

Cardiorespiratory arrest during the first rituximab infusion in a patient with refractory chronic inflammatory demyelinating polyradiculoneuropathy: a case report

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Case Report

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Abstract

Background

Rituximab is used off-label as rescue therapy in selected patients with refractory chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), but severe immediate infusion-related reactions can occur.

Case presentation:

A 69-year-old man with progressive, refractory CIDP received rituximab after an insufficient response to intravenous immunoglobulin and intolerance to plasma exchange. After approximately 40 mL of the first infusion, he developed abrupt respiratory compromise, hemodynamic collapse, and asystolic cardiac arrest. Return of spontaneous circulation was achieved after 10 minutes of advanced cardiopulmonary resuscitation. He required mechanical ventilation and transient vasopressor support, subsequently recovered without recurrent cardiovascular instability, and rituximab was discontinued. The precise mechanism of the reaction could not be established because serum tryptase, interleukin-6, and formal allergy testing were not obtained.

Conclusion

Severe and potentially fatal reactions may occur within the first milliliters of an initial rituximab infusion. Continuous monitoring and immediate access to advanced resuscitation are essential, particularly in medically complex patients.

Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is an acquired immune-mediated neuropathy characterized by progressive or recurrent weakness, sensory impairment, and reduced or absent tendon reflexes. First-line treatments include intravenous immunoglobulin, corticosteroids, and plasma exchange. However, a subgroup of patients (approximately 20%–30%) has an insufficient response, loses response, or develops treatment-limiting adverse events.[1, 2]

Rituximab is a chimeric anti-CD20 monoclonal antibody that depletes B lymphocytes. Its use in CIDP is off-label, and available evidence remains heterogeneous. Prospective observational data suggest benefit in selected refractory patients, whereas a recent randomized trial did not demonstrate superiority over placebo in preventing deterioration after immunoglobulin withdrawal.[3, 4]

Immediate reactions to rituximab include infusion-related reactions, cytokine-release reactions, type I hypersensitivity, and mixed phenotypes.[7] They may cause bronchospasm, hypoxemia, hypotension, arrhythmia, and, rarely, cardiac arrest. We report a cardiorespiratory arrest during the first rituximab

infusion in a patient with refractory CIDP. This case report was prepared in accordance with the CARE guidelines.

Case presentation

A 69-year-old man had a one-year history of sensorimotor axonal and demyelinating CIDP, arterial hypertension, hypothyroidism, and dyslipidemia. He also had a history of prolonged occupational exposure to glyphosate. He had previously received intravenous immunoglobulin and two plasma-exchange sessions. During a plasma-exchange session in 2025, he had experienced a cardiorespiratory arrest attributed in the medical record to possible hypoglycemia or hypocalcemia, with no neurologic sequelae.

He was admitted after five months of progressive neurologic deterioration, with increasing gait limitation, predominantly distal weakness, reduced handgrip, hyporeflexia, dysarthria, dysphonia, and urinary retention. During this hospitalization, he received treatment for *Klebsiella* bacteremia and *Clostridioides difficile* infection without severity criteria; both were clinically improving when rescue immunotherapy was considered.

Neurology prescribed intravenous immunoglobulin at 30 g every 24 hours for five days. The response was insufficient, and plasma exchange was considered unsuitable because of the previous arrest. Given continued functional decline, rituximab was selected as a third-line, off-label treatment after assessing risks and benefits.

During the first rituximab administration, after approximately 40 mL of the preparation had been infused and while tolerance was being monitored for rate titration, the patient developed abrupt clinical deterioration. An initial dose of epinephrine did not produce an adequate response; profound oxygen desaturation and cardiorespiratory arrest followed at 09:40, with asystole as the initial rhythm. He was intubated with a 7.5-mm endotracheal tube and received advanced cardiopulmonary resuscitation for 10 minutes, including three doses of epinephrine, before return of spontaneous circulation.

The subsequent course was favorable, allowing withdrawal of life support. A 24-hour Holter recording showed sinus rhythm, complete right bundle branch block, rare supraventricular and ventricular ectopy, and no pauses, atrial fibrillation, or ventricular tachycardia. No recurrent cardiovascular instability occurred. Rituximab and plasma exchange were avoided, and outpatient neurologic follow-up was arranged.

Discussion

Refractory CIDP is therapeutically challenging when intravenous immunoglobulin, corticosteroids, or plasma exchange are ineffective or not tolerated. Rituximab has been used as rescue therapy, particularly in antibody-associated or otherwise selected phenotypes, but its efficacy is not uniform and the risk–benefit assessment must be individualized.[2–4]

The patient's occupational history of prolonged glyphosate exposure raises the question of a possible environmental contribution to his neuropathy. However, the epidemiological evidence linking glyphosate to peripheral nervous system disease remains inconclusive. A systematic review of 25 epidemiological studies found no association between glyphosate exposure and any neurological outcome in humans, including peripheral nerve conduction velocity[5]. In contrast, isolated case reports have linked glyphosate-based herbicide exposure to peripheral neuropathy, but these describe acute, high-level dermal or ingestional exposure with confirmed vasculitic changes on nerve biopsy, a pattern distinct from the chronic, low-level occupational exposure described in our patient.[6] Given this discrepancy in exposure pattern and the absence of supportive biopsy or serologic findings implicating a toxic or vasculitic mechanism in our case, we regard glyphosate exposure as a noteworthy but unproven contextual factor rather than an established etiologic contributor to this patient's CIDP.

In this patient, collapse occurred during the first exposure and after a small infused volume, establishing a strong temporal association. Immediate rituximab reactions represent overlapping clinical endotypes: common infusion-related reactions may be rate dependent; cytokine-release reactions are often characterized by fever, chills, and systemic symptoms; type I reactions may present with bronchospasm, hypotension, urticaria, or anaphylaxis; and mixed reactions combine these features.[7]

The absence of documented rash or angioedema, the rapid progression from desaturation and shock to asystole, and the incomplete initial response to epinephrine do not exclude anaphylaxis but also do not distinguish it from severe cytokine release or another infusion-related mechanism. Serum tryptase, interleukin-[6], and formal allergy testing were not obtained; therefore, the precise mechanism remains indeterminate.

Regulatory information warns that rituximab may cause severe or fatal infusion reactions and that approximately 80% of reported fatal reactions occurred with the first infusion.[8] Cytokine-release syndrome with cardiovascular collapse has also been described after rituximab, supporting immediate discontinuation and intensive support when severe symptoms appear.[9] Sudden death after an initial infusion has been reported in other clinical settings.[10]

The cardiorespiratory arrest during plasma exchange one year earlier is also relevant. That episode was attributed to possible metabolic disturbances and does not establish a shared mechanism, but it may indicate reduced physiologic reserve or susceptibility to abrupt hemodynamic stress. Recent infection was another potential confounder; however, clinical improvement before infusion and the immediate temporal relationship make rituximab the most plausible trigger of the index event.

When rituximab is not tolerated or is contraindicated, as in this patient after his index event, alternative anti-CD20 strategies may be considered. Ofatumumab, a fully human anti-CD20 monoclonal antibody, has lower immunogenicity than the chimeric rituximab and has been reported to induce sustained remission in cases of relapsed or refractory CIDP unresponsive to conventional immunotherapy.[11, 12] Its subcutaneous administration and distinct CD20-binding epitope may offer an alternative treatment

strategy; however, safety after a severe rituximab infusion reaction is unknown, and evidence in CIDP remains limited to case reports.

A strength of this report is the detailed documentation of event timing, initial rhythm, resuscitation duration, post-arrest blood gases, cardiac monitoring, and outcome. Limitations include the absence of confirmatory biomarkers or allergy testing, incomplete characterization of the prior arrest, and the inherent inability of a single case to establish causality. Future infusions in similarly complex patients should be planned in settings with continuous monitoring, trained personnel, and immediate access to advanced resuscitation.

Conclusions

Rituximab may cause an immediate, severe, and potentially fatal infusion reaction within the first milliliters of an initial administration. In this patient with refractory CIDP, the close temporal association, asystolic arrest, and absence of a subsequent arrhythmic explanation support rituximab as the most plausible trigger, although the specific reaction phenotype could not be confirmed. Careful selection, continuous monitoring, slow initial infusion, and immediate resuscitation capability are essential.

Declarations

Ethics approval and consent to participate

The authors declare that no experiments involving humans or animals were conducted for this report.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

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Availability of data and materials

The data supporting the conclusions of this case report are included within the article. No additional dataset was generated.

Authors' contributions

Maria Fernanda Velasco Hoyos: Conceptualization; Investigation; Writing – original draft; Writing – review and editing. Carolina Gómez Idrobo: Investigation; Writing – review and editing. Laura Carvajal: Investigation; Writing – review and editing. All authors read and approved the final manuscript.

Patient perspective

Not available.

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