# Overlap syndrome of systemic lupus erythematosus and systemic sclerosis in a person living with HIV: the paradox of immunodeficiency and autoimmunity coming together

# Síndrome de overlap entre lupus eritematoso sistêmico e esclerose sístemica em pessoa vivendo com HIV: o paradoxo da imunodeficiência e autoimunidade

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**ABSTRACT**
The existence of autoimmune dysfunction in HIV/AIDS patients is intriguing. Many cases are being reported around the world of the combination of HIV with systemic autoimmune diseases. We report a case of an HIV-infected patient that presented alopecia, symmetric polyarthritis, skin thickening and raynaud's phenomenon. Diagnosis of overlap syndrome of SS and SLE was made and treatment with prednisone, methotrexate and nifedipine started. No HIV flare was documented.

**Keywords:** HIV, systemic sclerosis, systemic lupus erythematosus, autoimmune diseases.

**RESUMO**
A existência de disfunções auto-imunes em doentes com VIH/SIDA é intrigante. Muitos casos estão a ser relatados em todo o mundo da combinação do VIH com doenças auto-imunes sistémicas. Relatamos um caso de um doente infectado com VIH que apresentava alopecia, poliartrose simétrica, espessamento da pele e fenómeno de raynaud. Foi feito o diagnóstico de síndrome de sobreposição de SS e LES e iniciado o tratamento com prednisona, metotrexato e nifedipina. Não foi documentada nenhuma erupção de HIV.

**Palavras-chave:** VIH, esclerose sistémica, lúpus eritematoso sistémico, doenças auto-imunes.

## 1 INTRODUCTION

The existence of autoimmune dysfunction in HIV/AIDS patients is intriguing. The status of the HIV infection has changed from fatal to chronic with the improvement of anti-retroviral therapy (HAART), making the discovery of new clinical features of the disease, such autoimmune dysfunction, possible. This feature may increase the risk of developing autoimmune diseases.[1,2]

This is indeed a great paradox. Many cases are being reported around the world of the combination of HIV with systemic autoimmune diseases, such as rheumatoid arthritis, systemic lupus erythematosus (SLE), systemic sclerosis (SS), and sjögren's syndrome.[3–5]

Proving itself as a noteworthy theme we are proud to report, to the best of our knowledge, the first case of an HIV-infected patient that presented an overlap syndrome of SLE and SS.

## 2 CASE REPORT

A 41-years-old female patient was diagnosed with HIV infection in 2014 during a routine test. She was referred to the local infectious disease reference hospital. Lab results: viral load test was 39.530 copies and log 4,5 and her CD4+ levels were 237. Treatment with biovir and efavirenz was started, with good acceptability and efficacy. After 6 months of treatment, the patient's viral load test was not detectable and her CD4+ levels increased to 556. Treatment continued until 2017 when the HAART was changed to tenofovir, Lamevidine, and Efavierenz. The patient continued to be asymptomatic, with good control of the HIV infection.

In 2018, during an appointment with the infectologist, the patient started complaining of polyarthritis, pale fingers and alopecia. She was recommended to a rheumatologist. On physical examination: alopecia, symmetric polyarthritis of small joints, skin thickening with Rodnan score of 22 (**Figure 1**) and raynaud's phenomenon were seen. Lab results showed: anaemia of chronic disease, leukopenia, lymphopenia, hypocomplementaemia, ANA 1:1280 nuclear large speckled pattern, Anti-Scl-70 = 0.7, VHS = 100 mm, Anti-Sm = 480 and Anti-RNP = 240, CPK = 489 (23–190). A skin biopsy was done, showing excessive accumulation of extracellular matrix components.

A diagnosis of overlap syndrome of SS and SLE was made according with the classification criteria seen in **table 1**. Both the infectologist and the rheumatologist were concerned about the possibility of HIV flare with the use of immunosuppressant therapy. However, treatment with prednisone 60 mg per day, methotrexate 25 mg per week, nifedipine 40 mg per day, folic acid, and $CaCO_3$ + vitamin D was started, and the patient was followed-up closely with biweekly consultations. The patient indicated improvement of the arthritis, Raynaud phenomenon and alopecia. HIV treatment continued, and the patient's viral load was still not detected with good CD4+ levels.

## 3 DISCUSSION

The coexistence of autoimmunity in an immunosuppressed patient is an important topic. Diagnosis and treatment is complex, requiring a multidisciplinary approach and knowledge about the association between HIV infection and autoimmune diseases. To help other doctors in a similar situation, we have written a review of this topic, highlighting some points that doctors should be aware of.

The onset of autoimmune diseases in such cases can be a direct product of the HIV infection due to the association between HIV and immune dysregulation, or it can be a result of immune restoration during HAART. Four stages of the autoimmune manifestations related to HIV/AIDS was proposed. During stage I, the patient has acute infection with a high viral load and good CD4+ levels. In stage II, the CD4+ levels drop, but they are still within normality, and the viral load are high. In stage III, there are low CD4+ level and the viral load remains high. Finally, stage IV occurs after HAART is started, and the CD4+ levels rise and the viral load drops.[1,4]

The importance of such stages is because, most of the cases happens in stage IV. The HAART increases immunocompetence and repopulates CD4+ levels, causing an immune reconstitution inflammatory syndrome and making the onset of autoimmune diseases possible.[6,7] In the presenting case, the patient developed the overlap syndrome 4 years after HIV treatment – which is considered stage IV.

Diagnosis is a real challenge because HIV can cause multiples rheumatological symptoms and lab results, such as musculoskeletal pain, arthralgia, arthritis, myalgia, skin rash, lymphadenophaty, cytopenias, renal and nervous system involvement, positive ANA antibodies, positive Anti-DNAds, and positive anti-Sm and anti-cardiolipin antibodies. In our case, the patient had classical features of SLE and SS, such as arthritis, alopecia, skin thickening, Raynaud phenomenon, anaemia, leukopenia, lymphopenia, hypocomplementaemia, positive ANA, and positive anti-Sm and anti-RNP. It is important to note that hypocomplementaemia has not been documented in HIV patients, which makes it a suitable marker for SLE flare.[4,5,8–10]

Regarding treatment, our patient used corticosteroids, hydroxychloroquine, and methotrexate for control of the immune diseases. In the literature, most articles are case reports; therefore, no treatment guideline can be made with so little studies. We have found that most of the patients respond well to DMARDs. Corticosteroids and hydroxychloroquine seem safe for symptom control. Hydroxychloroquine actually inhibits HIV infectivity and viral replication and increases CD4+ T cells. For the corticosteroids, we have to be aware that ritonavir inhibits steroid metabolism; therefore, the dose needs to be adjusted case by case. Lastly, DMARDs such methotrexate can only be used if CD4+ levels are higher than 200 counts/cells/$m^3$ and the viral activity is suppressed.[4,5,10]

There are many autoimmune diseases associated with HIV. The association betwen SLE and HIV is well documented, with several case reports around the world. SS and HIV are very rare, and there are only a few reported cases. Despite this, an overlap syndrome of these two

diseases in a person living with HIV has never been reported, making this case exceedingly important and enlightening for doctors that might face similar situations.

## 4 CONCLUSION

This is the first case of overlap syndrome of SS and SLE in an HIV-infected patient. The possible explanation of the coexistence of autoimmunity and immunodeficiency is that during phase IV of HIV, after HAART has been started, the immune restoration is responsible for the autoimmunity. Careful management of such cases is needed in order to not cause an HIV flare. Since this is a very rare association, more studies about management are needed in order to guide doctors around the world who face similar challenging situations.

## INFORMED CONSENT

Written informed consent for patient information and images to be published was provided by the patient.

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## CONFLICT OF INTEREST

The Author(s) declare(s) that there is no conflict of interest.

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**Figure**

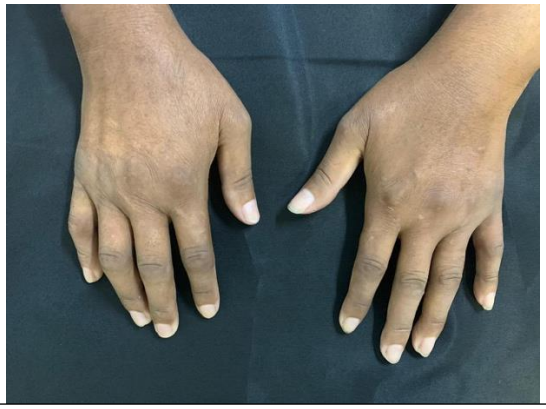

**Figure 1.** Hands with infiltrated and ticked skin and synovitis in proximal interphalangeal and metacarpophalangeal joints.

**Table**

Table 1: Classification criteria fulfilled for SLE and SS

| **2019 Classification criteria for systemic lupus erythematosus (ACR/EULAR)** | | **2013 Classification criteria for systemic sclerosis (ACR/EULAR)** | |
|---|---|---|---|
| **Criteria** | Points | Criteria | Points |
| **FAN + > 1:80** | Entry criteria | Skin thickening of the fingers | 9 |
| **Leukopenia** | 3 | Raynaud's phenomenon | 3 |
| **Non-scaring alopecia** | 2 | | |
| **Joint involvement** | 6 | | |
| **Anti-Sm +** | 6 | | |
| **Total** | 17 points | Total | 12 points |