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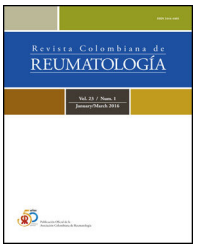

Case report

Utility of bronchoalveolar lavage in connective tissue diseases: A case report

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ABSTRACT

Interstitial lung diseases are a heterogeneous group of respiratory diseases that are difficult to diagnose. The study of bronchoalveolar lavage (BAL) by flow cytometry can define typical cell patterns in different diseases, providing some help in differential diagnosis. In this article, we present a case of interstitial lung disease of unknown origin, in a patient previously diagnosed with rheumatoid arthritis who received treatment with methotrexate.

Utilidad del lavado broncoalveolar en enfermedades del tejido conectivo: a propósito de un caso

Palabras clave:
Citometría de flujo
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RESUMEN

Las enfermedades pulmonares intersticiales difusas son un grupo heterogéneo de enfermedades respiratorias difíciles de diagnosticar. El estudio del lavado broncoalveolar (BAL) mediante citometría de flujo puede definir patrones celulares típicos en diferentes enfermedades, proporcionando algo de ayuda en el diagnóstico diferencial. En este documento se presenta un caso de enfermedad pulmonar intersticial difusa de origen desconocido, en paciente previamente diagnosticado de artritis reumatoide que recibe tratamiento con metotrexato.

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Diffuse interstitial lung diseases (DILDs) are a heterogeneous group of pathologies that predominantly affect the pulmonary interstitium.

The diagnostic process is complex and challenging for the clinical staff, for different reasons, among which a non-specific and common clinical picture, a varied etiology and a lack of uniform consensus stand out.

Bronchoalveolar lavage (BAL) is a method that allows the study of the lower respiratory tract through the analysis of the cellular and biochemical forms of the sample.[1]

We present the case of an 80-year-old man who came to our hospital with dyspnea, cough, obstructive sleep apnea syndrome (OSAS) and a history of rheumatoid arthritis. The chest X-ray revealed patchy ground-glass pulmonary lesions affecting the left lung and the right upper lobe. The study was complemented with a non-contrast computed tomography (CT), which reported the presence of faint infiltrates of interstitial predominance in both upper lobes, with a patchy distribution and left predominance. The image observed was very non-specific and seemed to be related to a complication of inflammatory-infectious nature. In addition, right basal laminar atelectasis and incipient paraseptal emphysema were observed. Lymphadenopathies, tumors or pulmonary effusion were not detected.

In the second CT study, performed 15 days later, it was concluded a rapid evolution of the lesion, from faint ground-glass infiltrates to alveolar condensation and ground-glass lesions that affected the entire left lung and the upper and middle lobes of the right lung in a patchy manner. Given the rapid evolution of the lesions in a relatively short period of time, it was suspected a possible infectious, pharmacological (the patient was receiving treatment with methotrexate [MTX]), or inflammatory diagnosis related to the previous arthritis that the patient already had.

Firstly, in order to rule out lung damage associated with opportunistic infection (a common clinical picture in patients with osteoarthritis who receive treatment with MTX, which causes immunosuppression and increases the risk of opportunistic infections, the most frequent of which is produced by *Pneumocystis jiroveci*), a microbiological culture was performed. No bacterial or fungal growth was observed, while the PCR tests for viruses (rhinovirus, enterovirus, influenza) were negative. In addition, urinary antigen tests for legionella and pneumococcus were also performed, which were negative.

Secondly, in view of the previous results in culture and imaging tests, it was decided to carry out more invasive tests such as a BAL study.

The BAL study showed: 86% lymphocytes, 2% monocytes and 12% polymorphonuclear cells, with a CD4+/CD8+ ratio of 1.33. On the other hand, a ratio of 0.31 was observed in peripheral blood, compared to 1.33 in the BAL.

The pattern of lymphocytic alveolitis with an increase in CD4+ lymphocytes, together with the rapid evolution of lung lesions, confirms the diagnosis of MTX-induced diffuse interstitial lung disease.

The diagnostic usefulness of BAL has been the subject of numerous studies. Most of them agree on the diagnostic value of certain pathologies, however, there are many works that still discuss its usefulness in many other DILDs, where it seems to have a guidance value.[2]

In the case of connective tissue disorders, such as rheumatoid arthritis, the BAL provides valuable information about the course of the disease.[3]

MTX is a drug used as an antineoplastic and anti-inflammatory agent, which works by competitively inhibiting dihydrofolate reductase, as well as DNA synthesis. One of the most serious adverse effects described is acute interstitial pneumonitis.[4]

In patients with rheumatoid arthritis, the toxicity associated with MTX presents with non-specific symptoms, both respiratory and systemic, which can rapidly progress to respiratory failure.[5]

The frequency of toxicity associated with MTX ranges from 0.3 to 7.5%, being this complication the most frequent cause of treatment interruption. In addition to pulmonary toxicity, the adverse effects associated with MTX include: gastrointestinal intolerance, cutaneous or genitourinary disorders, of which the most serious are hepatic complications, myelosuppression and pulmonary complications.[6]

MTX-related pulmonary complications are mainly inflammatory, opportunistic infections, or of lymphoproliferative type.

In complications of a non-infectious nature, as was our case, different types of pulmonary patterns may occur (interstitial fibrosis, bronchiolitis obliterans with organizing pneumonia or acute interstitial pneumonitis). The most severe and common complication is acute interstitial pneumonitis, described in this case.

There are different hypotheses that seem to explain the pulmonary toxicity associated with MTX, and they are based on the appearance of a prolonged inflammatory response in individuals who have certain genetic or environmental factors that favor its development, which ultimately leads to interstitial pulmonary fibrosis.[7]

The symptomatology that occurs is varied, with dry or productive cough, progressive dyspnea and acute respiratory distress being frequent; in addition, these symptoms can lead to other complications such as pleural effusion or pulmonary fibrosis.

It is not possible to make an imaging diagnosis of pulmonary toxicity due to MTX, making its diagnosis complicated, which in many cases is established by ruling out other pulmonary pathologies.

Thus, there are some scoring-based systems that help guide the diagnosis of MTX toxicity, one of which is the one proposed by Searles and Mckendry[8] in 1987, which takes into account the following criteria: dyspnea of less than 8 weeks, tachypnea and non-productive cough, oxygen saturation lower than 90%, blood leukocytes $< 15{,}000/mm^3$, histopathological report of hypersensitivity pneumonitis, negative microbiological studies, restrictive pattern in pulmonary function tests, and presence of alveolar or interstitial infiltrates in the chest X-ray.

In relation to the diagnosis by means of the BAL study, drug-induced pulmonary toxicity, in general, can reflect any type of alveolitis, with lymphocytic alveolitis with increased CD8+ being frequent. This occurs in the majority of cases, but not with MTX, in which a predominance of CD4+ T lymphocytes can be observed.[5,9]

In conclusion, although the diagnostic power of BAL still seems to be debated, in our case BAL presented an important diagnostic value that allowed us to clarify the etiology and rule out the damage associated with arthritis or other systemic autoimmune diseases with pulmonary symptoms, as well as to rule out infectious causes.

With respect to treatment, the most important thing in these cases is to rule out the infectious cause, and once ruled out, it is essential to withdraw the drug. Treatment with corticosteroids is not endorsed by studies, however, there is available literature that supports their use.[10]

Ethical considerations

Approval by the Clinical Research Ethics Committee.

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Conflict of interest

None.

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