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## **Primary Cerebral Lymphoma and Autoimmune Hepatitis: An Unusual Case Associated with Prolonged Treatment with Mycophenolate Mofetil.**

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### **ABSTRACT:**

The initial approach to autoimmune hepatitis is based on the use of immunosuppressants and corticosteroids. The first-line immunosuppression options include azathioprine or mycophenolate mofetil. Long-term immunosuppression predisposes patients to the development of neoplastic diseases. In this case, chronic AIH treatment with mycophenolate mofetil was associated with the onset of primary cerebral lymphoma, which was treated with methotrexate and rituximab. Rituximab is an interesting therapy for AIH, and in this case, it was able to treat both conditions.

### **1. INTRODUCTION.**

Autoimmune hepatitis (AIH) is a chronic immune-mediated disease that requires lifelong clinical follow-up and prolonged individualized immunosuppression, which in turn increases the predisposition to developing malignancies.

### **2. CASE PRESENTATION.**

A 63-year-old woman with a history of type 1 AIH diagnosed in 2009 without chronic liver disease, initially treated with azathioprine and corticosteroids but did not achieve complete biochemical remission. In 2017, the treatment was modified to mycophenolate mofetil (MMF) and budesonide, achieving complete normalization of

liver function test.

In 2023, the patient was admitted with a sudden onset of instability, paresthesia, diplopia, hemiparesis, and dysphagia. Neurological studies revealed lymphocytosis and hyperproteinorrachia in cerebrospinal fluid (CSF), as well as supratentorial white matter involvement with subcortical frontal lesions and attenuation in the pons on imaging tests (Fig. 1). Histological analysis confirmed the presence of primary cerebral lymphoma (PCL), associated with immunosuppression and Epstein-Barr virus positivity. No infiltration was found in the extension study.

MMF was discontinued, and treatment with dexamethasone, rituximab (RTX), and methotrexate was initiated, leading to complete remission. The patient continues to receive periodic rituximab and follow-up. She has shown a good clinical evolution, with partial recovery of neurological deficits and no liver function alterations.

As a post-treatment complication, she experienced an episode of deep vein thrombosis and pulmonary embolism secondary to immobilization, for which indefinite anticoagulation with edoxaban was initiated. Currently, she remains stable, in complete biochemical remission, and without signs of hepatic disease decompensation.

### 3. DISCUSSION AND CONCLUSION.

Chronic immunosuppression predisposes patients to malignant diseases due to immune system dysregulation and pathogen-associated cancer proliferation. MMF is a widely used immunosuppressant due to its lower rate of side effects. Previous cases have associated MMF-related immunosuppression with the development of PCL in conditions such as myasthenia gravis<sup>2</sup>, polymyositis, rheumatoid arthritis, systemic sclerosis<sup>3</sup>, systemic lupus erythematosus<sup>4</sup>, and post-renal transplant. However, to date, no cases of PCL associated with MMF as a treatment for AIH have been reported.

The treatment of PCL includes methotrexate-based chemotherapy and rituximab. Recent studies have reported the efficacy of RTX as a third-line drug for AIH<sup>5</sup>. Thus, RTX emerges as a relevant therapeutic alternative, capable of addressing both diseases in an integrated manner, making it a promising option, particularly in the context of AIH.

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#### 5. FIGURES.



FIGURE 1 - Illustration 1 - Brain MRI without contrast, T1 FLAIR"