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

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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).

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.

This case demonstrates the importance of early recognition of DIIHA (which can cause severe, sometimes fatal, reactions) and cessation of the causative agent 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.

Mechanisms of DIIHA

Potential Complications of CIIHA