

Diffuse Infiltrative Lymphocytosis Syndrome with Interstitial Pneumonia in a Patient with HIV

Síndrome de linfocitosis infiltrativa difusa con neumonía intersticial en un paciente con VIH

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Received: 6/17/2022

Accepted: 8/18/2022

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ABSTRACT

Diffuse infiltrative lymphocytosis syndrome (DILS) occurs in association with HIV infection; it requires that diagnostic criteria are met and other infectious and autoimmune diseases are discarded. We present the case of a 47-year-old woman who consulted for bilateral parotid swelling, sicca syndrome, cough and impregnation syndrome; chest tomography showed patchy bilateral ground glass infiltrate. The patient was diagnosed with HIV, and fiberoptic bronchoscopy with bronchoalveolar lavage (BAL) was performed, without pathogen growth. It is interpreted as lymphoid interstitial pneumonia associated with DILS. Antiretroviral therapy was started, with good evolution and disappearance of symptoms and pulmonary infiltrates.

Key words: Diffuse infiltrative lymphocytosis syndrome (DILS); Human immunodeficiency virus; Interstitial pneumonia

RESUMEN

El síndrome de linfocitosis infiltrativa difusa se produce en asociación con la infección por virus de la inmunodeficiencia humana; requiere cumplir con los criterios diagnósticos y descartar otras patologías infecciosas y autoinmunes. Se presenta el caso de una mujer de 47 años que consultó por edema parotídeo bilateral, síndrome sicca, tos y síndrome de impregnación. Se observó en la tomografía de tórax infiltrado en "vidrio esmerilado", parcheado y bilateral. Se realizó diagnóstico de virus de la inmunodeficiencia humana positivo y fibrobroncoscopia con lavado broncoalveolar sin desarrollo de patógenos. Se interpreta como neumonía intersticial linfoidea asociada a síndrome de linfocitosis infiltrativa difusa. Se inició terapia antirretroviral con buena evolución y desaparición de los síntomas y de los infiltrados pulmonares..

Palabras clave: Síndrome de linfocitosis infiltrativa difusa; Virus de la inmunodeficiencia humana; Neumonía intersticial linfoidea

INTRODUCTION

DILS is associated with the human immunodeficiency virus (VIH), characterized by dry eyes and dry mouth (sicca syndrome), lymphadenopathies, bilateral parotitis and extra-glandular involvement. It was initially identified in 1985 as lymph node hyperplasia and parotid gland enlargement in HIV patients.¹ Then, in 1989, this complex was called DILS, and its association with host factors was defined as antigens of the major histocompatibility complex and increased frequency of HLA-DR5, thus determining the presence of a genetically defined immune response to HIV infection.² The estimated prevalence is 7.8% in the era before the antiretroviral therapy (ART), which was then reduced to 1.5% with said treatment.³⁻⁴

We present a case of sicca syndrome associated with recent diagnosis of HIV infection with lymphoid interstitial pneumonia (LIP) and DILS.

CASE REPORT

47-year-old female patient with history of smoking and hypothyroidism. She presented with a six-month history of painless edema in bilateral parotid region, dry cough, dry mouth and dry eyes, night sweating, and weight loss (20 kg).

The neck ultrasound showed enlarged parotid glands of diffuse heterogeneous aspect. Lab results: blood count

without eosinophilia; PCR: 4.7 mg/d, positive serology for HIV, with CD4+ 253 mm³ /CD8+ 1159 mm³ values, viral load of 186.340 copies/ml, negative collagenogram, normal IgE values, normal proteinogram.

The chest CT showed patchy ground glass infiltrate with bilateral involvement and diffuse distribution; subtle presence of predominantly peripheral reticulum and some isolated cysts (Fig. 1). A fiberoptic bronchoscopy with BAL was performed, evidencing 28% lymphocytosis without microbiological isolates and negative PCR for *Pneumocystis jirovecii*. The patient refused to undergo a biopsy of the parotid due to the possible complications of this procedure. The symptoms were interpreted as lymphoid interstitial pneumonia related to DILS, so the patient began antiretroviral therapy.² Currently without respiratory symptoms, parotid glands reduced in size, undetectable viral load with increased CD4/CD8 ratio.

DISCUSSION

Sicca syndrome is one of the rheumatologic manifestations that can be present in patients with HIV.^{5,6} The DILS is defined as an entity associated with HIV and is characterized by the Sicca syndrome, adenopathies, bilateral parotitis and extra-glandular involvement, which is based on tissue destruction due to CD8+lymphocyte infiltration. At the peripheral blood level, we observe lymphocytosis with expansion of CD8+ cells, and a low CD4/CD8 ratio. Clinical manifestations secondary to the extra-glandular visceral involvement depend on the

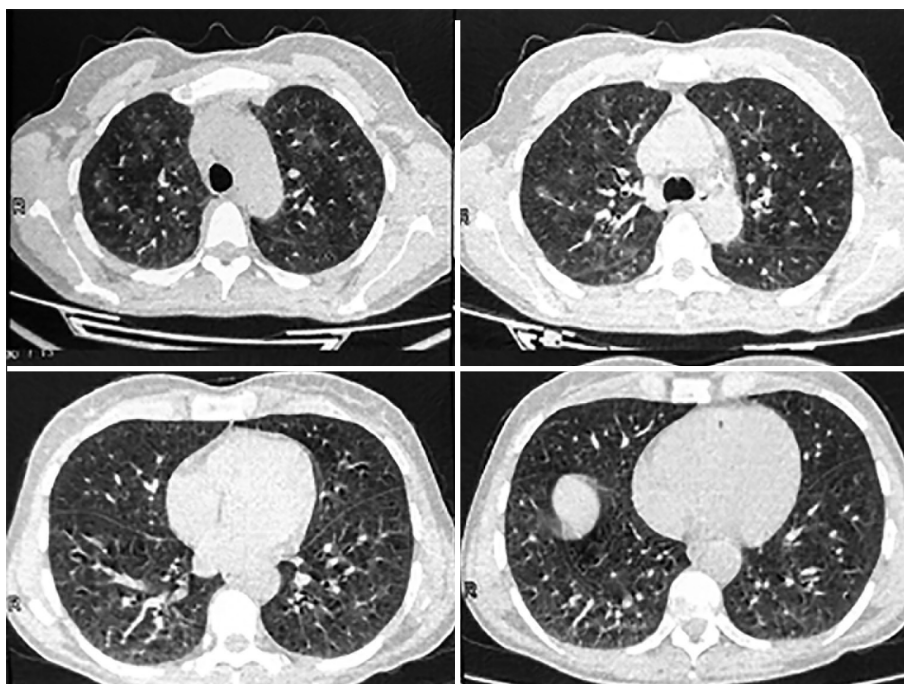


Figure 1. Chest CT: patchy, ground glass areas are observed, with bilateral and diffuse involvement.

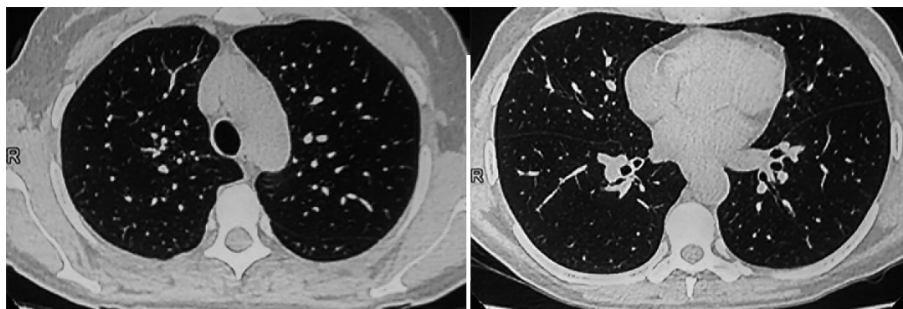


Figure 2. Chest CT shows clear improvement of previously described infiltrates after beginning antiretroviral therapy.

affected organ: nervous system with aseptic meningitis, polyneuropathy of acute or sub-acute onset, paralysis of the facial nerve, lymphocytic hepatitis, tubulointerstitial nephritis, cystitis and gastrointestinal infiltration.⁷⁻⁸

The prevalence of pulmonary involvement varies according to the different series in 33 to 66% of the cases. The most common clinical and radiological presentation is lymphoid interstitial pneumonia (LIP). The chest CT shows areas of bilateral ground glass infiltrate, ill-defined centrilobular nodules, thin-walled cysts, septal thickening and interlobular reticulations.⁹

No consensus has been reached regarding the diagnostic criteria for DILS, and no standards have been established, either. However, some authors such as *Itescu et al* propose the following diagnostic criteria:

- 1) Positive serology for HIV.
- 2) Bilateral swelling of salivary glands or dry mouth with persistence of signs or symptoms for at least 6 months.
- 3) Histological confirmation of lymphocytic infiltration of the salivary or lacrimal glands without granulomatous or neoplastic involvement.¹⁰

BAL is useful for discarding an underlying opportunistic infection, and typical findings include an increase in the total white blood count with lymphocytosis and a normal count in the CD4/CD8 ratio.

The differential diagnosis includes the Sjögren syndrome (SS), which has the same signs as the Sicca syndrome, parotitis, extra-glandular manifestations (mainly involving the lung, the nervous system and the kidney) and hypergammaglobulinemia. In the SS, we can observe the presence of autoantibodies: FAN with anti-SSA/Ro, anti-SSB/

La in SS and organ infiltration by CD4+ lymphocytes, whereas in DILS there will always be HIV patients and infiltration by CD8+¹¹lymphocytes. We must also exclude other “Sjögren-like” syndromes such as IgG4-related disease, chronic hepatitis C and chronic graft-versus-host disease.

With regard to the treatment, most authors agree on the administration of ART, also considering the use of steroids according to the severity of the symptoms.¹²

In the case presented herein, the systemic clinical characteristics and pulmonary radiographic features, the absence of autoantibodies and favorable clinical evolution after beginning antiretroviral therapy allow us to presume a DILS diagnosis, since the histological confirmation couldn't be obtained due to patient's refusal.

CONCLUSION

DILS is a multisystem syndrome with a currently low prevalence. Interstitial pneumonia can be one manifestation and must be included in the differential diagnosis.

Conflict of interest

Authors have no conflict of interest to declare.

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