CASE REPORT

Borrelia Burgdorferi, a Root Cause of Inflammatory Bowel Disease: A Case Report of Successful Treatment and Remission

Elliot Dinetz, MD; Yusuf Saleeby, MD

ABSTRACT

Background • The Borrelia species is recognized to cause a myriad of non-specific symptoms among Lyme patients. It has also been documented in the literature to have the ability to incite autoimmune responses. Despite this, very few clinical cases have ever put together the autoimmune connection to such infections, including in Crohn's disease.

Case Presentation • A 14-year-old adolescent male with a previous diagnosis of Crohn's disease was discovered to have underlying Lyme disease caused by *Borrelia*

Elliot Dinetz, MD, is a Functional Medicine specialist located at Timeless Health in Miami, FL. **Yusuf Saleeby, MD,** is Functional Medicine specialist located at Carolina Holistic Medicine in Mt Pleasant, SC.

Corresponding author: Elliot Dinetz, MD E-mail: dr@elliotdinetz.com

Crohn's disease is an autoimmune condition causing longterm inflammation in the gastrointestinal (GI) tract typically appearing in young adults, but also now affecting more children.¹ While the etiology of the disease is still being debated, it is well recognized as an autoimmune disorder. The literature also recognizes the overlapping symptom between Crohn's disease and chronic Lyme disease being arthralgia. Crohn's disease strikingly overlaps with Lyme disease, in particular the Borrelia burgdorferi (Bb) sensu lato group, in certain areas of the United States and in Europe.^{2,3} The prevalence of Lyme infection has also been noted in autoimmune disease cohorts who were receiving immune suppressive therapy which resulted in worsened infections, in particular Crohn's disease and Irritable Bowel Disease cases.⁴ This is a concern as the worldwide incidence of Lyme disease has been increasing and is as high as 15% of the population in certain areas around the world according to a recent meta-analysis.⁵ Lyme disease and other coinfections associated with tick borne illness (very *burgdorferi* infection. Identifying this as a potential cause of his autoimmune condition, an integrative medical approach was initiated, resulting in successful treatment and complete remission.

Conclusions • Lyme disease should be recognized as a potential trigger of autoimmune conditions, especially Crohn's disease. This underlying cause is novel to the literature and may help many patients obtain the proper diagnosis so that curative treatment may be received. (*Altern Ther Health Med.* 2023;29(5):86-89).

often Bartonella, Babesia, Ehrlichia, for example) are known as a masquerading condition in how it mimics other disease processes including creating autoimmunity.⁶ Unfortunately, the many symptoms of Lyme disease, especially in children, which overlap with Crohn's disease are often dismissed and no connection is established. This makes Lyme disease of great concern as a potential unmasked cause of a myriad of chronic disease states including Crohn's disease. In our case report, a pediatric patient struggling with uncontrolled Crohn's disease was properly re-diagnosed and treated for Lyme disease using an integrative medicine approach, and as a result, remains in remission to this day. This is the first case study reported in the literature of a pediatric Crohn's disease patient successfully brought into remission after a focused treatment regimen for Lyme disease.

CASE STUDY

A 14-year-old Hispanic male with a Body Mass Index (BMI) of 16 presented with brain fog (diminished executive cognitive function), fatigue and four to eight bouts of daily hematochezia and GI pain for several months prior to arrival at our clinic. He was not questioned on any musculoskeletal joint pains by his primary care physician, nor gastroenterologist, as it was discovered later. The gastroenterology team ordered basic laboratory testing, a colonoscopy and CT enterography, which provided a diagnosis of terminal ileitis likely from Crohn's disease (laboratory results shown below). His

physical exam was unremarkable including no evidence of erythema migrans or other rashes, no facial palsy or other neurological findings. After Crohn's disease began interfering with his activities of daily life (ADL's), he was taken out of school as his gastroenterology team failed to help control symptoms using a trial of Budesonide therapy and Mesalamine suppositories. This was followed by discussions of immune suppressive therapy with the patient's family. The family elected to delay this treatment as much as possible when the risks and complications of immune suppressive therapy were discussed, especially since an adolescent young male may have to take this medication for life. At this point, they sought Integrative Functional Medicine with the aim for an alternative approach with deeper evaluation and treatment possibilities. The systems biology approach with Integrative Functional Medicine helps to elicit the root cause of ailments, and often uses safer alternative therapeutics to treat, not simply pharmaceuticals. Upon the family's visit to our practice, detailed questioning of the patient revealed transient migratory joint pains. There was no travel to any Lyme disease endemic regions in the United States that they were aware of, however, there were many trips to Ecuador. The patient appeared fatigued and initially could not recall specific dates of events when things began to change in his health, which is not typical according to him or his family. His physical exam was unremarkable, and vital signs were in normal range for his age.

Initial Gastroenterologist ordered 9/21:

CRP: 45.6 mg/L (reference range: <8 mg/L)

Sedimentation Rate: 14 mm/hr (reference range >15 mm/hr) Vitamin D 25-OH: 23 ng/L (reference range: 30 ng/L -100ng/L) Stool microbiology, negative for all: *Yersinia, Salmonella/ Shigella, Shiga toxin, Campylobacter, Clostridium difficille* Initial Colonoscopy 5/21: moderately severe colitis in the rectum

CT Enterography 9/21: Terminal Ileitis most likely from Crohn's disease

Repeat Colonoscopy 10/21: Proctitis and possible Ileitis

Additional labs ordered by Integrative Medical team 11/21:

Absolute CD57: 41 uL (reference range: 60-360 uL) This is a marker of Natural Killer (NK) cell lymphocyte subset. Lyme disease has been associated with decreased CD57 levels and innate immune suppression.⁷

Lyme serology using Vibrant America Labs Tickborne 2.0 ImmunoBlot 11/19/21:

IgG + detected: Borrelia burgdorferi p23-25 (OspC), p30,p31 (OspA), p45 Borrelia Afzelii OspA, Borrelia Bavariensis DbpA, Borrelia Bavariensis VlsE1, Borrelia Spielmanii DbpA. Additional Borrelia species: Borrelia Miyamotoi, Borrelia Yangtzensis

These results do not satisfy the criteria set forth by the CDC/ IDSA guidelines for diagnosing Lyme. Coinfections detected: Anaplasma phagocytophilum Msp5 IgG Epstein Barr Virus Epstein Barr Virus EBNA1 IgG Parvovirus B19 Parvovirus B19 VLP VP1/Vp2 Co Capsid IgG Toxoplasma gondii Crude Extract, p24 and p29 IgG Herpes simplex virus 2 IgM Human herpesvirus 6 IgG Streptococcal A IgG

Repeat Lyme serology using Vibrant America Labs 10/27/22:

IgG + levels dropped from High [≥ 20.1] to moderate [10.1 ~ 20.0] in the following: Borrelia burgdorferi p30 IgG Borrelia bavariensis VlsE1 IgG Borrelia miyamotoi EKG: Normal Sinus Rhythm with no ST-T wave changes nor evidence of heart block.

It was decided to treat the patient for Lyme disease based mainly on his clinical presentation, the classic migratory arthralgia and persistent neuropsychiatric symptoms. Understanding the margin for error with the current CDC/ IDSA guidelines, particularly suboptimal sensitivity, plus the patient's history and symptoms suggestive of Lyme disease infection, remain at the forefront of this decision to treat and should be considered by conventional medicine standards.8 We would later determine if treating coinfections would be warranted. He was first started on Low Dose Naltrexone (LDN) 1.5 mg and titrated to 4.5 mg with 1.5 mg incremental increases weekly as LDN has evidence to induce remission in Crohn's disease.⁹ This was to initiate symptom relief while determining the most appropriate antimicrobial therapy in a young male. Unfortunately, there was no improvement after 8 weeks, so the initiation of Samento (Cat's claw / Uncaria tomentosa) and Banderol (bark of the Banderilla /Otoba parvifolia) tree) titrating to 30 drops each twice daily of a standardized preparation was implemented. This is given the known safety profile of each in treating Lyme disease and comparable antimicrobial effect to antibiotics.¹⁰ After 4 weeks, noticeable improvement was reported by the patient and his parents. At 12 weeks of therapy, the patient showed an 80% overall improvement clinically. This was self-reported by having no more migratory arthralgia and complete resolution of bloody bowel movements as well as a resolution of his GI pain. He still was reporting significant brain fog, however, and couldn't focus or re-enter school consequently. It was next decided to start Cryptolepis sanguinolenta and discontinue the Banderol to cycle therapy and prevent resistance by another safe anti-Borrelia herbal medicine shown to have comparable effects to antibiotics.¹¹ Despite initiating this herb, the patient remained at this plateau for 4-weeks with no improvement. After reviewing his low CD57 laboratory value and suspected NK cell deficiency, it was then postulated that perhaps the patient needed more than anti-microbial therapy and would benefit from improving his immune function by modulating the inflammatory response. It was then decided

to add an immune modulating peptide Thymosin alpha 1 (Ta1) 2 mg/ml, which was intended to help boost his NK cells to sufficient levels and modulate the inflammatory response.¹² Ta1 was initiated at 0.4 mg subcutaneous (SQ) injections daily for 2 weeks, then increased to 0.8 mg units daily for 4 weeks. At the end of this course 4-weeks later, the patient was completely symptom free. His clinical remission persists to this day 1 year later. The patient and his family did not wish to have any further imaging nor repeat colonoscopy given how difficult his past experience was for him. Repeat serology 2 months after remission did confirm improvement in 3 different Borrelia species IgG antibody titers.

DISCUSSION

Crohn's disease remains a mystery to physicians regarding how it develops, and bacterial organisms are among the causes in that debate.¹³ While advancements have been made in treatment, major adverse events such as cancer from chronic immune suppressive medicines, like TNF alpha inhibitors, cannot be overlooked.14 More evidence is emerging in the literature that suggest Lyme disease may play a role as a causative agent. A recent case report of an adult with Crohn's disease had a significant reduction of symptoms once Lyme disease was diagnosed and treated where the authors concluded the importance of exploring other etiologies like infections in Crohn's disease patients.¹⁵ Since Lyme disease has been implicated in other autoimmune conditions, a recent publication suggested that the differential diagnosis should include Lyme disease in order to initiate proper treatment.¹⁶ According to the publication, it would be reasonable to suggest that all autoimmune patients undergo screening for Lyme disease, especially in those with overlapping symptoms.¹⁷ Given the difficulty in reliance on confirmatory laboratory testing and the myriad of triggers we know that can cause autoimmunity, clinical acumen remains at the forefront of a clinician's armament. Immune suppressive therapy may therefore actually worsen (or be contraindicated) in cases of Crohn's disease due to such infectious etiology.

With regards to treatment, the decision to use these modalities is based first on safety in a pediatric patient. Common harmful side effects of Tetracyclines, for example, are now known to go beyond tooth staining and cause disruption of the microbiome which is associated with numerous chronic diseases and immune dysregulation.¹⁸ LDN was started in order to help modulate the inflammatory response seen in Crohn's disease via reduced intestinal proinflammatory cytokine profile.^{19,20} When this was noted to be of no aid, it indicated that antimicrobial therapy would be best to start next to target the infection in hopes of some resolve. Samento, Banderol and Cryptolepis were chosen since they have a well-documented safety profile and have shown effectiveness in treating Borrelia clinically as noted. Banderol, an extract from the bark of the Banderilla (Otoba parvifolia) tree from Peru, is a known anti-inflammatory and anti-Borrelia agent.²¹ Samento (a proprietary TOA-free chemotype of Cat's claw) is known to be well tolerated and safe

while also effective against Borrelia species, and was therefore used without adverse events noted in our patient.⁸ Cat's claw, otherwise referred to as Una de Gato or *Uncaria tomentosa*, is a woody vine growing wild in the Amazon rainforest and other areas of Central and South America. It is used medicinally in traditional indigenous medicine for hundreds of years with reported benefit for autoimmune conditions. *Cryptolepis sanguinolenta*, also known as Ghanaian quinine or yellow-dye root, is a botanical used to treat a myriad of illnesses in similar context with known safety.²² In our review of the literature, there was no shown efficacy of our treatment strategies against any other confections the patient had, further reinforcing his successful treatment thus far was not due to other organism eradication.

Treatment significantly improved his Lyme disease symptoms where the patient was no longer having GI bleeding and symptoms, but he did however reach a plateau with persistent brain fog to no avail. Since the patient still couldn't attend school due to persistent brain fog, it appeared necessary to consider additional options in the patient's treatment. We decided it would be most appropriate to use the peptide known as Ta1 in order to help fight off infections given that his immune system, specifically CD57, a marker of Natural Killer (NK) function, was low.²³ This therapy, originating in the 1960's, has been found to work on the thymus gland to improve NK cells and modulate inflammation including use and documented benefit in conditions like Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) as well as similar neurological symptoms.²³ Issues with Thymus involution are associated with numerous chronic diseases and infections as we age. The thymus gland deteriorates over time, whereby at age fifty, approximately 80% of the thymus gland is involuted and dysfunctional.²⁴ This further is associated with longevity given the critical role of immune function as we age.25 There are two ways we theorize in which this peptide helped our patient. First, based on this patient's low CD57 count, the peptide helped by restoring his depleted NK cells so his innate immune system could function more optimally. This could have compensated for what the antimicrobial herbal tinctures could not. Second, this peptide helped by modulating inflammation by way of restoring T regulatory cell function.²⁶ This could explain how his brain fog was able to be resolved. After only 4-weeks, the patient no longer needed the Ta1 and was declared in clinical remission with close observation for an additional 2 months. Such a therapeutic approach warrants further evaluation, however, this shouldn't stop it from being used immediately to stimulate proper immune functionality. This is the benefit of an integrative medical approach; the ability to have a larger armament towards fighting disease while also focusing on the immune system concomitantly. Upon repeat serology testing for Lyme disease 2 months after remission began, it revealed reduced levels of Borrelia burgdorferi p30 IgG antibodies which are against the outer surface protein p30 present in all 3 subspecies of B. burgdorferi sensu lato. Along with this, the other antibodies of Borrelia bavariensis VlsE1 IgG, and

Borrelia miyamotoi also decreased from high to moderate levels. This further supports a successful treatment strategy. Given that Ta1, LDN, Banderol, Samento, and Cryptolepis have not been shown to be harmful at such doses, further studies are warranted to see if they may interact with other pharmaceuticals and long-term remission rates. Per our published literature search, this is the first case of Lyme disease identified as the cause of Crohn's disease in a pediatric patient who was successfully treated and as a result remains in clinical remission several months later.

CONCLUSION

Bacteria have been thought to contribute to Crohn's disease, but only until more recently has Lyme disease (Bb) emerged as a potential causative agent. While it is still early to tell what percentage of patients with Crohn's disease may have underlying Lyme disease, future studies should aim at determining this. This case report is on the heels of growing research suggesting that infections like Borrelia may be an occult cause of Crohn's disease and autoimmune disorders.²⁷ Clinical acumen and suspicion should be at the forefront of diagnosis given Lyme disease's mimicking characteristics and difficulty with standard diagnosis. In doing so, clinicians may offer a new hope for some Crohn's disease sufferers and those struggling with autoimmune conditions globally, especially in the younger populations. Given the improvements noted, the approach of both antimicrobial therapy with immune modulation appears to be of great benefit and perhaps warrants further clinical study, not just with Crohn's disease due to Lyme disease, but with chronic Lyme disease patients themselves. This may spare unnecessary and potentially harmful therapy in patients and may lead to remission in those struggling with Crohn's disease.

REFERENCES

- Rosen MJ, Dhawan A, Saeed SA. Inflammatory Bowel Disease in Children and Adolescents. JAMA Pediatr. 2015;169(11):1053-1060. doi:10.1001/jamapediatrics.2015.1982
- Horowitz R, Freeman PR. Precision Medicine: The Role of the MSIDS Model in Defining, Diagnosing, and Treating Chronic Lyme Disease/Post Treatment Lyme Disease Syndrome and Other Chronic Illness: Part 2. *Healthcare (Basel)*. 2018 Dec; 6(4): 129. Published online 2018 Nov 5. doi:10.3390/healthcare6040129 PMCID: PMC6316761 PMID: 30400667.
- Roberts SE, Thorne K, Thapar N, et al. A Systematic Review and Meta-analysis of Pediatric Inflammatory Bowel Disease Incidence and Prevalence Across Europe, *Journal of Crohn's and Colitis*, Volume 14, Issue 8, 1 August 2020, Pages 1119–1148. doi:10.1093/ecco-jcc/jjaa037. PMID: 32115645.
- Maraspin V, Bogovič P, Rojko T, Ogrinc K, Ružić-Sabljić E, Strle F. Early Lyme Borreliosis in Patients Treated with Tumour Necrosis Factor-Alfa Inhibitors. J Clin Med. 2019;8(11):1857. PMID:31684103 doi:10.3390/jcm8111857
- Dong Y, Zhou G, Cao W, et al. Global seroprevalence and sociodemographic characteristics of Borrelia burgdorferi sensu lato in human populations: a systematic review and meta-analysis. BMJ Glob Health. 2022;7(6):e007744. doi:10.1136/bmjgh-2021-007744
- Singh SK, Girschick HJ. Lyme borreliosis: from infection to autoimmunity. Clin Microbiol Infect. 2004;10(7):598-614. PMID:15214872 doi:10.1111/j.1469-0691.2004.00895.x
- Stricker RB, Burrascano J, Winger E. Longterm decrease in the CD57 lymphocyte subset in a patient with chronic Lyme disease. Ann Agric Environ Med. 2002;9(1):111-113. PMID:12088407
- Moore A, Nelson C, Molins C, Mead P, Schriefer M. Current Guidelines, Common Clinical Pitfalls, and Future Directions for Laboratory Diagnosis of Lyme Disease, United States. *Emerg Infect Dis.* 2016;22(7):1169-1177. doi:10.3201/eid2207.151694
- Smith JP, Stock H, Bingaman S, Mauger D, Rogosnitzky M, Zagon IS. Low-dose naltrexone therapy improves active Crohn's disease. *Am J Gastroenterol.* 2007;102(4):820-828. PMID:17222320 doi:10.1111/j.1572-0241.2007.01045.x
- Feng J, Leone J, Schweig S, Zhang Y. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of *B. burgdorferi*. Front Med (Lausanne). 2020;7:6. PMID:32154254 doi:10.3389/fmed.2020.00006
- Zhang Y, Alvarez-Manzo H, Leone J, Schweig S, Zhang Y. Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani. Front Cell Infect Microbiol. 2021;11:624745. Published 2021 Mar 8. doi:10.3389/fcimb.2021.624745
- Dominari A, Hathaway Iii D, Pandav K, et al. Thymosin alpha 1: A comprehensive review of the literature. World J Virol. 2020;9(5):67-78. PMID:33362999 doi:10.5501/wjv.v9.i5.67

- Zhang L, Liu F, Xue J, Lee SA, Liu L, Riordan SM. Bacterial Species Associated With Human Inflammatory Bowel Disease and Their Pathogenic Mechanisms. *Front Microbiol*, 2022;13:801892. doi:10.3389/fmi.b2022.801892
- Li J, Zhang Z, Wu X, Zhou J, Meng D, Zhu P. Risk of Adverse Events After Anti-TNF Treatment for Inflammatory Rheumatological Disease. A Meta-Analysis. *Front Pharmacol.* 2021;12:746396. doi:10.3389/fphar.2021.746396
- Qamar K, Tiwari, A, Arora, A. Lyme Arthritis Mimicking Inflammatory Bowel Disease-Associated Arthritis in Patient With Crohn's Disease. *The American Journal of Gastroenterology*: October 2020 - Volume 115 - Issue - p S1186 doi:10.14309/01.ajg.0000710996.87550.4f.
- Arvikar SL, Steere AC. Diagnosis and treatment of Lyme arthritis. Infect Dis Clin North Am. 2015;29(2):269–280. PMID:25999223 doi:10.1016/j.idc.2015.02.004
- Vojdani A, Pollard KM, Campbell AW. Environmental triggers and autoimmunity. Autoimmune Dis. 2014;2014:798029. doi:10.1155/2014/798029
- Ahn Y. Young Jung J, Kweon O. Impact of Chronic Tetracycline Exposure on Human Intestinal Microbiota in a Continuous Flow Bioreactor ModelAntibiotics (Basel). 2021;10(8):886. doi:10.3390/ antibiotics10080886
- Lie MRKL, van der Giessen J, Fuhler GM, et al. Low dose Naltrexone for induction of remission in inflammatory bowel disease patients. J Transl Med. 2018;16(1):55. Published 2018 Mar 9. doi:10.1186/s12967-018-1427-5
- Younger J, Parkitny L, McLain D. The use of low-dose naltrexone (LDN) as a novel antiinflammatory treatment for chronic pain. *Clin Rheumatol.* 2014;33(4):451-459. doi:10.1007/ s10067-014-2517-2
- Weiss J. Herb-Drug Interaction Potential of Anti-Borreliae Effective Extracts from Uncaria tomentosa (Samento) and Otoba parvifolia (Banderol) Assessed In Vitro. Molecules. 2018;24(1):137. doi:10.3390/molecules24010137
- Zhang Y, Alvarez-Manzo H, Leone J, Schweig S, Zhang Y. Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani. Front Cell Infect Microbiol. 2021;11:624745. doi:10.3389/fcimb.2021.624745
- Nielsen CM, White MJ, Goodier MR, Riley EM. Functional significance of CD57 expression on human NK cells and relevance to disease. *Front Immunol.* 2013;4:422. doi:10.3389/ fimmu.2013.00422
- Rezzani R, Nardo L, Favero G, Peroni M, Rodella LF. Thymus and aging: morphological, radiological, and functional overview. Age (Dordr). 2014;36(1):313-351. doi:10.1007/s11357-013-9564-5
- Lin'kova NS, Poliakova VO, Trofimov AV, Sevost'ianova NN, Kvetnoi IM. [Influence of peptides from pineal gland on thymus function at aging]. Adv Gerontol. 2010;23(4):543-6. Russian. PMID: 21510076.
- King R, Tuthill C. Chapter Seven Immune Modulation with Thymosin Alpha 1 Treatment, Editor(s): Gerald Litwack, Vitamins and Hormones, Academic Press, Volume 102, 2016, Pages 151-178, ISSN 0083-6729, ISBN 9780128048184, doi:10.1016/bs.vh.2016.04.003.
- Campbell AW. Autoimmunity and the gut. Autoimmune Dis. 2014;2014:152428. doi:10.1155/2014/152428