarditis is commonly reported in 6% of patients in the United States and 9% according to Reiseter *et al.* [12]. Conduction abnormalities have been described in approximately 20% of patients, though they are typically benign and do not impact vital prognosis [11].

Regarding gastrointestinal involvement, epigastric pain was reported in 60% of cases, and heartburn in 40%. Hiatal hernia was identified in 60% of patients via esophagogastroduodenoscopy, with one case of cardial incontinence. In the Norwegian series, Gunnarsson *et al.* noted esophageal dysmotility in 50% of patients [10], with epigastric pain being the predominant symptom. Similarly, an American series reported epigastric complaints in 38% of patients, followed by dysphagia [4].

In our study, no renal or neurological complications were identified.

From a biological standpoint, two patients presented with an inflammatory syndrome, characterized by inflammatory anemia, a positive C-reactive protein, and one case of polyclonal hypergammaglobulinemia. No leukopenia or lymphopenia was observed. These hematologic abnormalities are more frequently encountered in mixed connective tissue disease (MCTD), as confirmed by American, Norwegian, and Italian studies, with a reported prevalence of approximately 44% [4] [10]. However, such findings are non-specific and commonly seen in other autoimmune diseases.

Antinuclear antibodies (ANA) and anti-U1RNP antibodies were positive in all patients. This finding is consistent with Gabonese, Japanese, and American series, where positivity reached 100% [4] [9] [11]. Anti-U1RNP antibodies were present at high titers, exceeding 241. These immunological markers are consistently positive across studies, as they constitute a diagnostic criterion in the various classi-

fication systems used. Nonetheless, these autoantibodies are not pathognomonic of MCTD and may also be present at lower titers in other autoimmune conditions, such as systemic lupus erythematosus (SLE) [11]. Furthermore, their titers tend to decrease over the course of the disease.

Other antibodies were also detected in our cohort, including anti-SSa/Ro in 40% of cases and anti-SSb/La in 20%. These autoantibodies are not specific to MCTD and may suggest coexisting primary or secondary Sjögren's syndrome.

In our study, one patient tested positive for anti-native DNA antibodies. In Morocco, Ayoub *et al.* reported this antibody in over 54% of patients. Although anti-dsDNA antibodies are more sensitive markers of SLE, their presence may indicate overlap syndromes or progression towards a defined connective tissue disease [11].

The most commonly used diagnostic criteria in our series were those proposed by Sharp, applied in 80% of patients (**Figure 7**). However, these criteria are infrequently used in clinical studies. In a comparative analysis, the Alarcón-Segovia criteria demonstrated better sensitivity (62.5%) and specificity (86.2%) compared to other classification systems. Thus, the use of these criteria is recommended for a more accurate diagnostic approach [17].

In terms of treatment, all patients received corticosteroids and synthetic antimalarials, with 60% receiving methotrexate. Articular manifestations were the most frequent clinical feature, justifying the use of disease-modifying therapies, with prednisone administered at anti-rheumatic doses. Despite the lack of standardized treatment guidelines, therapeutic strategies were similar in other cohorts. In the Italian series, corticosteroids were prescribed in 82% of cases, immunosuppressants including methotrexate in 58%, and hydroxychloroquine in 45% [12]. Similarly, in the Algerian study, all patients were on prednisone, and four out of six received hydroxychloroquine [8]. Calcium channel blockers and azathioprine were each prescribed to one patient—respectively for Raynaud's phenomenon and for management of interstitial lung disease.

The mean follow-up duration was 4.4 years, ranging from 1 to 9 years. A longer follow-up period appears to be associated with a higher rate of complications (**Figure 8**), highlighting the importance of long-term monitoring and early detection strategies to improve both functional outcomes and survival. In our series, two patients developed interstitial lung disease, one had a cardiac complication (left anterior fascicular block), and two had gastrointestinal manifestations including epigastric pain and heartburn.

5. Conclusion

Autoimmune diseases are relatively uncommon and often lead to delayed diagnosis. In sub-Saharan Africa, limited awareness of these conditions, the heterogeneity of clinical manifestations, and insufficient diagnostic infrastructure contribute to challenges in their management. Internal medicine plays a key role as a diagnostic and therapeutic specialty, particularly in the care of systemic diseases such

as mixed connective tissue disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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