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CASE STUDY

The use of rituximab in the treatment of multiple sclerosis: a case study

El uso de rituximab en el tratamiento de la esclerosis múltiple: un estudio de caso

O uso de rituximab no tratamento de esclerose múltipla: um estudo de caso

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Abstract

This study aimed to present the case of rituximab in the treatment of a patient with multiple sclerosis, providing preliminary evidence of its efficacy. This case study included a review of the patient's medical records and an analysis of scientific literature from databases such as PubMed, Google Scholar, and SciELO. The results demonstrated a significant reduction in disease exacerbations and an improvement in the progression of functional disability. Although adverse events were reported, they were successfully managed with premedication. The conclusion is that rituximab may be a promising therapeutic option for refractory cases of multiple sclerosis, although prospective studies are needed to confirm these results.

Descriptors: Multiple Sclerosis; Rituximab; Idiopathic Thrombocytopenia; Treatment; Neurology.

Resumén

Este estudio tuvo como objetivo presentar el caso de rituximab en el tratamiento de un paciente con esclerosis múltiple, aportando evidencia preliminar de su eficacia. Este estudio incluyó una revisión de la historia clínica del paciente y un análisis de la literatura científica en bases de datos como PubMed, Google Scholar y SciELO. Los resultados demostraron una reducción significativa de las exacerbaciones de la enfermedad y una mejora en la progresión de la discapacidad funcional. Si bien se reportaron eventos adversos, estos se manejaron con éxito con premedicación. La conclusión es que rituximab puede ser una opción terapéutica prometedora para casos refractarios de esclerosis múltiple, aunque se requieren estudios prospectivos para confirmar estos resultados.

Descriptores: Esclerosis Múltiple; Rituximab; Trombocitopenia Idiopática; Tratamiento; Neurología.

Resumo

Objetivou-se apresentar o caso do uso de rituximab no tratamento de uma paciente com esclerose múltipla, fornecendo evidências preliminares sobre sua eficácia. Trata-se de um estudo de caso, incluindo a revisão do prontuário médico da paciente e a análise de literatura científica proveniente de bases de dados como PubMed, Google Acadêmico e SciELO. Os resultados demonstraram uma redução significativa nas exacerbações da doença e uma melhora na progressão da incapacidade funcional. Embora eventos adversos tenham sido relatados, eles foram controlados com sucesso por meio de pré-medicação. Conclui-se que o rituximab pode ser uma opção terapêutica promissora para casos refratários de esclerose múltipla, embora estudos prospectivos sejam necessários para confirmar esses resultados.

Descritores: Esclerose Múltipla; Rituximab; Trombocitopenia Idiopática; Tratamento; Neurologia.

Introduction

Multiple sclerosis (MS) is a chronic neuroinflammatory disease characterized by the loss of the myelin sheath in the central nervous system, primarily caused by an autoimmune response involving both T cells and B cells. This pathology affects approximately 2.5 million people worldwide and results in neurological dysfunctions that can compromise mobility, motor coordination, and other essential cognitive functions[1]. Given the complexity of its pathogenesis and the variability of symptoms, the treatment of MS continues to be a clinical challenge, especially in cases refractory to first-line treatments.

Immune Thrombocytopenic Purpura (ITP) is an acquired autoimmune disease characterized by thrombocytopenia resulting from autoantibodies directed against platelet antigens. This disease is a diagnosis of exclusion, meaning it is made after screening other diseases that can be identified through laboratory tests. It has an estimated incidence of 2 to 5 per 100,000 people in the general population[2]. The first-line treatment used is corticosteroids in immunosuppressive doses; however, in refractory cases, the guidelines allow for expanded management, using splenectomy, rituximab, or thrombopoietin receptor agonist.

In recent years, rituximab, an anti-CD20 monoclonal antibody that selectively depletes B cells, has emerged as an effective alternative in the treatment of relapsing-remitting multiple sclerosis (RRMS). Studies suggest that rituximab works by decreasing neuroinflammation, reducing the number of flare-ups and lesions visible on MRI[3]. Although the drug is already widely used in the treatment of lymphomas and rheumatological diseases, its use in MS is still considered "off-label", that is, outside the approved indications, which makes the analysis of its benefits and risks in this context crucial.

The main problem addressed in this work is the need to investigate the benefits of using rituximab in the treatment of MS, considering that there are still gaps in knowledge about its long-term effects and its relationship with the risk of infections[3,4]. This issue is particularly relevant not only because of the high prevalence of the disease but also because of the importance of therapies that combine clinical efficacy with a favorable safety profile. Such treatments are crucial for improving patients' quality of life and reducing the burden on healthcare systems.

Solving this problem could have significant implications for the management of multiple sclerosis, offering an additional therapeutic option for patients who do not respond adequately to conventional treatments. The use of rituximab may lead to a decrease in disability progression, preventing recurrent flare-ups, and potentially reducing long-term treatment costs[5].

This study aims to report the benefits observed with rituximab in the treatment of multiple sclerosis and idiopathic thrombocytopenic purpura (ITP), based on a case study. The analysis aims to provide evidence that can contribute to a deeper understanding of how rituximab can be incorporated into the multiple sclerosis therapeutic arsenal, promoting better clinical outcomes for patients. The objective is to present the case of a patient with relapsing-remitting multiple sclerosis who experienced significant clinical benefits with the use of rituximab as part of the pharmacological treatment for this condition.

Methodology

This is a case study of a patient followed from 2018 to 2020 in a municipality in the state of Minas Gerais. The information for this study was obtained through an approximately two-hour interview with the patient, in addition to a detailed analysis of her medical records for data collection. The patient's identity will be kept strictly confidential when the results are published.

The theoretical framework was based on 13 scientific articles extracted from Google Scholar, PubMed, and SciELO databases. The keywords used in the search were: "Multiple Sclerosis," "Idiopathic Thrombocytopenic Purpura," "Rituximab," and "Treatment." The exclusion criteria included publications in journals with an impact factor lower than 2. The inclusion criteria included articles addressing the use of rituximab in the treatment of multiple sclerosis and idiopathic thrombocytopenic purpura, as well as those discussing the drug's mechanism of action and the development of these diseases.

Regarding ethical aspects, the patient signed the Free and Informed Consent Form, and the research was registered and approved by the Research Ethics Committee of the Atenas University Center in Paracatu, State of Minas Gerais, through CAAE: 82942024.1.0000.0169 and Opinion: 7.091.148.

Case Presentation

Patient M.M.O., a 20-year-old and 10-month-old female, presents with idiopathic thrombocytopenic purpura (ITP) and relapsing-remitting multiple sclerosis (RRMS) with inactive disease status. In September 2013, she developed a high fever for 3 days, diagnosed with tonsillitis, and began antibiotic therapy. Approximately 15 days later, she returned to the emergency room with bruises all over her body and was diagnosed with ITP. She received intravenous immunoglobulin infusions (400 mg/kg) in September and October of the same year and continued treatment with oral corticosteroids until September 2014 to control thrombocytopenia.

On December 8, 2018, she woke up with blurred vision in her left eye and pain with eye movement. These symptoms progressively worsened over two weeks, resulting in difficulty seeing colors, only seeing outlines. She was evaluated by an ophthalmologist, who found no abnormalities and referred her to a specialist at an ophthalmology hospital in Brasília. After a further ophthalmological evaluation revealed no abnormalities, an optical coherence tomography scan was requested, which diagnosed optic neuritis in her left eye. At that point, the patient was referred to the neurology emergency room (ER).

On December 19, 2018, she was admitted to a hospital in Minas Gerais, where a neurologist ordered magnetic resonance imaging (MRI) of the skull, cervical, lumbar, and orbital regions, as well as a lumbar puncture and

methylprednisolone pulse therapy. A brain MRI performed on December 20, 2018, showed lesions in the supra- and infratentorial white matter suggestive of demyelinating disease, without active inflammatory signs. An MRI of the cervical spine showed focal spinal cord lesions also suggestive of demyelinating disease, without active inflammatory signs. An MRI of the thoracic and lumbar spine showed no significant changes. Cerebrospinal fluid collected on May 10, 2019, showed the presence of oligoclonal bands.

For treatment, methylprednisolone pulse therapy was prescribed for 5 days, resulting in marked improvement within 48 hours of the first infusion. She was discharged on December 25, 2018, with a prescription for 60 mg of prednisone until her outpatient appointment. Subsequently, she was seen by a neurologist who prescribed Rebif 22® (interferon beta) three times a week intramuscularly, starting treatment on February 21, 2019.

A blood count performed on March 26, 2020, revealed a recurrence of ITP, and the physician prescribed immunosuppressive doses of prednisone until September of that year. However, the condition proved refractory to oral corticosteroids, and on September 8, 2020, the patient was hospitalized. She had a platelet count of 12,000 and received intravenous immunoglobulins to stabilize her condition. She was subsequently referred to as a rheumatologist, who, along with the immunologist, decided to use rituximab to treat both conditions with a single drug.

The patient took rituximab for approximately 1 year, with no precise documentation of the start or end of treatment. She reported no significant adverse effects, and the medication was discontinued due to the stabilization of thrombocytopenia and the medical team's concern about the zero B lymphocyte count, which increased the risk of serious infections. Therefore, she was started on fingolimod, which was not well accepted by the body, resulting in recurrent infections such as pharyngotonsillitis and candidiasis. Subsequently, the patient and her doctors opted for natalizumab infusions, which she continues to use without major complications and with adequate control of ITP and MS.

Discussion

Multiple sclerosis presents its pathophysiology in three forms: relapsing-remitting, primary progressive, and secondary progressive, characterized by the action of encephalitogenic T cells that are capable of crossing the blood-brain barrier (BBB) and initiating robust neuroinflammation that leads to lesions in the brain and spinal cord. Characterized as an inflammatory autoimmune disease, MS causes progressive disability and affects the quality of life of patients, making it essential to search for medications that alleviate the symptoms generated by this condition[6,7].

The updated guideline of the American Society of Hematology, published in 2019, determines that second-line medications should be chosen when the patient is refractory to the use of oral corticosteroids, so that they require more than 5 mg/day of prednisone to maintain platelet levels above 30 X 109. If the patient values remission without treatment and wishes to avoid surgery, rituximab is the preferred treatment[8].

Rituximab is an anti-CD20 monoclonal antibody that has demonstrated efficacy in RRMS and other neurological, rheumatological, and hematological conditions, offering a unique opportunity to investigate and identify these mechanisms. The drug is known to act by reducing the number of B cells in the periphery, thus controlling both diseases, given that B cells are present in MS lesions and attack platelets in ITP[9,10].

Preclinical and observational studies indicate that rituximab may be effective in reducing multiple sclerosis activity by promoting the selective depletion of B cells, which are responsible for antigen presentation and cytokine production, without compromising B cell reconstitution or preexisting humoral immunity. The profound depletion of CD20+ B cells is expected to modify B cell-mediated antigen presentation, subsequent T cell activation, antibody production, and possibly the circulation of Epstein-Barr virus, which resides in B cells and has been implicated as a factor potentially associated with the pathogenesis of multiple sclerosis[2,9].

The safety profile of rituximab is generally considered favorable. The most common side effects include infusion reactions and an increased risk of infections, especially in patients with comorbidities. These results indicate that rituximab use in MS patients is accompanied by frequent, but not serious, adverse events, which generally decrease with subsequent infusions. Therefore, rituximab is considered sufficiently safe for these patients, based on the patient's report of no significant adverse reactions[2,11].

A comparative analysis with other disease-modifying therapies (DMTs), such as natalizumab and fingolimod, was also performed. Individuals who started or switched to low-dose rituximab off-label had a reduced risk of relapses and were less likely to switch therapy compared to those who started on approved MS alternatives[12].

The use of rituximab in multiple sclerosis has been supported by growing evidence of efficacy, especially in patients who do not respond to other DMTs. The case of the patient reported here is in line with the literature, which suggests that B-cell depletion can result in effective control of disease activity[7-13].

Therefore, well-designed studies should be conducted to validate the therapeutic efficacy of rituximab in the treatment of MS, as this would benefit those with this condition. Among the medications available for the treatment of MS, RTX is known to have one of the best cost-benefit ratios. Furthermore, it has proven efficacy in the treatment of rheumatological and hematological diseases, allowing personalized therapy according to each patient's clinical condition. The above report highlights a promising example of rituximab's use in the treatment of multiple sclerosis. Although its use was off label for this disease and its efficacy still needs to be confirmed by larger clinical studies, its positive response to treatment suggests that rituximab may be a viable option for MS patients with other diseases that may benefit from this drug.

Conclusion

The use of rituximab in the treatment of relapsing-remitting multiple sclerosis (RRMS) has proven to be a promising alternative for patients refractory to conventional treatments. In this case report, rituximab administration resulted in significant improvement in both the control of multiple sclerosis and the patient's idiopathic thrombocytopenic purpura (ITP), offering an effective therapeutic approach for the concomitant management of these conditions.

Although the results are encouraging, it is important to emphasize that the use of rituximab for RRMS is still considered off-label. Therefore, larger-scale prospective and controlled studies are needed to validate the long-term safety and efficacy of this treatment. The clinical application of therapies targeting B cells, such as rituximab, could redefine the management of patients with multiple sclerosis, especially those with inadequate responses to first-line therapies.

This case highlights the potential of rituximab as a viable and effective therapy for RRMS, stabilizing the patient's clinical condition. Personalized treatment, based on the specific characteristics of each case, allows for a more effective and targeted approach, with significant benefits for patients' quality of life and the healthcare system.

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