Disseminated Lyme Presenting as Pancytopenia Complicated by Hemophagocytic Lymphohistiocytosis

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Introduction

- Since its identification in 1976, the prevalence of Lyme in the US has rapidly increased.
- With projected healthcare costs approaching a billion dollars and the risk of chronic complications, early recognition of presenting symptoms is necessary.

Case Presentation

A 67-year-old female with a history of type 1 diabetes mellitus, post-ablative hypothyroidism secondary to Graves' disease, CAD status post-CABG complicated by STEMI and free wall rupture presented with 4 weeks of myalgias and generalized fatigue accompanied with 2 weeks of subjective fever & chills.

Vitals on admission: T 36.4°C, HR 70s, BP 87/51 → 110/50 mmHg, RR 20, SpO2 97% on room air

Pertinent Physical Exam Findings:

- General: uncomfortable appearing, rigoring
- Abdomen: diffusely tender to palpation without guarding or rebound
- Integumentary: diffuse pruritic, tender, macular erythematous blanching rash on back and lower extremities.

Pertinent Labs: WBC 1.44 k/uL (ANC 330), Hgb 10.4 g/dL without hemolysis, Platelets 164 k/uL, ESR 119 mm/hr, CRP 100.8 mg/L.

Imaging: mildly dilated CBD on CT of the abdomen with normal subsequent US.

Clinical Course

- Patient was started on Ceftriaxone and Metronidazole empirically for persistent fevers; switched to Cefepime for febrile neutropenia.
- Differential diagnosis included malignancy *vs.* autoimmune process *vs.* infectious etiology.
- Bone marrow biopsy was negative for malignancy or myelodysplastic syndrome.
- Unremarkable autoimmune work-up and negative infectious work-up (viral, fungal, and malarial sources).
- Tick-borne testing: +++ Lyme antibody with confirmatory western blot; negative for anaplasmosis, babesia, and ehrlichiosis.
- HLH-score=166: Fevers, Pancytopenia, ↑Ferritin ↑Triglycerides, ↑AST → <u>40-54% probability of hemophagocytic syndrome</u>
- Patient started on Doxycycline with symptomatic improvement, and resolution of neutropenia.

Diagnostic criteria of hemophagocytic lymphohistiocytosis: HLH-2004

Diagnosis will be established if one of either (A) or (B) is fulfilled	***Patient's results***
(A) Molecular diagnosis consistent with HLH	
(B) Diagnostic criteria for HLH fulfilled (5 out of the 8 criteria shown below)	
① Fever ≥38.5°C for ≥7 days	**Criterion met**
② Splenomegaly ≥3 finger breadth below the left subcostal margin	
③ Cytopenias affecting ≥2 of 3 lineages in peripheral blood	**Criterion met**
Hemoglobin <9 g/L	*Hemoglobin 6.9 g/L*
Platelets <100×10⁹/L	↓ to 103×10⁹/L
Absolute neutrophil count <1.0×10⁹/L	*ANC 330x10⁹/L*
④ Hypertriglyceridemia and/or hypofibrinogenemia	**Criterion met**
Fasting triglycerides ≥265 mg/dL, Fibrinogen ≤1.5 g/L	*Triglycerides 417 mg/dL*
⑤ Hemophagocytosis in the bone marrow or spleen or lymph node	
⑥ Low or absent NK cell activity	*Not tested*
⑦ Ferritin ≥500 µg/L	**Criterion met**
⑧ Soluble CD25 (sIL-2 receptor) ≥2,400 U/mL	*Not tested*

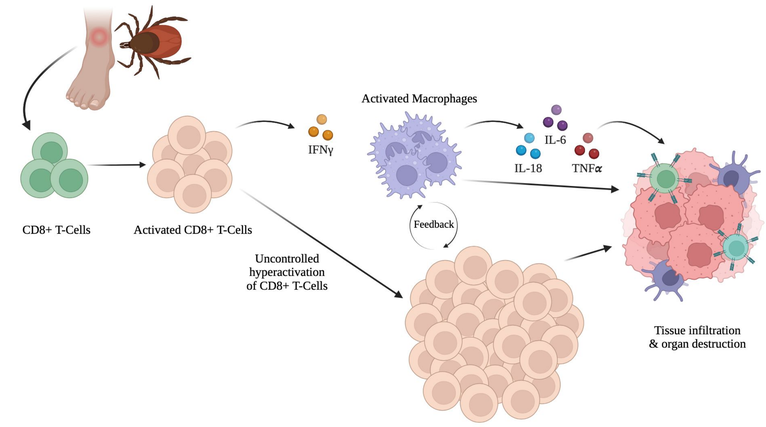

Figure. The proposed immunologic response in our patient with hemophagocytic syndrome post-disseminated Lyme disease

Discussion

This case serves to illustrate an uncommon presentation of disseminated Lyme featuring pancytopenia, atypical rash, and indicators of HLH. HLH constitutes a life-threatening syndrome characterized by excessive cytokine (interferons, interleukins, tumor necrosis factor and macrophages stimulating factors) release due to immune overactivity *(Figure)*. This leads to tissue infiltration and organ destruction, and subsequently multi-organ dysfunction. Secondary HLH can be due to infections, mainly viruses (EBV, CMV, HIV), and but also bacteria.

Conclusion

Few case reports of pancytopenia or HLH due to Lyme are in the literature. This case highlights dilemmas in diagnosing a common disease presenting uncommonly—reinforcing the need to keep tick-borne illnesses on the differential in endemic regions.

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