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Looking younger, growing sicker: a case of late-onset sharp syndrome in a cameroonian woman

Observation d'un syndrome de Sharp à début tardif chez une femme âgée camerounaise présentant une apparence rajeunie paradoxale

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Clinical Case

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ABSTRACT

Mixed connective tissue disease (MCTD) is a condition that combines signs borrowed from major connective tissue diseases such as systemic lupus erythematosus, systemic scleroderma, and idiopathic inflammatory myopathies, with high titers of anti-U1RNP antibodies, which are currently the biomarker for this condition. It most often affects young adults, and its late onset is rare or even exceptional. We report the case of a 71-year-old woman with MCTD meeting Sharp's criteria, with cutaneous, osteoarticular and hematological involvement. We discuss the issue of late-onset MCTD and its management in a context of limited resources.

RESUME

La connectivite mixte (CM) est une pathologie qui allie des signes d'emprunt des connectivites majeures que sont le lupus systémique, la sclérodermie systémique et les myopathies inflammatoires idiopathiques, avec la forte positivité des anticorps anti U1RNP qui sont à ce jour le biomarqueur de cette affection. Elle concerne le plus souvent l'adulte jeune, sa survenue tardive est une situation rare voire exceptionnelle. Nous rapportons le cas d'une femme de 71 ans présentant une CM remplissant les critères de Sharp avec atteinte cutanée, ostéoarticulaire et hématologique. Nous discutons la problématique de la survenue tardive de la CM et de la prise en charge en contexte de ressources limitées.

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Introduction

Connective tissue diseases (CTDs) represent a heterogeneous group of autoimmune disorders characterized by complex clinical manifestations involving multiple organ systems. Among them, systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) are two well-defined entities with distinct immunological profiles, yet they may occasionally overlap creating diagnostic and therapeutic challenges [1,2]. Mixed connective tissue disease (MCTD), first described by Sharp in 1972 is a rare autoimmune condition defined by high titres of anti-U1-ribonucleoprotein (U1-RNP) antibodies and by clinical features of at least two CTDs, including SLE, SSc and inflammatory myopathies [3]. Although overlap features between SLE and SSc may occur within the spectrum of MCTD, their combined presentation remains relatively uncommon in older adults. Furthermore, data from sub-Saharan Africa are scarce, and the condition may be underdiagnosed due to limited awareness and overlapping symptomatology with more prevalent diseases [4]. The co-occurrence of SLE and SSc in an older adult presents unique diagnostic challenges as symptoms may be attributed to age-related comorbidities or may follow an atypical course [1,2]. Early recognition is essential to prevent severe complications and guide appropriate immunosuppressive therapy. In this context, we report the case of a 71-year-old Cameroonian woman diagnosed with MCTD combining features of SLE and SSc. This case highlights the diagnostic challenges and clinical implications of this rare presentation in an older patient in our setting.

Case Observation

We report the case of a 71-year old female brought by her daughter who noticed changes on her face. Indeed the daughter think her mother appear younger with reduce wrinckles. Furthermore, the patient report a 1-year history of inflammatory polyarthralgias predominantly in the hands. She also report hardening of her hands which hinder her ability to perform instrumental activities of daily living (IADLs) namely housekeeping, laundry and cooking. It was associated with sicca syndrome involving the mouth. There was no fever nor weight loss. She had no Raynaud phenomenon nor muscle weakness. She has a past medical history of hypertension treated with amlodipine and hydrochlorothiazide. On general physical examination, she showed a diffuse skin thickening on her face, hands and legs associated with bilateral phalangeal arthritis and a positive prayer's sign (figure 1 and 2). The squezzing sign was absent. The modified Rodnan Skin Score (mRSS) was 11. The biological workups showed high titer of antinuclear, anti-Sm and anti-U1RNP antibodies (Table 1). She also had inflammatory syndrome with an elevated C-reactive protein (CRP) at 48 mg/L. There was no erosive arthritis on hands x-ray. The chest x-ray was normal. Echocardiogram showed left ventricular hypertrophy and no signs of pulmonary hypertension. The kidney function was normal and there was no proteinuria on urinary dipstick. The full blood count showed moderate leukopenia at 2800/µL the rest was unremarkable. Fasting blood sugar and thyroid stimulating hormone values were in normal ranges.

Table I : Immunological features

Auto-antibodies	Titers
Antinuclear	1/1280
Anti-ENA	14 UI/mL
Anti-Sm	12 UI/mL
Anti-U1RNP	>241 UI/mL
Anti-DNA	Negative
Anti-CCP	Negative
Rheumatoid factor	Negative
Anti-Scl 70	Negative
Anti-centromere	Negative
Anti-SSa	Negative
Anti-SSb	Negative

CCP citrullinated peptide, DNA desoxyribonucleic acid, ENA extractable nuclear antigen, Sm Smith, U1-RNP U1 ribonucleoprotein

The patient met criteria for MCTD including the presence of U1-RNP antibodies and four Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) criteria for SLE and one criteria of the American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) for SSc. According to the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2k) disease activity was at 7. She was diagnosed with a MCTD and patient was given hydroxychloroquine 200mg twice daily and 10mg daily maintenance dose of prednisone 5 mg/day. The joint pain improved rapidly but the patient was lost to follow up after 6 weeks.

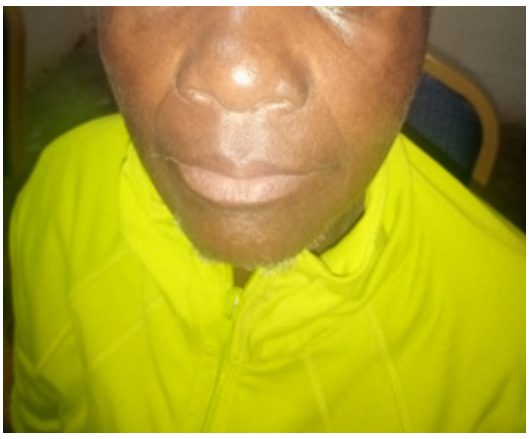

Figure 1 : reduction of wrinckles of the face

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Figure 2 : skin thickening of the fingers with a positive prayer's sign

Discussion

MCTD is a rare autoimmune condition defined by high titres of anti-U1-ribonucleoprotein (U1-RNP) antibodies and by clinical features of at least two overlapping CTDs, including SLE, SSc, inflammatory myopathies and rheumatoid arthritis [3,5]. Multiple attempts have been made to develop classification criteria for MCTD, but there are currently no internationally agreed-upon diagnostic criteria. Most clinicians agree on a diagnosis if the following criteria are met : the presence of a high titer of anti-U1-RNP antibodies and Raynaud phenomenon, puffy digits or hand edema [3]. Our patients has high titer of ribonucleoprotein (U1-RNP) antibodies although she had not report Raynaud phenomenon. Anti-U1-RNP antibodies are necessary for the diagnosis of MCTD, but they are also prevalent in other connective tissue diseases, especially SLE, from which distinction remains challenging [6]. The presence of anti-Smith (Sm) antibodies in our patient may have hindered the final diagnosis. However, the co-occurrence of features of SSc, particularily skin thickening in presence of positive U1-RNP was highly suggestive of an overlap syndrome [7].

The patient's age at presentation makes this case noteworthy. Late onset reflects timing of clinical expression, not a distinct disease mechanism [1,2]. The fundamental autoimmune mechanism remains the same, but aging shifts the balance from immune control to immune dysregulation allowing MCTD to emerge later in life. A central explanation for late-onset MCTD is immunosenescence associated with inflammaging, which alter immune regulation in aging leading to less immune tolerance [8]. The pathophysiology of MCTD itself does not fundamentally change with age however, several age-related changes but also comorbidities and environmental factors help explain why its phenotype may differ in older adults [3].Case reports of late-onset MCTD describe clinical and pathological features that differ from the classic phenotype observed in younger patients. In a case report of a 74-year-old man, disease onset was marked by proximal muscle weakness and inflammatory arthritis without typical cutaneous features or Raynaud phenomenon, leading to an initial presentation dominated by myositis-like symptoms rather than overt overlap manifestations [9]. In another case a 69-year-old female, the presentation lacked early, prominent cutaneous or joint symptoms and instead involved an uncommon gastrointestinal mechanical complication, underscoring the broad spectrum of organ involvement that may predominate in older patients with MCTD rather than the expected vasospastic or joints-related symptoms commonly emphasized in younger cohorts [2,10,11].

Our patient has sicca syndrome, a hallmark of Sjögren's syndrome and arthritis. In older patients, musculoskeletal complaints, skin changes but also sicca syndrome are frequently attributed to degenerative or age-related conditions, which may hinder early recognition of inflammatory rheumatic diseases. In this case, the initial trigger for medical consultation was not pain or disability but the daughter's observation of apparent facial rejuvenation, which was related to diffuse skin thickening. Skin involvement, particularly facial skin thickening, is a hallmark of SSc and may reduce wrinkles in older adults, giving an appearance of youthfulness. This unusual presenting concern underscores the importance of careful clinical examination and consideration of CTDs when confronted with unexplained skin changes in older adults. Despite diffuse skin involvement, the patient did not demonstrate major organ complications commonly associated with SSc, such as pulmonary arterial hypertension or sclerodermal renal crisis. Cardiac evaluation revealed only left ventricular hypertrophy, likely related to longstanding hypertension. Findings that may reflect either early disease recognition or a less aggressive disease course in this older patient.

Treatment with hydroxychloroquine and low-dose prednisone led to rapid improvement in inflammatory joint symptoms, consistent with existing evidence supporting hydroxychloroquine as a cornerstone therapy in SLE and overlap syndromes [12,13]. However, the patient was lost to follow-up after six weeks, highlighting a common challenge in chronic disease management in resource-limited settings. Limited access to specialized care, financial constraints but also health literacy barriers may all contribute to poor long-term follow-up and outcomes of MCTD in our setting. This case highlights several key clinical messages. First, CTDs should remain part of the differential diagnosis in older patients presenting with inflammatory arthritis and skin changes. Second, overlap syndromes and MCTD, though rare, can present late in life and with atypical complaints. Finally, heightened clinical awareness is essential, particularly in low-resource settings, to

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avoid diagnostic delay and missed opportunities for early intervention.

Conclusion

This case demonstrates that MCTD with features of SLE and SSc can present late in life in our setting. It challenges the perception that CTDs are rare in older African populations and highlights the likelihood of underdiagnosis.

Conflict of interest: none

Ethical considerations: Written informed consent was obtained from the patient prior to case report and we also had obtained the necessary consent to publish patient information.

Author's contributions: MJNE and SRSN collected data. MJNE drafted the manuscript. SRSN, JRN, CNO, BF and MNS provided substantial feedbacks on the manuscript. All authors read and approved the final amnuscript.

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