
Rituximab as a Single Agent for Granulomatous Lymphocytic Interstitial Lung Disease in Common Variable Immune Deficiency

Tessarín G¹, Bondioni MP², Rossi S¹, Palumbo L³, Soresina A³, Badolato R¹, Plebani A¹, Lougaris V¹

¹*Pediatrics Clinic, Department of Clinical and Experimental Sciences, University of Brescia, ASST Spedali Civili of Brescia, Brescia, Italy*

²*Pediatric Radiology, University of Brescia, ASST Spedali Civili di Brescia, Brescia, Italy*

³*Pediatrics Clinic, ASST-Spedali Civili of Brescia, Brescia, Italy*

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Common variable immune deficiency (CVID) is the most common symptomatic primary immunodeficiency and is characterized by hypogammaglobulinemia that may be associated with T-cell defects. The clinical hallmarks are recurrent infections, autoimmune manifestations, and lymphoproliferation [1]. Lung involvement is common and may manifest as recurrent infection, chronic lung disease, and interstitial lung disease [1,2]. A small subset of patients with CVID develop granulomatous lymphocytic interstitial lung disease (GLILD), a restrictive interstitial lung disease characterized by a mixed pattern of granulomata and lymphocytic infiltration. Prognosis is unfavorable [2]. Recent data suggest that diagnosis of GLILD in patients CVID reduces life expectancy by 50% [3]. Studies on lung biopsy specimens from CVID patients with GLILD have shown the formation of a tertiary lymphoid structure (TLS) in the lung [4].

There is currently no consensus on a standardized treatment protocol for CVID-associated GLILD. Available data are limited to small case series and expert opinions [5]. Management to date has been with intravenous immunoglobulin, systemic corticosteroids, and combined immunosuppressive therapies, although the results have been variable [5-7]. There is growing evidence on the efficacy of the anti-CD20 monoclonal antibody rituximab in monotherapy for treatment of CVID-associated GLILD [8]. In addition, recent evidence attributes an important role to B cells in the initiation and maintenance of a TLS [8,9].

We present the case of a 37-year-old woman with CVID receiving regular treatment with subcutaneous immunoglobulins. Her clinical history was remarkable for autoimmune thyroiditis, psoriasis, and multiple allergic reactions to drugs (ie, amoxicillin-clavulanate, levofloxacin, azithromycin, and contrast media for computed tomography [CT] scan).

In April 2018, the patient experienced productive cough, mild fever, and dyspnea on exertion. A month later, her physical examination at a local clinic was normal, and a

chest x-ray showed multiple nodular lesions on the left lung. Given her immunological status, she was admitted to hospital, where she received empirical antibiotic therapy (meropenem and doxycycline) for suspected multilobar pneumonia. Biochemical and clinical parameters returned to normal. She was re-admitted a week after discharge for relapsing fever and underwent further investigations. A chest CT scan showed multiple nodular lesions on the left lung; culture of bronchoalveolar lavage (BAL) fluid excluded bacterial infections, mycobacteria, and pneumocystosis. Given the positive galactomannan result in BAL, the patient started antifungal therapy (itraconazole). The 2-month follow-up chest CT scan revealed lesions on the contralateral lung. Lung biopsy revealed numerous non-necrotizing epithelioid cell granulomata and interstitial lymphocytic infiltrates, which were suggestive of GLILD.

Given the patient's immunodeficiency, we decided not to use classical immunosuppressive drugs. Treatment was started with rituximab infusion at 375 mg/m² (total dose, 500 mg) every 4 weeks (total of 4 infusions) after premedication with intravenous hydrocortisone (500 mg) and chlorphenamine (10 mg), owing to her past history of drug-related allergic reactions. Her symptoms improved considerably after 2 doses of rituximab, and she reported a reduction in dyspnea on exertion and resolution of cough. At the end of the fourth infusion, a chest CT scan showed a marked reduction in all lesions (Figure). During treatment, no infections or other adverse effects were observed.

CVID is a clinically complex and heterogeneous condition. GLILD is considered a major complication for which treatment guidelines are lacking and underlying mechanisms are only starting to be unraveled. In the case we report, rituximab in monotherapy proved effective in controlling and reducing progression of GLILD, without the need for additional immunosuppressive treatment (such as azathioprine), which could further complicate the clinical course of affected patients in terms of opportunistic infections and increased risk of lymphoproliferation. During treatment, no severe

adverse events or infectious complications were recorded. The present report provides supporting data regarding the efficacy and safety of rituximab in controlling and remitting GLILD in CVID [6,8]. Further studies on larger cohorts of affected patients are warranted to define the efficacy and outcome of rituximab for treatment of CVID-associated GLILD.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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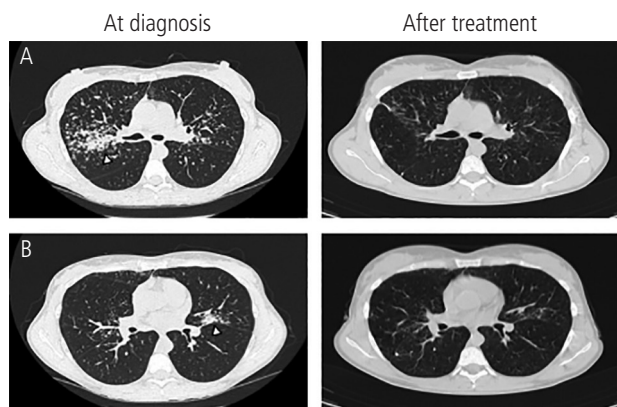


Figure. Axial lung computed tomography scan showing multiple lesions at diagnosis (left column) and their resolution after treatment with rituximab (right column). A, Diffuse lesions in the right upper lobe (white triangle) at diagnosis (left), with complete resolution upon treatment (right). B, Lesions in the lingula at diagnosis (white triangle) (left), with almost complete resolution upon treatment (right).

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Vassilios Lougaris

E-mail: vlougarisbs@yahoo.com