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ACUTE MYOCARDIAL DYSFUNCTION ASSOCIATED WITH RITUXIMAB IN A PATIENT WITH SCHILDER-TYPE MULTIPLE SCLEROSIS: A CASE REPORT

DISFUNÇÃO MIOCÁRDICA AGUDA ASSOCIADA AO RITUXIMABE EM UM PACIENTE COM ESCLEROSE MÚLTIPLA DO TIPO SCHILDER: RELATO DE CASO

DISFUNCIÓN MIOCÁRDICA AGUDA ASOCIADA AL RITUXIMAB EN UN PACIENTE CON ESCLEROSIS MÚLTIPLE TIPO SCHILDER: REPORTE DE CASO

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ABSTRACT

Introduction: Rituximab is an anti-CD20 monoclonal antibody widely used in the treatment of autoimmune and hematologic diseases, including off-label use in aggressive forms of multiple sclerosis. Although its overall safety profile is considered favorable, rare and potentially severe cardiovascular adverse events have been increasingly reported, particularly as its use expands beyond oncology settings.

Objective: To report a case of acute myocardial dysfunction temporally associated with rituximab infusion in a young patient with Schilder-type multiple sclerosis and no prior history of cardiac disease, and to discuss its clinical implications.

Methods: This is a case report based on a retrospective review of clinical, laboratory, electrocardiographic, and echocardiographic data obtained from the electronic medical record, complemented by a narrative review of the recent literature on anti-CD20–associated cardiotoxicity.

Case report: A 30-year-old female patient with Schilder-type multiple sclerosis developed sudden chest pain during rituximab infusion, associated with marked elevation of cardiac troponin levels and left ventricular systolic dysfunction documented by echocardiography. The infusion was immediately discontinued, and standard heart failure therapy was initiated, resulting in clinical improvement and recovery of cardiac function. Due to the adverse event, immunomodulatory therapy was subsequently changed.

Conclusion: This case suggests an association between rituximab use and acute myocardial dysfunction, even in young patients without traditional cardiovascular risk factors. It highlights

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the importance of early recognition of rare adverse events, appropriate monitoring during infusions, and multidisciplinary management to enhance the safety of immunobiological therapies.

Keywords: Multiple Sclerosis. Rituximab. Cardiotoxicity. Monoclonal Antibodies. Case Report.

RESUMO

Introdução: O rituximabe é um anticorpo monoclonal anti-CD20 amplamente utilizado no tratamento de doenças autoimunes e hematológicas, incluindo o uso off-label em formas agressivas de esclerose múltipla. Embora seu perfil geral de segurança seja considerado favorável, eventos adversos cardiovasculares raros e potencialmente graves têm sido cada vez mais relatados, especialmente à medida que seu uso se expande para além do contexto oncológico.

Objetivo: Relatar um caso de disfunção miocárdica aguda temporalmente associada à infusão de rituximabe em uma paciente jovem com esclerose múltipla do tipo Schilder e sem histórico prévio de doença cardíaca, bem como discutir suas implicações clínicas.

Métodos: Trata-se de um relato de caso baseado na revisão retrospectiva de dados clínicos, laboratoriais, eletrocardiográficos e ecocardiográficos obtidos do prontuário eletrônico, complementada por uma revisão narrativa da literatura recente sobre cardiotoxicidade associada a anti-CD20.

Relato de caso: Paciente do sexo feminino, 30 anos, com esclerose múltipla do tipo Schilder, desenvolveu dor torácica súbita durante a infusão de rituximabe, associada a elevação acentuada dos níveis de troponina cardíaca e disfunção sistólica do ventrículo esquerdo documentada por ecocardiografia. A infusão foi imediatamente interrompida e instituída terapia padrão para insuficiência cardíaca, resultando em melhora clínica e recuperação da função cardíaca. Em decorrência do evento adverso, a terapia imunomoduladora foi posteriormente modificada.

Conclusão: Este caso sugere uma associação entre o uso de rituximabe e disfunção miocárdica aguda, mesmo em pacientes jovens sem fatores de risco cardiovasculares tradicionais. Ressalta-se a importância do reconhecimento precoce de eventos adversos raros, do monitoramento adequado durante as infusões e do manejo multidisciplinar para aumentar a segurança das terapias imunobiológicas.

Palavras-chave: Esclerose Múltipla. Rituximabe. Cardiotoxicidade. Anticorpos Monoclonais. Relato de Caso.

RESUMEN

Introducción: El rituximab es un anticuerpo monoclonal anti-CD20 ampliamente utilizado en el tratamiento de enfermedades autoinmunes y hematológicas, incluido su uso fuera de indicación en formas agresivas de esclerosis múltiple. Aunque su perfil general de seguridad se considera favorable, se han reportado cada vez más eventos adversos cardiovasculares raros y potencialmente graves, especialmente a medida que su uso se expande más allá del ámbito oncológico.

Objetivo: Reportar un caso de disfunción miocárdica aguda temporalmente asociada a la infusión de rituximab en una paciente joven con esclerosis múltiple tipo Schilder y sin antecedentes de enfermedad cardíaca, así como discutir sus implicaciones clínicas.

Métodos: Se trata de un reporte de caso basado en la revisión retrospectiva de datos clínicos, de laboratorio, electrocardiográficos y ecocardiográficos obtenidos del historial clínico electrónico, complementada por una revisión narrativa de la literatura reciente sobre cardiotoxicidad asociada a anti-CD20.

Reporte de caso: Paciente femenina de 30 años con esclerosis múltiple tipo Schilder desarrolló dolor torácico súbito durante la infusión de rituximab, asociado a una marcada elevación de los niveles de troponina cardíaca y disfunción sistólica del ventrículo izquierdo documentada por ecocardiografía. La infusión fue interrumpida de inmediato y se inició tratamiento estándar para insuficiencia cardíaca, lo que resultó en mejoría clínica y recuperación de la función cardíaca. Debido al evento adverso, la terapia inmunomoduladora fue modificada posteriormente.

Conclusión: Este caso sugiere una asociación entre el uso de rituximab y la disfunción miocárdica aguda, incluso en pacientes jóvenes sin factores de riesgo cardiovasculares tradicionales. Destaca la importancia del reconocimiento temprano de eventos adversos raros, el monitoreo adecuado durante las infusiones y el manejo multidisciplinario para mejorar la seguridad de las terapias inmunobiológicas.

Palabras clave: Esclerosis Múltiple. Rituximab. Cardiotoxicidad. Anticuerpos Monoclonales. Reporte de Caso.

1 INTRODUCTION

Multiple sclerosis is a chronic, immune-mediated, inflammatory demyelinating disease of the central nervous system characterized by heterogeneous clinical presentation and variable long-term disability, with substantial impact on functional capacity and quality of life[1]. Among its clinical variants, Schilder-type multiple sclerosis represents a rare and aggressive form, typically associated with extensive demyelinating lesions, higher inflammatory burden, and poorer functional prognosis when compared with classical phenotypes[2]. Due to this aggressive course, early initiation of high-efficacy disease-modifying therapies is often required to control disease activity and prevent irreversible neurological damage[3].

Over the past two decades, the therapeutic landscape of multiple sclerosis has expanded considerably, particularly with the introduction of monoclonal antibodies targeting specific immune pathways[4]. These agents have demonstrated superior efficacy in reducing relapse rates, radiological activity, and disability progression when compared with traditional immunomodulatory therapies[5]. Among them, rituximab, a chimeric monoclonal antibody directed against the CD20 antigen expressed on B lymphocytes, has gained widespread use in clinical practice, despite its off-label status for multiple sclerosis[6].

Rituximab induces selective B-cell depletion, thereby modulating antigen presentation, cytokine production, and autoantibody-mediated immune responses, mechanisms that play a central role in the pathophysiology of multiple sclerosis[7]. Observational studies and real-world data have consistently demonstrated significant efficacy of rituximab in reducing inflammatory disease activity and relapse frequency, particularly in patients with highly active or treatment-refractory disease[8]. As a result, rituximab has become a commonly used therapeutic option in several centers worldwide, including for aggressive phenotypes such as Schilder-type multiple sclerosis[9].

Overall, rituximab is considered to have a favorable safety profile, with infusion-related reactions, including fever, chills, and transient hypotension, being the most frequently reported adverse events[10]. However, as its use has expanded beyond oncological indications and into younger, non-oncological populations, rare but potentially serious adverse events have been increasingly recognized[11]. Among these, cardiovascular complications such as arrhythmias, acute heart failure, myocarditis, and left ventricular systolic dysfunction have been reported, predominantly through case reports and pharmacovigilance studies[12].

Cardiotoxicity associated with immunobiological therapies represents an emerging clinical challenge and differs conceptually from classical chemotherapy-induced cardiotoxicity, which is typically dose-dependent and cumulative[13]. In the context of monoclonal antibodies, proposed mechanisms include cytokine release syndrome, immune-

mediated myocardial inflammation, endothelial dysfunction, and autoimmune cross-reactivity affecting cardiac tissue[14]. Nevertheless, the precise mechanisms underlying rituximab-associated cardiotoxicity remain incompletely understood, and its true incidence is likely underestimated, particularly in patients without pre-existing structural heart disease[15].

Although well-established cardio-oncology guidelines exist for monitoring patients receiving known cardiotoxic agents, no specific recommendations currently address cardiovascular surveillance for rituximab when used outside oncological settings, such as in autoimmune neurological diseases[16]. This lack of standardized guidance underscores the importance of individual case reports in expanding clinical awareness, characterizing potential risk profiles, and informing future preventive strategies. Reports involving young patients without traditional cardiovascular risk factors are particularly valuable, as they broaden the recognized spectrum of susceptibility to rituximab-associated cardiac events[17].

In this context, the present study aims to report a case of acute myocardial dysfunction temporally associated with rituximab infusion in a young patient with Schilder-type multiple sclerosis and no prior history of cardiovascular disease[18]. By detailing the clinical presentation, diagnostic findings, management, and outcome, this report seeks to contribute to the growing body of evidence regarding rituximab-associated cardiotoxicity and to highlight the importance of early recognition, multidisciplinary management, and individualized risk–benefit assessment in patients receiving anti-CD20 therapies[19].

2 OBJECTIVES

The primary objective of this study is to describe a case of acute myocardial dysfunction temporally associated with rituximab infusion in a young patient with Schilder-type multiple sclerosis and no prior history of structural heart disease.

The secondary objectives are to discuss potential pathophysiological mechanisms underlying rituximab-associated cardiotoxicity, to critically contextualize this event within the existing literature on cardiovascular adverse effects related to anti-CD20 therapies, and to highlight the clinical implications for monitoring, risk assessment, and therapeutic decision-making in patients with autoimmune neurological diseases treated with immunobiological agents.

3 METHODOLOGY

This study is an observational descriptive report of a single clinical case. Data were collected retrospectively from the patient's electronic medical records, including clinical history, physical examinations, laboratory findings, electrocardiographic recordings,

echocardiographic assessments, and documented clinical evolution during hospitalization and outpatient follow-up.

Clinical data were reviewed and organized chronologically, from the administration of rituximab infusion through the onset of cardiovascular symptoms, diagnostic evaluation, therapeutic management, and subsequent clinical outcome. Particular attention was given to cardiovascular signs and symptoms, hemodynamic parameters, cardiac biomarkers, imaging findings, and response to treatment.

To support the discussion and provide scientific context, a narrative review of the literature was conducted using established medical databases, including PubMed and SciELO. Articles published within the last ten years were prioritized, focusing on rituximab, anti-CD20 therapies, cardiotoxicity, cardiovascular adverse events, and multiple sclerosis. Relevant case reports, observational studies, reviews, and clinical guidelines were included.

The study was conducted in accordance with ethical principles governing research involving human subjects. All patient data were anonymized to ensure confidentiality, and no identifiable personal information is included in this report. The preparation of this manuscript followed internationally accepted recommendations for the reporting of clinical case studies.

4 CASE REPORT

A 30-year-old female patient with a diagnosis of relapsing–remitting multiple sclerosis of the Schilder type was under regular neurological follow-up. Her medical history was significant for class III obesity and schizophrenia. She also had a prior history of deep vein thrombosis of the left lower limb in 2020, which was treated with warfarin for one year, as well as a history of fetal demise at the age of 20. She denied tobacco use, alcohol consumption, or known drug allergies. Family history was notable for ischemic stroke and myocardial infarction in her father at the age of 70, and three episodes of ischemic stroke in her mother.

Neurological follow-up began in 2017 after an initial presentation characterized by ataxia, visual blurring, and dysarthria, which progressed to impaired consciousness requiring orotracheal intubation and admission to the intensive care unit. Initial disease-modifying therapy with dimethyl fumarate was initiated; however, recurrent clinical relapses occurred in 2018, prompting treatment with high-dose corticosteroid pulse therapy. Given disease progression and the aggressive clinical phenotype, rituximab therapy was initiated in 2019 and maintained thereafter.

The patient was receiving rituximab according to a regimen consisting of one weekly infusion for four consecutive weeks every six months. Concomitant medications included quetiapine, fluoxetine, promethazine, and clonazepam. Magnetic resonance imaging

performed in 2024 demonstrated multiple supratentorial and spinal demyelinating lesions without evidence of active inflammation, consistent with chronic evolution of Schilder-type multiple sclerosis.

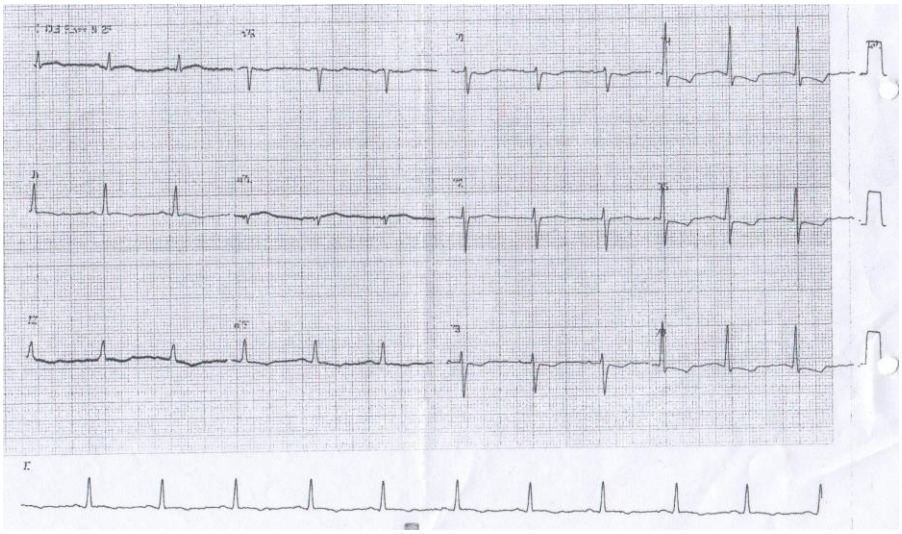
On January 27, 2025, at 08:00 a.m., the patient was admitted for the second infusion of her scheduled six-month rituximab cycle. She was asymptomatic and in good general condition at admission. Physical examination and routine laboratory tests revealed no significant abnormalities, and the first infusion administered one week earlier had been uneventful.

Shortly after the initiation of the infusion, the patient developed sudden-onset chest pain described as intense, constrictive, non-radiating, and associated with diaphoresis and headache. She reported no prior history of chest pain. On physical examination, cardiac rhythm was regular with normal heart sounds and no audible murmurs. Pulmonary auscultation revealed mildly reduced breath sounds at the lung bases without adventitious sounds. Peripheral perfusion was preserved. Vital signs showed a blood pressure of 110/60 mmHg, heart rate of 82 beats per minute, and peripheral oxygen saturation of 97% on room air.

The rituximab infusion was immediately discontinued, and diagnostic evaluation was initiated with serial electrocardiograms, cardiac biomarker assessment, chest radiography, and transfer to the emergency department for continuous monitoring. The admission electrocardiogram demonstrated sinus rhythm, narrow QRS complexes, and diffuse ventricular repolarization abnormalities without ST-segment elevation or ischemic changes. Subsequent electrocardiograms showed no dynamic ST-segment alterations. Chest radiography was unremarkable. Bedside cardiac ultrasound suggested diffuse hypokinesia of the left ventricle.

Figure 1

Patient's admission electrocardiogram. Examination performed at the time of the adverse event following rituximab infusion, used for initial assessment of cardiac function



The first high-sensitivity troponin measurement, obtained at 13:26, was markedly elevated at 4481 ng/L, with a subsequent decrease to 3902 ng/L at 22:12. D-dimer levels were within normal limits. The patient experienced chest pain for approximately three hours, with gradual and spontaneous resolution. Given the evidence of left ventricular dysfunction, treatment with enalapril 10 mg twice daily and intravenous furosemide 40 mg twice daily was initiated.

Transthoracic echocardiography revealed mild global left ventricular systolic dysfunction, with an estimated ejection fraction of 45%, diffuse mild hypokinesia, and mild left ventricular dilation. The left atrium measured 4.0 cm, the aortic root 3.3 cm, left ventricular systolic diameter 4.8 cm, and diastolic diameter 6.2 cm. Septal and posterior wall thickness were both 0.9 cm. Grade I diastolic dysfunction and mild holosystolic mitral regurgitation were also observed.

On January 28, 2025, the patient was transferred to the coronary care unit for further diagnostic evaluation and clinical observation. During hospitalization, she remained hemodynamically stable, with complete resolution of chest pain. Serial troponin measurements showed progressive decline (4481 → 3902 → 1185 → 305 ng/L). Creatine kinase-MB levels remained within normal limits, and renal function was preserved.

Between January 29 and February 1, the patient remained clinically stable, without recurrence of chest pain. Carvedilol 3.125 mg twice daily and spironolactone 25 mg daily were added to the therapeutic regimen, and furosemide was transitioned to oral administration at a dose of 40 mg daily. On February 2, she was asymptomatic, with

normalized laboratory parameters, and was discharged with prescriptions for furosemide 40 mg daily, carvedilol 3.125 mg twice daily, enalapril 5 mg twice daily, and spironolactone 25 mg daily, along with outpatient cardiology follow-up.

At neurological follow-up on February 19, 2025, the patient reported mild exertional chest discomfort relieved by rest. Neurological examination was unchanged, and her Expanded Disability Status Scale score was 1.5. Further evaluation was planned following cardiology reassessment to determine the continuation of rituximab therapy.

At cardiology follow-up, optimized medical therapy for heart failure was maintained, with favorable clinical evolution. After one month, the patient was asymptomatic from a cardiovascular standpoint. On March 20, 2025, at subsequent neurological follow-up, neurological examination and disability status remained unchanged. In light of the cardiovascular event temporally associated with rituximab infusion, a multidisciplinary decision involving neurology and cardiology was made to discontinue rituximab and initiate treatment with cladribine, contingent upon updated laboratory testing and magnetic resonance imaging of the brain and spinal cord prior to therapy initiation.

5 DISCUSSION

The temporal association between rituximab infusion and the onset of acute myocardial dysfunction observed in this case strongly suggests a drug-related adverse cardiovascular event, particularly in the absence of prior cardiac symptoms or known structural heart disease[20]. The rapid development of chest pain shortly after infusion initiation, accompanied by marked elevation of cardiac biomarkers and echocardiographic evidence of left ventricular systolic dysfunction, supports the plausibility of a causal relationship[20]. Furthermore, the favorable clinical evolution following prompt discontinuation of rituximab and initiation of guideline-directed heart failure therapy reinforces the likelihood of a rituximab-associated cardiotoxic event[20].

From a pharmacovigilance perspective, several classical criteria used to assess adverse drug reactions are fulfilled in this case, including temporal proximity, biological plausibility, reversibility after drug withdrawal, and lack of a more probable alternative diagnosis[21]. Although formal causality assessment tools, such as the Naranjo algorithm, were not systematically applied, the chronological sequence of events and objective diagnostic findings are consistent with a probable adverse drug reaction[21]. Importantly, the patient's young age and absence of previously documented cardiovascular disease broaden the clinical spectrum of patients potentially at risk for rituximab-associated cardiotoxicity[21].

The differential diagnosis of acute chest pain with elevated troponin levels includes acute coronary syndrome without ST-segment elevation, viral myocarditis, stress-induced cardiomyopathy, and immune-mediated myocarditis[22]. In this case, the absence of ischemic electrocardiographic changes, normal chest radiography, preserved hemodynamic stability, and rapid clinical improvement make a classic atherothrombotic coronary event less likely[22]. Additionally, the lack of prodromal infectious symptoms or systemic inflammatory signs argues against viral myocarditis as the primary etiology[22].

Stress-induced cardiomyopathy, also known as Takotsubo syndrome, represents a relevant diagnostic consideration, particularly in the setting of acute physiological stress, including infusion-related reactions[23]. However, the presence of diffuse rather than regional wall motion abnormalities, along with the magnitude of troponin elevation observed, is less characteristic of Takotsubo cardiomyopathy[23]. While cardiac magnetic resonance imaging could have provided additional tissue characterization to further refine the diagnosis, its absence does not negate the strong clinical association between rituximab exposure and myocardial dysfunction in this case[23].

The pathophysiological mechanisms underlying rituximab-associated cardiotoxicity remain incompletely understood and are likely multifactorial[24]. One proposed mechanism involves acute cytokine release during infusion, leading to systemic inflammatory responses that may transiently impair myocardial contractility[24]. Elevated levels of proinflammatory cytokines such as tumor necrosis factor alpha and interleukin-6 have been implicated in myocardial depression and endothelial dysfunction, potentially contributing to the observed cardiac manifestations[24].

Another hypothesis relates to the role of B lymphocytes in cardiovascular immune homeostasis[25]. Experimental and clinical studies have suggested that abrupt B-cell depletion may disrupt immunoregulatory pathways, facilitating inflammatory myocardial processes or autoimmune cross-reactivity[25]. Although cardiomyocytes do not significantly express the CD20 antigen, indirect immune-mediated mechanisms, including complement activation and autoantibody production, may play a contributory role in myocardial injury[25].

Current evidence regarding rituximab-associated cardiotoxicity is largely derived from case reports and pharmacovigilance databases, which inherently limits accurate estimation of incidence and identification of definitive risk factors[26]. Nevertheless, reported events include acute heart failure, arrhythmias, myocarditis, and dilated cardiomyopathy, occurring both in patients with pre-existing cardiovascular disease and in those without known cardiac pathology[26]. Retrospective analyses have suggested that asymptomatic left ventricular

dysfunction may be underrecognized in routine clinical practice, further underscoring the need for heightened clinical vigilance[26].

Traditional risk factors for cardiotoxicity, such as advanced age, prior exposure to cardiotoxic agents, and baseline cardiovascular comorbidities, have been proposed but do not fully explain the occurrence of events in younger, otherwise healthy individuals[27]. The present case adds to the growing body of evidence indicating that rituximab-associated cardiac events may also occur in patients without classical risk factors, particularly when used in non-oncological settings such as autoimmune neurological diseases[27].

At present, no specific guidelines recommend routine cardiovascular monitoring for patients receiving rituximab outside the oncological context[28]. Existing cardio-oncology protocols primarily address agents with well-established cardiotoxic profiles and may not adequately account for immunobiological therapies used in autoimmune diseases[28]. Given the expanding use of rituximab and other anti-CD20 agents in neurology, rheumatology, and dermatology, this gap highlights the importance of individualized risk assessment and careful monitoring during and after infusions[28].

From a practical standpoint, this case emphasizes the importance of administering rituximab in adequately equipped healthcare settings, with access to continuous monitoring and rapid intervention capabilities[29]. Early recognition of symptoms, immediate interruption of the infusion, and prompt initiation of appropriate cardiovascular management were crucial to the favorable outcome observed in this patient[29]. Moreover, multidisciplinary collaboration between neurology and cardiology played a pivotal role in therapeutic decision-making and subsequent modification of disease-modifying therapy[29].

Several limitations of this report should be acknowledged[30]. The absence of advanced cardiac imaging, such as cardiac magnetic resonance, limits definitive etiological characterization of myocardial injury[30]. Additionally, as an observational case report, causality cannot be conclusively established[30]. Nonetheless, the consistency of clinical, laboratory, and imaging findings strongly supports a rituximab-associated adverse cardiac event.

Despite these limitations, this case contributes meaningful clinical insight by documenting acute myocardial dysfunction associated with rituximab in a young patient without known cardiovascular disease, within the context of Schilder-type multiple sclerosis[31]. By expanding awareness of this rare but potentially serious complication, the present report underscores the importance of pharmacovigilance, individualized therapeutic strategies, and future prospective studies aimed at elucidating mechanisms, identifying predictive factors, and developing evidence-based monitoring recommendations for patients treated with anti-CD20 therapies[31].

6 CONCLUSION

This case report describes an episode of acute myocardial dysfunction temporally associated with rituximab infusion in a young patient with Schilder-type multiple sclerosis and no prior history of cardiovascular disease. The clinical presentation, characterized by sudden chest pain, marked elevation of cardiac biomarkers, and transient left ventricular systolic dysfunction, followed by clinical improvement after drug discontinuation and standard heart failure therapy, strongly suggests a rituximab-related adverse cardiac event.

The increasing use of rituximab and other anti-CD20 therapies in autoimmune diseases, particularly in off-label neurological indications, highlights the clinical relevance of recognizing rare but potentially serious cardiovascular complications. This report reinforces that cardiotoxicity may occur even in patients without traditional cardiovascular risk factors, expanding the spectrum of individuals who may be susceptible to such adverse events.

Prompt interruption of the infusion, early cardiovascular evaluation, and multidisciplinary management involving neurology and cardiology were crucial to the favorable outcome observed. These measures underscore the importance of administering immunobiological therapies in appropriately equipped settings and ensuring that healthcare teams are trained to rapidly identify and manage acute infusion-related complications.

Although the observational nature of a single case limits definitive causal inference, the temporal relationship, objective diagnostic findings, and clinical course provide meaningful evidence supporting an association between rituximab and acute myocardial dysfunction. This case adds to the growing body of literature emphasizing the need for heightened clinical vigilance, systematic reporting of adverse events, and individualized risk–benefit assessment when selecting disease-modifying therapies.

In conclusion, this report underscores the importance of integrating cardiovascular safety considerations into the management of patients receiving anti-CD20 therapies for autoimmune neurological diseases. Further prospective studies and pharmacovigilance efforts are warranted to better define the mechanisms, incidence, and risk factors of rituximab-associated cardiotoxicity and to inform future monitoring strategies aimed at optimizing patient safety.

REFERENCES

1. Alping, P., Frisell, T., Novakova, L., et al. (2023). Disease-modifying therapies in multiple sclerosis. Nature Reviews Neurology, 19(10), 635–651.

2. Langer-Gould, A., Bebo, B., & Cree, B. A. C. (2024). Rituximab for multiple sclerosis: Hiding in plain sight. Neurology, 102(19), Article e1835–e1837.

3. Salzer, J., Svenningsson, R., Alping, P., et al. (2016). Rituximab in multiple sclerosis: A retrospective observational study on safety and efficacy. Neurology, 87(20), 2074–2081.

4. Granqvist, M., Boremalm, M., Poorghobad, A., et al. (2018). Comparative effectiveness of rituximab and other initial treatment choices for multiple sclerosis. JAMA Neurology, 75(3), 320–327.

5. Roos, I., Hughes, R., Zhao, Y., et al. (2023). Rituximab versus ocrelizumab in relapsing–remitting multiple sclerosis. JAMA Neurology, 80(7), 676–685.

6. Elgenidy, A., Abdelazeem, B., AlHefnawy, M., et al. (2024). Hypogammaglobulinemia and infections in patients with multiple sclerosis treated with anti-CD20 therapies: A systematic review and meta-analysis. Multiple Sclerosis and Related Disorders, 84, Article 105444.

7. Kimby, E. (2014). Tolerability and safety of rituximab. Blood, 123(13), 1948–1956.

8. Kridin, K., Mruwat, N., Weinstein, O., et al. (2023). Association of rituximab with risk of long-term cardiovascular and metabolic outcomes in patients with pemphigus. JAMA Dermatology, 159(1), 63–71.

9. Al-Yafeai, Z., Al-Badr, W., Alharthi, M., et al. (2022). Novel multiple sclerosis agents–associated cardiotoxicity: A pharmacovigilance study. International Journal of Cardiology, 364, 71–77.

10. Lyon, A. R., López-Fernández, T., Couch, L. S., et al. (2022). 2022 ESC Guidelines on cardio-oncology. European Heart Journal, 43(41), 4229–4361.

11. Tschöpe, C., Van Linthout, S., Spillmann, F., et al. (2021). Myocarditis and inflammatory cardiomyopathy: Current evidence and future directions. Nature Reviews Cardiology, 18(3), 169–193.

12. Bermea, K., Masson, R., Handzlik, M. K., et al. (2022). The role of B cells in cardiomyopathy and heart failure. Current Heart Failure Reports, 19(4), 173–186.

13. Hajjar, L. A., Costa, I. B. S., da Silva, E. A. B., et al. (2020). Brazilian cardio-oncology guideline – 2020. Arquivos Brasileiros de Cardiologia, 115(5), 1006–1043.

14. Farooq, M., Siddiqui, A., Khan, S., et al. (2021). Rituximab-associated cardiotoxicity: A pharmacovigilance study. Journal of Oncology Pharmacy Practice, 27(5), 1095–1101.

15. Keswani, A. N., Mohammad, A., Sykes, J. A., & Gaba, R. C. (2015). Rituximab-induced acute ST-elevation myocardial infarction. Case Reports in Oncological Medicine, 2015, Article 601098.

16. Ng, K. H., Dearden, C., & Gruber, P. C. (2015). Rituximab-induced Takotsubo syndrome: More cardiotoxic than it appears? BMJ Case Reports, 2015, Article bcr2014209070.

17. Girkar, N., Zaki, S., & Kabadi, S. (2022). Reversible cardiomyopathy after rituximab treatment in a chronic lymphocytic leukemia patient. Journal of Pharmacy Practice, 35(5), 855–859.

18. Sharif, K., Watad, A., Bragazzi, N. L., et al. (2017). Anterior ST-elevation myocardial infarction induced by rituximab infusion: A case report and review of the literature. Journal of Clinical Pharmacy and Therapeutics, 42(3), 356–362.

19. Ndukwu, P. O., Patel, A., Raza, S., et al. (2025). Rituximab-induced acute coronary syndrome. Cureus, 17(2), Article e78777.

20. Tschöpe, C., Van Linthout, S., Klein, O., et al. (2019). Targeting CD20+ B lymphocytes in inflammatory dilated cardiomyopathy with rituximab improves clinical course. European Heart Journal Case Reports, 3(3), Article ytz131.

21. Zhang, X., Zhang, Z., Zhuang, L., et al. (2022). Targeting B cells in cardiomyopathy and heart failure: Immunological mechanisms and therapeutic opportunities. Frontiers in Cardiovascular Medicine, 9, Article 869798.

22. Wattjes, M. P., Oreja-Guevara, C., Wuerfel, J., et al. (2024). Comparative safety profiles of ocrelizumab and rituximab in persons with multiple sclerosis. Annals of Neurology, 96(6), 919–929.

23. Fossum, I., Holmøy, T., Wergeland, S., et al. (2025). Early extended interval dosing of rituximab in multiple sclerosis: A prospective cohort study. Multiple Sclerosis and Related Disorders, 87, Article 105675.

24. Musigk, N., Sianis, M., & Tschöpe, C. (2024). The inflammatory spectrum of cardiomyopathies. Frontiers in Cardiovascular Medicine, 11, Article 1251780.

25. Barbuti, E., De Luca, G., Signori, A., et al. (2025). A real-world multicenter study of ocrelizumab outcomes in multiple sclerosis. Multiple Sclerosis and Related Disorders, 90, Article 105859.

26. Min, A., & Win, K. L. Y. (2022). Takotsubo cardiomyopathy or hidden cardiotoxic event by rituximab. Clinical Medicine (London), 22(Suppl. 4), 18–19.

27. Gupta, R. (2022). Takotsubo cardiomyopathy secondary to rituximab. American Journal of Therapeutics, 29(4), e469–e471.

28. Sheikh, M., Nugent, K., & Zaghla, H. (2015). Rituximab-induced left bundle branch block. Heart Views, 16(1), 25–27.

29. Cheungpasitporn, W., Kopecky, S. L., Specks, U., et al. (2017). Nonischemic cardiomyopathy after rituximab treatment for membranous nephropathy. Journal of Renal Injury Prevention, 6(1), 18–25.

30. Brili, S., Bei, E., Kounis, N. G., et al. (2021). Hypertensive crisis and pulmonary edema following rituximab-induced anaphylaxis. Acta Bio-Medica, 92(S1), Article e2021115.

31. Salem, J. E., Manouchehri, A., Moey, M., et al. (2020). Cardiovascular toxicities associated with immune checkpoint inhibitors: An observational pharmacovigilance study. Lancet Oncology, 21(7), e358–e369.