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Ceftriaxone-Induced Immune Hemolytic Anemia from Treatment of Post-Treatment Lyme Disease Syndrome

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INTRODUCTION

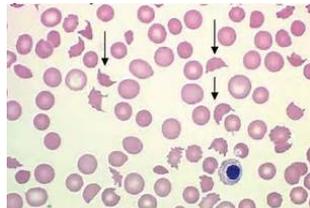
- Drug-induced immune hemolytic anemia (DIIHA) is a rare though likely underreported entity that is associated with significant morbidity and mortality.
- Ceftriaxone is a commonly used antibiotic with a well-documented association with DIIHA. The mechanism is a drug-dependent antibody, immune-complex mediated reaction which can be severe, leading to organ failure, shock, and even death.
- While the majority of cases are in children, a recent literature review had one-third of cases being adults, with up to 30-40% mortality in all ages.
- This case describes an adult patient treated for the controversial diagnosis of post-treatment Lyme disease syndrome (PTLDS) which resulted in ceftriaxone-induced immune hemolytic anemia (CIIHA).

CASE REPORT

- The patient is a 72-year-old active female from Minnesota with self-reported history of disseminated Lyme disease and Babesiosis diagnosed in the 1980s, Graves' disease, hypertension, and fibromyalgia.
- She presented with 3-4 weeks of progressive fatigue to being walker-dependent and mild cognitive impairment in setting of recently diagnosed normocytic anemia since starting 3x-weekly ceftriaxone-pulse therapy for PTLDS recommended by her PCP in California and prescribed by her local naturopathic doctor.

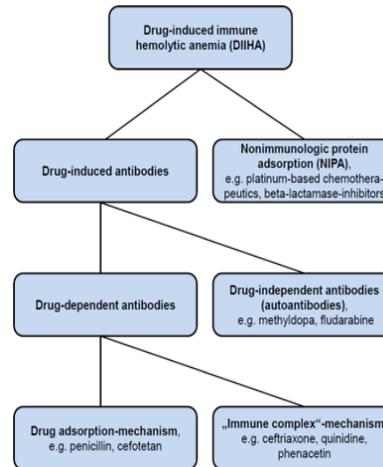
Evaluation:

CBC: WBC 6.4, Hgb 9.4 (baseline ~14) with MCV 88, Plt 288
CMP: Total bilirubin 1.3 (from 1.8 two days prior to admission)
Direct Coombs test: positive for IgG + complement, IgG
Peripheral smear: spherocytes, schistocytes
Haptoglobin: <30
LDH: 343
Reticulocyte index: 7.37
% retic: 16.7
Absolute retic count: 518
Ferritin 245, Fe 65
TIBC 408, %sat: 16
TSH 0.30, FT4 1.57

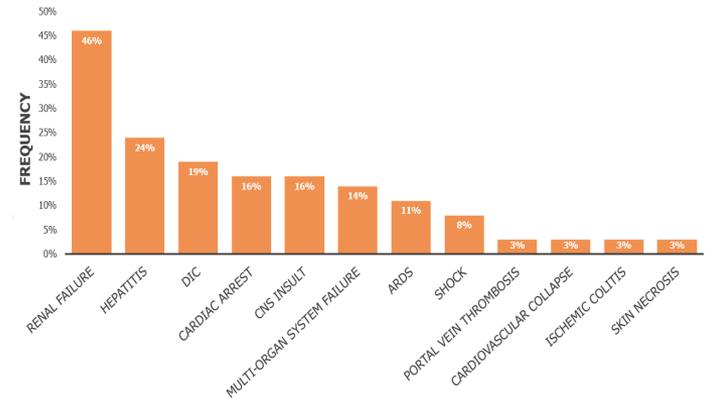


- Her ceftriaxone had already been discontinued 1 week prior to admission due to concern for DIIHA, which was consistent with her hospital workup. She was discharged home in fair but stable condition, and her anemia, energy, and cognition continued to improve in the weeks-months following.

FIGURES



Mechanisms of DIIHA



Potential Complications of CIIHA

DISCUSSION

- This patient was determined to have a subacute immune-mediated hemolytic anemia with symptoms that correlated temporally with her ceftriaxone infusions.
- DIIHA is a rare but potentially fatal entity with incidence of 1/1,000,000. Ceftriaxone (among other 2nd/3rd generation cephalosporins) and piperacillin, are commonly used antibiotics which have been associated with DIIHA. DIIHA has several mechanisms (see Figure 2). In the case of ceftriaxone, CIIHA is an immune complex-mediated reaction due to drug-dependent anti-ceftriaxone antibodies (acAb).
- Other features found in CIIHA patients include acute renal failure, hepatitis, and DIC (see Figure 3). One study suggested an increased risk of CIIHA in patients with underlying conditions such as sickle cell disease and HIV, or previous exposure to ceftriaxone such as in this patient.
- Treatment is withdrawing the offending drug and supportive measures as needed such as with blood transfusions. Some patients have been treated with plasmapheresis, corticosteroids, and IVIG.
- 2016 Infectious Disease Society of America (IDSA) State Policy Primer on PTLDS: "The potential benefit of long-term use of antibiotics for the treatment of Lyme disease has been examined and found ineffective in multiple well-done clinical trials. ... Long-term antibiotic therapy can cause many serious health consequences including protracted and intractable diarrhea, severe colitis, antibiotic resistance, allergic reactions, bloodstream infections and clots from intravenous catheters, and even death, without any scientifically-founded prospect of benefit."

CONCLUSION

- Early recognition of DIIHA (which can cause severe, sometimes fatal, reactions) and cessation of the causative agent is important to reduce the high morbidity and mortality associated with these patients.
- The role of antibiotics in (and even the diagnosis of) PTLDS is contended. Potential for serious adverse effects such as DIIHA among others should be considered prior to initiating antibiotics for PTLDS.