

Differential Diagnosis and Association of Acquired Immunodeficiency Syndrome and Systemic Erythematosus Lupus: A Brief Review

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Abstract

Acquired immunodeficiency syndrome and lupus erythematosus are multi-system diseases that can affect several organs and systems at different stages of disease evolution. Both diseases share common clinical manifestations, which may lead to diagnostic difficulties, especially at the onset of the disease. Another additional challenge is when there is an association of the two pathologies. The objective of this brief review is to describe the clinical manifestations of the diseases and to make considerations regarding the moment of onset of symptoms. Knowledge of these common manifestations and their peculiarities may alert clinicians to possible diagnoses and avoid errors in the evaluation and conduction of these patients.

Keywords

Acquired Immunodeficiency Syndrome, Systemic Lupus Erythematosus, Overlapping, Systemic Diseases

1. Introduction

Acquired immunodeficiency syndrome (AIDS) is a chronic, sexually transmitted infection, caused by the human immunodeficiency virus (HIV).

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can manifest with changes in various organs and systems.

HIV infection/acquired immunodeficiency syndrome and SLE share several clinical manifestations in common. The association of these two diseases in the

same patient is considered a real diagnostic challenge since the overlapping of symptoms can generate great difficulties in the elucidation of the medical picture and approach. HIV can mimic SLE symptoms and *vice versa*, which requires attention to distinguish the clinical manifestations of SLE. A high level of suspicion is required so that there is no underdiagnosis of any of these diseases [1] [2]. In 2004, Sommer *et al.* described a case that was misdiagnosed as SLE for 4 years when HIV was finally diagnosed [3].

SLE and HIV are known to be systemic diseases, with involvement of several organs and consequent similarity of symptoms, which may complicate the differential diagnosis even more. The classification criteria for SLE that can help in the diagnosis (Table 1) in this case are often not useful since patients with HIV infection alone may meet 4 or more criteria necessary for the diagnosis of SLE. For this reason, some authors have already suggested a re-evaluation of the classification criteria in this population [1] [4]. Another confounding factor is the manifestation of opportunistic infections, such as candidiasis, which may occur as a complication of immunosuppression in both diseases.

The objective of this brief review is to describe the common symptomatology as well as some clinical differences between these diseases to alert the attending physician about the possible diagnoses and guide the propaedeutics.

2. Clinical Manifestations: Similarities and Differences in Systemic Involvement

2.1. General Manifestations

General symptoms such as fever, weight loss, anorexia, adynamia, lymphadenopathy and myalgia, can occur in HIV and SLE, in several phases of these diseases [1] [4].

Table 1. 1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus Criterion Definition:

Criterion	Definition
Malar Rash	
Discoid Rash	
Photosensitivity	
Oral ulcers	
Arthritis	
Serositis	Pleuritis OR Pericarditis
Renal disorder	
Neurological disorder	Seizures OR Psychosis
Hematologic disorder	Hemolytic anemia OR Leukopenia OR Lymphopenia OR Thrombocytopenia
Immunologic disorder	Anti-DNA antibody OR anti-Sm OR Antiphospholipids antibody
Antinuclear antibody	

2.2. Articular Manifestations

Arthralgia and arthritis with varied patterns (mono, oligo or polyarticular) may occur in both SLE and HIV [1] [2] [3] [4] [5].

2.3. Hematological Manifestations

Anemia, leukopenia, lymphopenia and hypergammaglobulinemia are frequent manifestations in both diseases [1] [4].

2.4. Serosites

All types of serositis (pleuritis, pericarditis and peritonitis) have been described in HIV and are relatively common manifestations in SLE [1] [2] [3] [4] [5].

2.5. Neurological Manifestations

Psychoses, peripheral neuropathies, focal deficits, and stroke are neurological abnormalities shared by both diseases [6].

2.6. Cutaneous-Mucosal Manifestations

Oral ulcer and malar rash are classic manifestations of SLE, but may occur in HIV. Photosensitivity, characteristically described in SLE, is a common symptom in HIV and is generally considered a late manifestation in the course of infection.

The occurrence of discoid lupus erythematosus in HIV patients seems to be quite rare but has already been described in the literature [2] [7] [8].

2.7. Renal Manifestations

SLE and HIV present similarities to renal manifestations: both may present hematuria, proteinuria, frank nephropathy and even renal failure [6].

HIV-associated nephropathy (HIVAN) occurs most commonly in black patients and is characterized by nephrotic proteinuria, which progresses rapidly to renal failure in most cases [9]. Histologically, HIVAN is caused by focal and segmental glomerulosclerosis. Less frequently, membranoproliferative glomerulonephritis, IgA nephropathy, and thrombotic microangiopathy have been reported in patients with HIV-associated nephropathy [6]. Lupus nephritis appears to present a more varied clinical picture when compared to HIVAN and histologically there is deposition of immunocomplexes, causing the various patterns of lupus nephritis [10] [11] [12].

In 1999, Chang *et al.* Described 4 cases of patients with concomitant SLE and HIV who had renal changes. They were submitted to biopsy showing changes compatible with lupus nephritis in all of them. However, in 2 subjects there were still histological changes suggestive of HIVAN (tubular microcysts, podocyte hypertrophy and glomerular basement membrane collapse) and the authors concluded that there was an overlap of lupus nephritis and HIV-associated nephritis. The same authors reviewed another series of previously published

cases in which 7 patients with HIV and SLE had renal manifestations that were diagnosed as follows after histological study: 1 patient with class III lupus nephritis and 1 patient with class IV nephritis, 2 patients with nephritis class V, 1 patient with HIV-associated nephritis and 2 patients with mixed findings of lupus nephritis and HIVAN. In these two series there was a high proportion (55%) of pediatric cases (vertical transmission of HIV), a fact that raises doubts about the mechanisms involved in the genesis of nephritis in this population [6]. This trend of onset of nephritis in the pediatric population with SLE and perinatal HIV transmission has also been described in other publications [1] [11].

Another form of nephropathy that may cause great difficulties in the differential diagnosis with SLE: lupus-like nephritis has been described in HIV infection. It is a form of glomerulopathy with presence of immunocomplexes deposits and complement in immunofluorescence, in the absence of other clinical or laboratory manifestations of lupus [13] [14]. This form of nephritis has been described in the early stages of HIV infection, soon after seroconversion, and has been reported even in transplanted kidney of HIV patients [15] [16].

8) Other manifestations

SICCA syndrome, ocular and pulmonary manifestations, thromboembolic phenomena, can manifest in a similar way in both SLE and HIV [1] [2] [3] [4] [5] [17].

Table 2 shows a summary of the clinical manifestations of the two diseases.

3. Clinical Considerations Related to the Time of Onset of Diseases

3.1. Patients with HIV Infection and Subsequent Onset of SLE

Treatment with immunosuppressants required in cases of SLE may favor the onset of manifestations of a previously undiagnosed HIV infection or worsen the course of the disease in those known to be HIV positive. This fact probably results from increased viral replication [4] [7]. Alonso and Lozada described a case of a SLE patient who developed positive HIV serology but with an undetectable viral load. After pulse therapy with cyclophosphamide due to recurrent SLE crises, there was a marked increase in viral load which was reversed with suspension of the drug [18].

Another aspect to consider is treatment related to HIV infection. Since the beginning of highly active antiretroviral therapy (HAARV), there has been great progress in the treatment of HIV-infected patients with improved morbidity and mortality. However, after recovery of immunity from treatment, new symptoms known as “immune restoration inflammatory syndrome” (IRIS) have been observed, including symptoms and new diagnoses of autoimmune diseases such as SLE. Calabrese *et al* described, in a literature review, 4 new cases of SLE after HAARV [19].

Table 2. Systemic manifestations in AIDS and SLE [1]-[17].

MANIFESTATIONS	AIDS	SLE
General symptoms	Frequent	Frequent
Articular manifestations	Can occur	Frequent
Hematological manifestations	Frequent	Frequent
Serosites	Can occur	Frequent
Neurological manifestations	Can occur	Can occur
Cutaneous-mucosal manifestations	Frequent	Frequent
Renal Manifestations	Can occur (HIV-associated nephropathy)	Can occur (lupus nephritis)

An additional approach already published in the literature is that the emergence of SLE in advanced stages of HIV seems to favor a milder course of lupus evolution, probably due to the role of CD4 + T lymphocytes in its pathogenesis [5].

3.2. Patients with SLE Who Subsequently Develop HIV Infection

HIV infection in SLE patients appears to have a favorable impact on the progression of autoimmune disease. Several cases in the literature have described improvement and even remission of autoimmune disease after the onset of HIV. On the other hand, after initiation of HAART therapy and improvement of the immune status, reactivation of latent symptoms or signs of SLE activity may occur [1] [4].

3.3. Patients with Concomitant SLE and HIV

Because it is an association that is still rare and may present similar manifestations, concomitant signs of SLE and HIV generate great difficulties in management. Several case reports show different views of how HIV can interfere with the course and manifestations of SLE and *vice versa* [2]. In general, the symptoms of the two conditions may coexist at the time of diagnosis or manifest in the course of evolution, and it is sometimes a real dilemma to distinguish the cause.

4. Conclusion

HIV infection/acquired immunodeficiency syndrome and systemic lupus erythematosus (SLE) are multisystem diseases whose diagnosis and treatment remain challenging in medical practice. The knowledge of the clinical manifestations of these diseases can alert the physician to the correct differential diagnosis and consequently the appropriate management in possible associations of both diseases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this pa-

per.

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List of Abbreviations

HIV, human immunodeficiency virus
AIDS, acquired immunodeficiency syndrome
SLE, systemic lupus erythematosus
HIVAN, HIV-associated nephropathy
HAAV, highly active antiretroviral therapy
IRIS, immune restoration inflammatory syndrome