



Monoclonal antibody therapy for refractory chronic migraine-like headache related Lyme disease: a case report

Marlon Cantillo-Martínez^{1,2}, Cristian Correa-Arrieta^{1,2}, Fidel Sobrino-Mejía^{1,3}

¹Neurology Department, Universidad de La Sabana, Bogotá, Colombia

²Neuromuscular Disease Centre, Instituto Roosevelt, Bogotá, Colombia

³Headache Excelente Center, Unidad de Servicios de Salud Occidente de Kennedy, Bogotá, Colombia



Marlon Cantillo-Martínez.
marlonxcantillom@gmail.com

Edited by:

Raimundo Pereira Silva-Néto

Keywords:

Lyme disease
Chronic migraine-like
Colombia
Galcanezumab

Abstract

Introduction

Lyme disease, caused by *Borrelia burgdorferi*, can lead to diverse neurological manifestations, including headache. While most Lyme-associated headaches resolve with antibiotics, some may evolve into a refractory chronic migraine-like syndrome. We present a case of post-Lyme chronic migraine-like headache responsive to galcanezumab, a calcitonin gene-related peptide (CGRP) monoclonal antibody.

Case Report

A 42-year-old woman developed chronic migraine-like headaches following treatment for Lyme neuroborreliosis. The headaches were refractory to standard preventive therapies and only partially responsive to onabotulinumtoxinA. Administration of galcanezumab resulted in significant reduction of headache frequency, intensity, and impact on daily activities.

Comment

This case highlights the potential of CGRP-targeted therapies for persistent migraine-like headaches following Lyme neuroborreliosis. The favorable response to galcanezumab suggests a role for CGRP in the pathophysiology of post-Lyme headache. While further research is needed to establish efficacy and safety, clinicians should consider CGRP monoclonal antibodies for chronic migraine-like headaches refractory to standard treatments in the post-infectious phase of Lyme disease. The emergence of chronic migraine-like headaches following Lyme neuroborreliosis and the response to a CGRP monoclonal antibody in this case underscore the importance of considering targeted migraine therapies in the management of persistent headaches after antibiotic treatment. This report contributes to the understanding of Lyme disease sequelae and potential treatment options, warranting further investigation into the utility of CGRP-targeted therapies in this context.

Submitted: April 21, 2024
Accepted: June 23, 2024
Published online: June 30, 2024



Introduction

Lyme disease, a tick-borne infection caused by *Borrelia burgdorferi*, is transmitted by Ixodes ticks and is more prevalent in temperate northern hemisphere climates (1). Climate change, increased tick reproduction, and human migration are expected to contribute to a significant rise in cases worldwide (2). Lyme disease can affect the central nervous system (neuroborreliosis) in approximately 50% of cases, presenting with various symptoms, including headache (3). Diagnosis involves a two-step serological approach, with an ELISA followed by a confirmatory Western blot (4). Treatment with doxycycline should be initiated in all patients with suspected Lyme disease (4). While most headaches resolve with antibiotic treatment (5), this case report presents a patient with Lyme borreliosis who developed a refractory chronic migraine-like headache that responded favorably to galcanezumab, a monoclonal antibody targeting calcitonin gene-related peptide (CGRP).

Case Report

A 42-year-old woman from Bogotá, Colombia, presented in May 2022 with a progressive, intermittent, facially distributed exanthema, accompanied by migraine-like headaches occurring 20 times per month, joint pain, cutaneous allodynia, and paresthesias in the trigeminal nerve branches and scalp. She had traveled to Willowsford, Virginia, in October 2021. Physical examination revealed erythematous, round, well-demarcated, non-tender papules on the face, arms, and thighs (Figure 1). Brain MRI demonstrated hyperintensities on T2 and FLAIR images, with diffusion restriction and contrast enhancement in the bilateral frontal and left parietal white matter. Serological testing for *B. burgdorferi* was positive for IgM and IgG antibodies. Treatment with doxycycline and ceftriaxone resolved most symptoms, but the patient continued to experience chronic migraine-like headaches. Despite treatment with valproic acid, topiramate, propranolol, flunarizine, and onabotulinum toxin type A, the headaches persisted. Galcanezumab treatment significantly reduced headache frequency and intensity and improved daily activities and headache impact (Figure 2).



Figure 1. Clinical presentation of skin lesions in a patient with Lyme disease. Physical examination revealed multiple erythematous, round to oval-shaped, well-demarcated papules on the skin of the thighs. The lesions were non-tender upon palpation. This cutaneous eruption, while not classic for erythema migrans, can be seen in some cases of disseminated Lyme disease.

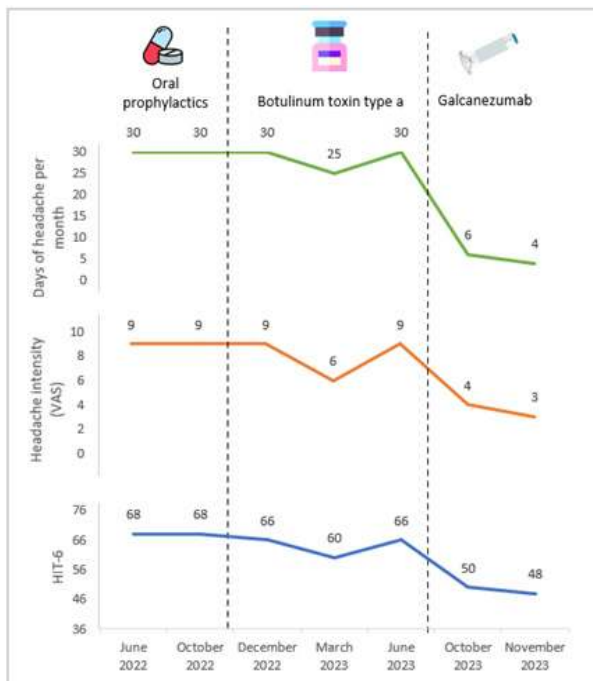


Figure 2. Changes in headache days per month, headache intensity and patient's HIT-6. HIT-6: Headache Impact Test-6; VAS: visual analogue scale.

Discussion

Lyme disease, primarily transmitted during summer and autumn (2), can manifest with diverse symptoms, including headache, which is common in neuroborreliosis (6,7). Headache can occur during active disease and as a residual symptom following antibiotic treatment (8). The clinical features of headache in Lyme disease are varied, often resembling tension-type headache but not fully meeting IHS criteria, and may be associated with systemic symptoms and neurological manifestations (9). A proposed pathophysiological mechanism is a local inflammatory process disrupting arachnoid villi, leading to an imbalance between CSF absorption and production (10). Although headache associated with Lyme disease often resolves with antibiotic treatment (5), it may evolve into a post-infectious chronic migraine-like syndrome refractory to standard preventive medications. In our case, Lyme disease was confirmed by serological testing, and while ceftriaxone resolved systemic manifestations, the patient developed chronic migraine-like features refractory to oral prophylaxis and only partially responsive to botulinum toxin therapy. These headaches resolved with CGRP monoclonal antibodies. This case underscores the potential benefit of specific migraine-directed treatments, including CGRP monoclonal antibodies, for patients with persistent post-Lyme migraine-like syndrome following appropriate antibiotic therapy.

Acknowledgements

The authors express their gratitude to the patient and her family for their participation in this case report.

References

1. Mead P. Epidemiology of Lyme Disease. *Infect Dis Clin North Am.* 2022 Sep;36(3):495-521. doi: 10.1016/j.idc.2022.03.004.
2. Dumic I, Severnini E. "Ticking Bomb": The Impact of Climate Change on the Incidence of Lyme Disease. *Can J Infect Dis Med Microbiol.* 2018 Oct 24;2018:5719081. doi: 10.1155/2018/5719081.
3. Roos KL. Neurologic Complications of Lyme Disease. *Continuum (Minneapolis Minn).* 2021 Aug 1;27(4):1040-1050. doi: 10.1212/CON.0000000000001015.
4. Ross Russell AL, Dryden MS, Pinto AA, Lovett JK. Lyme disease: diagnosis and management. *Pract Neurol.* 2018 Dec;18(6):455-464. doi: 10.1136/practneurol-2018-001998.
5. Scelsa SN, Lipton RB, Sander H, Herskovitz S. Headache characteristics in hospitalized patients with Lyme disease. *Headache.* 1995 Mar;35(3):125-30. doi: 10.1111/j.1526-4610.1995.hed3503125.x.
6. Nordberg CL, Bodilsen J, Knudtzen FC, Storgaard M, Brandt C, Wiese L, Hansen BR, Andersen AB, Nielsen H, Lebech AM; DASGIB study group. Lyme neuroborreliosis in adults: A nationwide prospective cohort study. *Ticks Tick Borne Dis.* 2020 Jul;11(4):101411. doi: 10.1007/s00431-022-047.
7. van Samkar A, Bruinsma RA, Vermeeren YM, Wieberdink RG, van Bommel T, Reijer PMD, van Kooten B, Zomer TP. Clinical characteristics of Lyme neuroborreliosis in Dutch children and adults. *Eur J Pediatr.* 2023 Mar;182(3):1183-1189. doi: 10.1007/s00431-022-047.
8. Dersch R, Sommer H, Rauer S, Meerpohl JJ. Prevalence and spectrum of residual symptoms in Lyme neuroborreliosis after pharmacological treatment: a systematic review. *J Neurol.* 2016 Jan;263(1):17-24. doi: 10.1007/s00415-015-7923-0.
9. Brinck T, Hansen K, Olesen J. Headache resembling tension-type headache as the single manifestation of Lyme neuroborreliosis. *Cephalalgia.* 1993 Jun;13(3):207-9. doi: 10.1046/j.1468-2982.1993.1303207.x.
10. Moses JM, Riseberg RS, Mansbach JM. Lyme disease presenting with persistent headache. *Pediatrics.* 2003 Dec;112(6 Pt 1):e477-9. doi: 10.1542/peds.112.6.e477.



Marlon Cantillo-Martínez
<https://orcid.org/0000-0002-8805-5051>
Cristian Correa-Arrieta
<https://orcid.org/0000-0003-2985-3026>
Fidel Sobrino-Mejía
<https://orcid.org/0000-0001-8334-6215>

Author's contribution: All authors contributed equally to this work.

Declaration of conflicting interests: The authors declare that there are no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding: None.