Patel D, Shoeb S, Shihora D, et al. Adult-Onset Still's Disease (AOSD) in Patient with Previous Lyme Disease. *Brown Hospital Medicine*. 2025;4(1):16-19. doi:10.56305/001c.124992

Case Reports

Adult-Onset Still's Disease (AOSD) in Patient with Previous Lyme Disease

Devanshi Patel[1], Sarah Shoeb[1], Dhvani Shihora[1], Andrew Zucker[2], Wajiha Khan[1], Hoa Pham[1], Isaac Daudelin[1], Jessica Wachtel, MD[2]

[1] Department of Medicine, Rutgers New Jersey Medical School,
[2] Department of Medicine, Cooperman Barnabas Medical Center

Journal of Brown Hospital Medicine
Vol. 4, Issue 1, 2025

Article Information

Keywords: adult onset still's disease, AOSD, lyme disease, lyme infection, autoimmune disorder, autoimmune disease

https://doi.org/10.56305/001c.124992

Submitted: July 14, 2024 EST

Accepted: October 20, 2024 EST

Published: January 01, 2025 EST

Abstract

Adult-onset Still's Disease (AOSD) is a rare autoimmune disorder causing systemic inflammation that presents with a rash, fever, polyarthritis, and a characteristic serum hyperferritinemia. There is a complex relationship between infections and autoimmune disease, however, the association of AOSD with lyme disease is not well established. Here we present a case of AOSD in a 29-year-old male with a recent history of lyme disease. After ruling out infection and malignancy, a diagnosis of AOSD was made. From this report, we aim to raise more awareness for AOSD and recommend providers consider this diagnosis as a potential sequela of lyme disease.

BACKGROUND

Adult-onset Still's Disease (AOSD), also referred to as systemic onset juvenile idiopathic arthritis, is a rare autoimmune disorder with systemic inflammation resulting in rash, fever, polyarthritis, characteristic finding of serum hyperferritinemia, and multisystem organ involvement of varying degrees.[1] As it is a rare disease, there is a lack of robust epidemiologic data, but the estimated prevalence has been reported to be between 0.73-6.77 per 100,000 individuals. There is a bimodal age distribution, with the first peak occurring between 16-25 years and a second peak between 36-46 years. The mean age of diagnosis is approximately 38 years, with no male or female predominance.[2] AOSD is a clinical diagnosis that is reached by the exclusion of other autoimmune conditions such as rheumatoid arthritis and lupus, infectious process, vasculitis, and malignancy in the setting of the typical symptoms of high spiking fevers, maculopapular rash, arthralgia or arthritis, and elevated levels of acute phase reactants, particularly ferritin.[2]

There is a complex relationship between bacterial or viral infections and autoimmune diseases such as AOSD, with many reports of infections triggering an underlying inflammatory process.[3,4] There is no consensus on the infection timeline to the onset of AOSD. Genetic predisposition, dysregulated immune system, and stressful life events are other triggers.[2] We present a rare case of AOSD disease associated with a recent infection of Lyme disease.

CASE PRESENTATION

A 29-year-old male living in New Jersey with a history of mononucleosis and Lyme disease and a family history of rheumatoid arthritis (unknown degree of relative) presented with debilitating fatigue for several months associated with drenching night sweats. Four months prior, he began to develop progressive bilateral joint pain and swelling that started in his shoulders and progressed caudally with worsening pain over the past two months. He also had noticed an erythematous, non-pruritic, macular salmon-colored rash on his chest, bilateral upper and lower extremities, and face, along with fever, lymphadenopathy, and a 30-pound weight loss over the past two months. He had been taking acetaminophen for fevers and non-steroidal anti-inflammatory drugs for pain with no improvement.

He had a significant history of infectious diseases, including mononucleosis in college when he was about 19 years old and two episodes of Lyme disease. The first episode of Lyme disease was two years ago in 2021, at which time he was treated with a 28-day course of doxycycline. During this episode, he also had similar symptoms of fatigue, lymphadenopathy, and night sweats but no rash or joint pain. His symptoms resolved with antibiotics. He was diagnosed with a second episode of Lyme early in 2023 due to a positive IgM Polymerase Chain Reaction (PCR). At that time, he was treated with doxycycline 100 mg twice daily for 45 days. However, his symptoms failed to improve this time, and he continued to have fatigue, lymphadenopathy, and night sweats. In addition, he was now presenting with a new rash and joint pain.

Table 1. Comprehensive laboratory workup

Lab	Value	Normal Range
WBC	**16.4 K/CMM (H)**	4.0-10.5 K/CMM
HGB	**12.6 g/dl (L)**	13.5-17.0 g/dl
Platelet	205 K/CMM	140-450 K/CMM
ESR	**42 mm/hr (H)**	0-15 mm/hr
Sodium	140 mmol/L	136-146 mmol/L
Potassium	4.2 mmol/L	3.5-5 mmol/L
Chloride	103 mmol/L	96-106 mmol/L
Bicarbonate	26 mmol/L	24-30 mmol/L
Procalcitonin	**0.14 ng/ml (H)**	<0.1 ng/ml
Ferritin	**3056 ng/ml (H)**	30-400 ng/ml
Anti dsDNA	Negative	
Rheumatoid factor	Negative	
IgG	1209 mg/l	60-1640mg/l
IgA	208 mg/l	47-310 mg/l
IgM	66 mg/l	50-300 mg/l
EBV IgG PCR	**60.7 U/ml (H)**	
EBV IgM PCR	<37 U/ml	
EBV Nuclear Antigen	**528 U/ml (H)**	
Monospot	**Positive**	
Lyme IgM PCR	**Positive**	

On admission, the patient was febrile to 100.6 F and found to have leukocytosis (16.4 K/mm^3) with a neutrophilic predominance and elevated inflammatory markers (ferritin (2056 ng/ml)) which are summarized in Table 1. There were no abnormalities in thyroid function tests, renal function tests, and liver function tests. His autoimmune workup was also negative, including negative antinuclear antibody, rheumatoid factor, and anti-dsDNA. His immunoglobulin levels were within the reference range. His infectious workup revealed a positive Lyme IgM PCR and positive EBV IgG PCR. In addition, fine needle aspiration of the right axillary lymph node and peripheral blood flow cytometry were both negative for any immunophenotypic evidence of malignancy.

A diagnosis of AOSD was made by exclusion, and he was treated with prednisone 160 mg for four days, followed by 80 mg for three days, followed by 40mg for four days, and scheduled with an outpatient rheumatology follow-up. He had significant symptomatic improvement with fewer night sweats, rashes, and joint pain after being started on prednisone.

DISCUSSION

AOSD is extremely rare, and its causes are not fully understood. Previous case reports have associated AOSD with EBV. However, AOSD associated with Lyme disease has been rarely reported in the literature.[3,4] Our case provides another data point linking AOSD with Lyme disease. The patient had a remote history of EBV, but this is less likely to be the trigger as it has been many years since these infections, and the patient's symptoms started soon after his Lyme infection. Genetic factors, such as the patient's family history of autoimmune disease, have also been hypothesized to predispose patients. However, overall, the condition is still considered nonfamilial and not hereditary.[5]

Lyme disease, an infection caused by the spirochete Borrelia burgdorferi, is suspected when a patient presents with fevers, fatigue, lymphadenopathy, and joint pain, especially in an endemic region such as the northeastern part of the United States.[6,7] In our case, the patient had an onset of these symptoms two years ago, during which time he was diagnosed with Lyme disease and treated with doxycycline. A couple of months ago, he presented with symptoms associated with Lyme, now with the addition of an evanescent rash and severe migratory joint pain. He had received a second course of treatment for Lyme disease due to a positive IgM without clinical improvement. Previous cases of AOSD have shown correlations between initiation of symptoms and high IgM or viral titers of a concurrent or previous infection.[8,9] This aligns with our case, as his positive IgM titers for Lyme could be the trigger for his AOSD. In addition, our patient had migratory polyarthritis, which is characteristic of Lyme disease, and an evanescent rash, which is characteristic of AOSD, establishing a possible overlap and link between the two conditions.

After ruling out other infections, malignant, or rheumatologic causes, this patient was diagnosed with AOSD and treatment with steroids led to clinical improvement.[10,11] There are three disease patterns - mono-

cyclic, polycyclic, and chronic. Treatment can vary based on pattern but generally starts with NSAIDs and steroids, especially for monocyclic. Systemic steroid therapy, such as with prednisone, dexamethasone, or methylprednisolone, has led to remission in approximately 65% of patients.[2] If patients are refractory or have polycyclic and chronic patterns, they may require immunosuppression with disease-modifying anti-rheumatic drugs (DMARDs) such as methotrexate. The next progression if DMARDs fail are biologics. The only FDA-approved biologic in the USA for AOSD is canakinumab. However, others, such as rilonacept and tocilizumab, have been used off-label.[2] Since our patient had persistent symptoms that did not appear to be cyclic and had previously not been trialed on steroids, we initiated his treatment with a prednisone taper.

Infectious diseases have been linked to the development of autoimmune conditions. Several studies have associated viral, especially DNA-based viruses, and bacterial infections with AOSD, which is hypothesized to be due to the inflammatory activation of the immune system, which causes the underlying condition to present itself.[12] There have been reports of the cytomegalovirus, parvovirus B19, echovirus, rubella, coxsackie B, EBV, Chlamydia pneumonia, Mycoplasma, and more being implicated in the initiation of AOSD.[8,9,11,13-15] In conclusion, we aim to raise more awareness of this rare diagnosis and recommend that providers consider this diagnosis in patients who are not responsive to antibiotics, as AOSD can be a potential sequela of Lyme disease.

Author Contributions

All authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the International Committee of Medical Journal Editors criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Disclosures/Conflicts of Interest

The authors declare they have no conflicts of interest

Corresponding Author

Devanshi Patel
Rutgers - New Jersey Medical School
185 S Orange Ave, Newark, NJ 07103
Email: dpp100@njms.rutgers.edu

REFERENCES

1. Mehta B, Efthimiou P. Ferritin in adult-onset still's disease: just a useful innocent bystander? *International journal of inflammation*. Published online 2012:298405. doi:10.1155/2012/298405

2. Efthimiou P, Kontzias A, Hur P, Rodha K, Ramakrishna GS, Nakasato P. Adult-onset Still's disease in focus: Clinical manifestations, diagnosis, treatment, and unmet needs in the era of targeted therapies. *Semin Arthritis Rheum*. 2021;51(4):858-874. doi:10.1016/j.semarthrit.2021.06.004

3. Smatti MK, Cyprian FS, Nasrallah GK, et al. Viruses and Autoimmunity: A Review on the Potential Interaction and Molecular Mechanisms. *Viruses*. 2019;11(8):762. doi:10.3390/v11080762

4. De Luca F, Shoenfeld Y. The microbiome in autoimmune diseases. *Clin Exp Immunol*. 2019;195(1):74-85. doi:10.1111/cei.13158

5. Ma Y, Meng J, Jia J, et al. Current and emerging biological therapy in adult-onset Still's disease. *Rheumatology (Oxford)*. 2021;60(9):3986-4000. doi:10.1093/rheumatology/keab485

6. Hamza S, Mrabet D, Cheour E, et al. Association arthrite idiopathique juvenile et maladie de Lyme: a propos d'une observation [Juvenile idiopathic arthritis and Lyme disease: a case report]. *La Tunisie medicale*. 2006;84(8):500-502.

7. Cimmino MA, Trevisan G. Lyme arthritis presenting as adult onset Still's disease. *Clinical and experimental rheumatology*. 1989;7(3):305-308.

8. Jia J, Shi H, Liu M, et al. Cytomegalovirus Infection May Trigger Adult-Onset Still's Disease Onset or Relapses. *Front Immunol*. 2019;10:898. doi:10.3389/fimmu.2019.00898

9. Anderson CW, Shah PA, Roberts JR. Adult-Onset Still's Disease: Is This Truly a Diagnosis of Exclusion? *Hawaii J Med Public Health*. 2017;76(11 Suppl 2):3-6.

10. Risal U, Subedee A, Pangeni R, et al. Case Report: Adult Onset Still's Disease after vaccination against Covid-19. *Wellcome Open Res*. 2022;6:333. doi:10.12688/wellcomeopenres.17345.2

11. Altuzarra-Ranedo Y, Gómez-Ramírez D, Rodríguez-Laguna M, et al. Parvovirus Infection Triggering Still's Disease. *Eur J Case Rep Intern Med*. 2022;9(1):003122.

12. Ocon AJ, Kwiatkowski AV, Peredo-Wende R, et al. Adult-onset Still's disease with haemorrhagic pericarditis and tamponade preceded by acute Lyme disease. *BMJ Case Rep*. 2018;2018:bcr2018225517. doi:10.1136/bcr-2018-225517

13. Wouters JM, van der Veen J, van de Putte LB, et al. Adult onset Still's disease and viral infections. *Ann Rheum Dis*. 1988;47(9):764-767. doi:10.1136/ard.47.9.764

14. Takeda H, Ling M, Ochi M, et al. A patient with adult Still's disease with an increased Chlamydia pneumoniae antibody titer. *J Infect Chemother*. 2002;8(3):262-265. doi:10.1007/s10156-002-0180-Z

15. Schifter T, Lewinski UH. Adult onset Still's disease associated with Epstein-Barr virus infection in a 66-year-old woman. *Scand J Rheumatol*. 1998;27(6):458-460. doi:10.1080/030097498442307