Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 26s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Rituximab for Progressive Interstitial Lung Disease and Vasculopathy in Mixed Connective Tissue Disease: A Case Report

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Cite this paper as: Swapnil Sinha, Vedika Verma, Deepika Sanapala, Sarath Chandra Ponnada, Rashi Bilgaiyan, Veldi Venkata Dileep Kumar, (2025) Rituximab for Progressive Interstitial Lung Disease and Vasculopathy in Mixed Connective Tissue Disease: A Case Report. *Journal of Neonatal Surgery*, 14 (26s), 54-58.

ABSTRACT

This case highlights the successful use of Rituximab in a patient with MCTD presenting with progressive ILD and vasculopathy, unresponsive to standard therapies. Symptoms included fever, myalgia, Raynaud's phenomenon, alopecia, skin rash, digital gangrene, dyspnoea, and digital ulcers. Clinical findings showed NSIP, positive autoimmune markers, and moderate restrictive lung pattern. Diagnosed with MCTD with myositis, NSIP, and vasculopathy. Treated initially with steroids and immunosuppressants; Rituximab was added during disease progression, leading to marked clinical improvement. Rituximab may be effective in refractory MCTD with progressive ILD and vasculopathy, supporting its role in individualized treatment strategies.

Keywords: *Mixed Connective Tissue Disease, Interstitial Lung Disease, Vasculopathy, Rituximab Therapy, Case Report*

1. INTRODUCTION

This case is notable for its chronic and progressive course of MCTD with simultaneous ILD and vasculopathy, unresponsive to standard immunosuppression. Improvement with Rituximab adds valuable insight into the treatment of refractory cases.

Patient Information

A 42-year-old female patient came to outpatient department. Upon presentation, the patient exhibited concerning symptoms including fever, generalized myalgia (muscle pain), and striking peripheral vascular changes characterized by cold fingers and toes displaying a blackish discoloration. Further findings include hair loss, the presence of a skin rash, and the development of ulcerative lesions (sores) on her fingers. Additionally, the patient reported experiencing dyspnea (difficulty in breathing), indicating potential respiratory involvement.

No known family history of autoimmune diseases was reported in the documented medical history. Information about the psychosocial stressors was not recorded. No genetic testing performed.

The patient had a history of prior treatment period from 2018 to 2024, involving several immunomodulatory and supportive medications. These included corticosteroids, Mycophenolate Mofetil, and Hydroxychloroquine, commonly used to manage autoimmune conditions. Additionally, vasodilators and prostaglandins were administered, likely targeting vascular symptoms. This multi-faceted treatment regimen resulted in a period of initial clinical stability for the patient.

Clinical Findings

Significant findings included digital ulceration, High-Resolution Computed Tomography revealed Nonspecific Interstitial Pneumonia with reticular and ground opacities and 20% lung involvement, **Forced Vital Capacity** of 55%, and strong positive autoimmune markers (Anti-Smith 3+, Antinuclear Antibodies 3+, Antiphospholipid Antibodies 3+ titres) with low complement levels.

Timeline

In 2018, the patient presented with digital gangrene and was diagnosed with Mixed Connective Tissue Disease (MCTD). From 2018 to 2024, she was managed with immunosuppressants and vasodilators, which helped control her symptoms and prevent disease progression. In 2024, she experienced a flare-up, marked by the development of a new digital ulcer, worsening breathlessness, and increased systemic symptoms such as fatigue, muscle pain, and Raynaud's phenomenon. After the flare, Rituximab was introduced to her treatment regimen, resulting in a significant clinical improvement, with stabilization of her symptoms and better overall management of her condition.

Diagnostic Assessment

The patient's high-resolution computed tomography revealed a pattern consistent with nonspecific interstitial pneumonia, indicating inflammation and scarring in the lungs. Pulmonary function tests showed a forced vital capacity of 55%, suggesting moderate restrictive lung disease. Autoimmune serology was positive for Anti-Smith antibodies, antinuclear antibodies, and antiphospholipid antibodies, which are commonly associated with autoimmune disorders. An echocardiogram revealed a normal ejection fraction of 60% with no signs of pulmonary arterial hypertension. These findings collectively support the diagnosis of mixed connective tissue disease with lung and cardiovascular involvement.

No significant logistical or financial challenges reported.

Mixed Connective Tissue Disease with myositis, NSIP (ILD), and vasculopathy. Differential diagnoses included SLE and systemic sclerosis initially.

Progressive disease course due to lung and vascular involvement, now stabilized post-Rituximab.

2. THERAPEUTIC INTERVENTION

The patient was managed with a combination of pharmacologic treatments aimed at controlling the underlying autoimmune disease, reducing inflammation, and improving organ function. The main categories of interventions included **immunosuppressants**, **vasodilators**, **corticosteroids**, and a **biologic agent (Rituximab)**. Immunosuppressants, such as Methotrexate, were used to reduce immune system activity and control autoimmune flare-ups, while corticosteroids helped manage inflammation. Vasodilators were prescribed to address the vascular issues related to Raynaud's phenomenon and digital gangrene. Rituximab, a biologic agent, was introduced to target B-cells, a key component in the autoimmune response, when the disease showed signs of progression despite earlier treatments.

Rituximab was administered as an intravenous infusion of 1.5 g, given in a spaced-out regimen, typically over a period of weeks, depending on clinical response and tolerability. This regimen allowed for effective suppression of the patient's immune response. Prior to Rituximab, the patient had been on oral immunosuppressants (such as Methotrexate) and vasodilators (such as Bosentan) to manage the symptoms of MCTD. These therapies were part of the patient's routine care to control the autoimmune activity and associated vasculopathy.

As the disease progressed, some adjustments to the medication regimen were necessary. **Bosentan**, which was initially used as a vasodilator, was replaced by **Ambrisentan**. This change was made due to Ambrisentan's improved efficacy and better tolerability in managing pulmonary arterial hypertension and other vascular complications in autoimmune diseases. Additionally, **steroids** were reintroduced to manage flare-ups and inflammation, and **Methotrexate** was added to provide stronger immune suppression and control disease activity. **Rituximab** was introduced because of the patient's inadequate response to the previous treatments and the progression of the disease, which included worsening systemic symptoms and new organ involvement. Rituximab, being a monoclonal antibody that targets CD20+ B-cells, specifically addresses the autoimmune response by depleting these cells, thus helping in reducing disease activity and preventing further organ damage. The combination of these interventions aimed to halt the disease progression, alleviate symptoms, and improve the patient's quality of life.

3. FOLLOW-UP AND OUTCOMES

The patient showed a **marked improvement** in her digital ulcers, with no new ulcers developing. Her Raynaud's symptoms, which had previously been severe and caused significant discomfort, also improved considerably. Additionally, **paraesthesia** (tingling or numbness in the extremities), which had been a troubling symptom, showed significant relief. Overall, the patient achieved **clinical stabilization**, with a reduction in disease activity and a noticeable improvement in her quality of life.

After 3 weeks of Rituximab treatment, **no new ulcers** were observed, indicating a positive response to therapy. Pulmonary function remained **stable**, with no further deterioration of lung function noted. The patient also reported **improved symptoms** across multiple domains, including reduced muscle pain, decreased fatigue, and better overall well-being. This suggests that Rituximab had a significant impact in controlling the disease's systemic effects, particularly the vasculopathy and autoimmune activity.

The patient **tolerated Rituximab** treatment well, with no adverse reactions or complications noted during the administration.

Adherence to the treatment regimen was carefully monitored both during hospitalization and through follow-up visits. The patient was regularly assessed for any signs of non-compliance or issues with medication intake. Given the improvements observed, adherence appeared to be excellent, and the patient showed a commitment to following the prescribed therapy plan.

No adverse effects were reported from Rituximab treatment. The patient did not experience any unexpected complications such as infusion reactions, infections, or other serious side effects typically associated with biologic therapies. The absence of any adverse events suggests that Rituximab was well tolerated, and its use was beneficial in managing the disease without introducing significant risks. Given the improvement in her clinical status and the lack of negative outcomes, Rituximab was considered an effective and safe intervention in this case.

4. STRENGTH

This case underscores the potential of Rituximab as an effective treatment for refractory **Mixed Connective Tissue Disease (MCTD)**. The patient's improvement in **digital ulcers**, **Raynaud's phenomenon**, and other systemic symptoms highlights the promising role of biologic therapies, particularly in cases that are resistant to traditional treatments. This case is supported by a growing body of literature demonstrating the efficacy of Rituximab in managing severe manifestations of connective tissue diseases, including **interstitial lung disease** (ILD) associated with these diseases (Maher et al., 2023; Seedat et al., 2024). The **systemic response** observed in this patient aligns with findings from similar case reports and clinical trials that suggest Rituximab's ability to modulate immune-mediated damage in diseases like MCTD (Pascual et al., 2015; Zhao et al., 2022).

5. LIMITATION

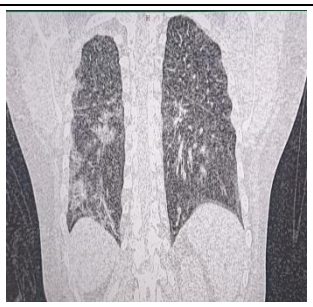
As with all single-patient case reports, the findings here should be interpreted with caution, as they may not be applicable to the broader patient population. Response to Rituximab can be variable, and its effectiveness may depend on the individual patient's disease characteristics (Wang & Li, 2023). Moreover, this report does not address the long-term efficacy or safety of Rituximab beyond the short follow-up period. Further studies involving larger cohorts are required to better understand the sustained effects and any potential late-onset side effects of Rituximab in **MCTD** (Maher et al., 2023; Adams et al., 2023).

Patient Perspective

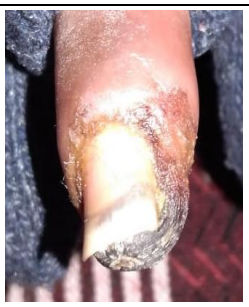
The patient reported significant relief from finger pain, improved breathing, and was satisfied with the outcome of Rituximab treatment after a long period of disease instability.

Informed Consent

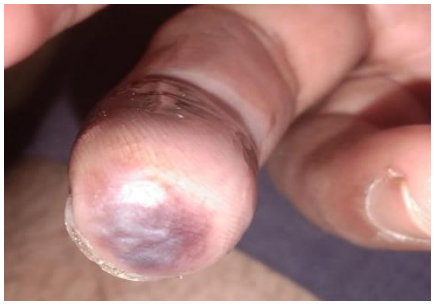
Informed written consent was obtained from the patient for publication of this case report and associated medical details.



HRCT Scan Of lung



Digital ulcer



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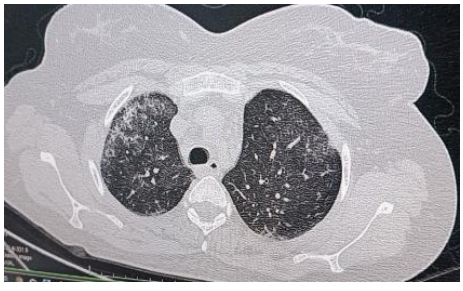

Hrct of lung

6. DISCUSSION

Rituximab, a **monoclonal antibody** targeting B-cells, has shown promising results in several autoimmune conditions, including **systemic lupus erythematosus** and **rheumatoid arthritis**, where immune dysfunction plays a critical role (Boppana et al., 2024). Specifically, in **connective tissue disease-associated ILD**, Rituximab has demonstrated potential in improving **pulmonary function** and controlling disease progression (Zhao et al., 2022). Studies comparing Rituximab with other immunosuppressive therapies like **intravenous cyclophosphamide** have shown that Rituximab may be equally or even more effective in reducing lung involvement in **connective tissue diseases** (Maher et al., 2023).

However, while Rituximab has shown positive outcomes in several case series and small trials, including in **MCTD**, the overall evidence base remains relatively small, with many studies reporting on limited sample sizes and varying treatment regimens (Seedat et al., 2024; Wang & Li, 2023). Additionally, combinations of Rituximab with other immunosuppressive drugs, such as **mycophenolate mofetil**, have been explored with some success in controlling ILD and other complications (Mankikian et al., 2023), though this combination therapy is still under investigation.

The mechanism by which Rituximab improves outcomes in autoimmune diseases like MCTD is primarily through its depletion of **B-cells**, which are implicated in the pathogenesis of these conditions by producing autoantibodies that attack the body's own tissues. This action significantly reduces **autoimmune activity** and helps mitigate systemic inflammation (Adams et al., 2023). In this case, Rituximab's efficacy in improving digital ulcers and **Raynaud's phenomenon** can be attributed to its impact on controlling the overactive immune response, which drives vasculopathy and skin changes (Pascual et al., 2015).

This case reinforces the growing role of **biologic therapies** like Rituximab in treating refractory MCTD, particularly in patients with progressive **lung disease** and **vasculopathy**. While this case represents a positive outcome, further research, including larger randomized controlled trials, is necessary to better establish Rituximab's long-term effectiveness and safety profile in MCTD and other connective tissue diseases with organ involvement (Vacchi et al., 2021; Zhao et al., 2022). The results of ongoing trials and systematic reviews continue to support the notion that Rituximab could become a cornerstone in the treatment of severe autoimmune diseases resistant to conventional therapies (Maher et al., 2023; Boppana et al., 2024).

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