Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

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DOI: 10.17235/reed.2024.10887/2024
Link: PubMed (Epub ahead of print)

Please cite this article as:
Vaquer-Grimalt Pere, Chausse Natalia, Ramis Estelrich Maria Dolors, Núñez María Belén, Escarda Aina , Bonet Llucia, Sastre Oliver Lydia, Vanrell Margalida. Interstitial pneumonitis due everolimus in a liver transplant recipient. Rev Esp Enferm Dig 2024. doi: 10.17235/reed.2024.10887/2024.

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Interstitial pneumonitis due everolimus in a liver transplant recipient

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Keywords: Everolimus. Interstitial pneumonitis. Liver transplantation.

Abbreviations:

BAL: bronchoalveolar lavage; CRP: c-reactive protein; CT: computed tomography; mTOR: mammalian target of rapamycin.

Conflict of interest: The authors declare no conflict of interest.

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Artificial intelligence: The authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

Dear Editor,

Transplant recipients commonly use immunosuppressive medications such as mammalian target of rapamycin (mTOR) inhibitors, everolimus and sirolimus, to prevent organ rejection. It is important to be aware of their side effects.

Case report

A 70-year-old female with a medical history of liver transplant due to secondary biliary cholangitis (April 2022) was admitted to our hospital with dyspnea and cough. She had no previous history of smoking, exposure to toxic material, or lung disease. Chest radiography and lung function tests prior to the liver transplant were normal. Three months ago, she presented neurotoxicity due to tacrolimus, so immunosuppressive treatment was switched from tacrolimus monotherapy to tacrolimus plus everolimus.

The physical examination revealed diminished breath sounds and an oxygen saturation level of 94%. Laboratory test results showed: C-reactive protein (CRP) 2.45 mg/dl (<0.5), 7.29 $x10^9$ leukocytes (4-11$x10^9$), tacrolimus 4.6 ng/mL, and everolimus 2.3 ng/mL. Chest radiography revealed interstitial infiltration at the upper lobes. Blood, sputum, and urine cultures were negative. Serologies for Mycoplasma pneumoniae, Chlamydophila pneumoniae, and Legionella were negative. CRP SARS-CoV-2 and Galactomannan were negative. Antibiotic treatment with amoxicillin and clavulanic acid was started. Computed tomography (CT) revealed linear thickening of the lung septa and patchy areas of increased ground-glass density predominantly in the upper lobes. A transthoracic echocardiogram ruled out structural heart disease and signs of heart failure. Treatment was modified to ceftriaxone and azithromycin. Bronchoscopy with bronchoalveolar lavage (BAL) was performed. Analysis of BAL fluid revealed a predominance of lymphocytes. Mycobacteria, viruses, fungi, and bacteria were negative in BAL cultures. Drug-induced interstitial pneumonia was considered when symptoms persisted, and the diagnostic workup came up negative. Everolimus was

stopped. Treatment with prednisone 40 mg/day in a tapering dose was initiated with tacrolimus 1 mg/day. After three months, the patient's condition improved clinically and radiologically with a decrease in oxygen requirement to room air (Figure 1).

Discussion

Everolimus-induced pneumonitis in transplant recipients is a diagnosis of exclusion, rare but potentially severe, that requires a high index of suspicion for diagnosis. Common symptoms include dyspnea, cough, and fever. Radiographic patterns are diverse, ranging from diffuse interstitial infiltrates to ground glass infiltrates. BAL shows lymphocytosis and increased eosinophil count. Differential diagnosis must include infections and primary interstitial pneumonitis. Therapeutic management involves the discontinuation of everolimus and, in severe cases, the use of corticosteroids to reduce pulmonary inflammation. Early identification and management of this condition can significantly improve clinical outcomes.

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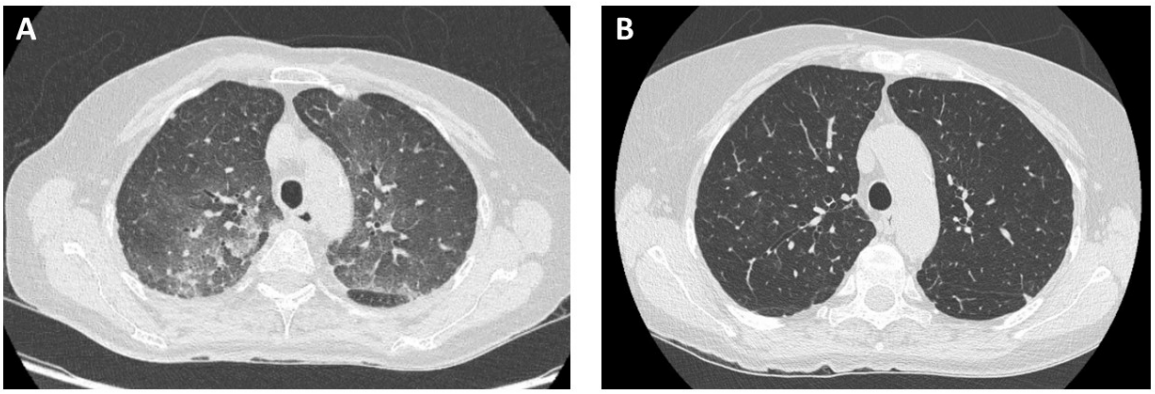

Fig. 1. A. Chest CT showing diffuse patchy ground glass opacities. B. Chest CT showing complete resolution of interstitial infiltrates at three months follow up.