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# Doxycycline Didn't Cure the Fever! An Interesting Case of Large Granular Lymphocytic (LGL) Leukemia with Secondary Hemophagocytic Lymphohistiocytosis (HLH).

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HLH: A rare association with LGL Leukemia

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### **Introduction**

Hemophagocytic lymphohistiocytosis (HLH) is a potentially fatal syndrome characterized by excessive immune activation. It is diagnosed in patients of all ages and is classified as either primary from gene mutations or secondary from various triggers. We present an interesting case of HLH in a patient with large granular lymphocytic leukemia (LGL).

### **Presentation**

A 53-year-old female with a questionable history of inflammatory osteoarthritis presented with fever and a diffuse papular erythematous rash. Her initial vital signs and labs were significant for temperature of 102.7F, HR 116/min, WBC 14000/mcl, platelets 96000/mcl, ALT 198 U/L, AST 185 U/L, and total bilirubin 1.8 mg/dl. Given initial concerns for flea-borne disease, antibiotics were initiated without improvement. Infectious disease consult recommended broadening antibiotics, but patient continued to deteriorate and was noted to have progressive pancytopenia and an elevated ferritin of 1610 ng/ml. Given suspicion for a non-infectious process, hematologic workup was initiated. Peripheral smear showed an expanded population of CD8+ T-cell large granular lymphocytes. Hematology was consulted and confirmed diagnosis of LGL by flow cytometry. At this point, patient rapidly deteriorated and developed hallucinations, confusion, and lethargy. Patient was noted to have developed acute hyponatremia with sodium levels dropping by more than 10 over 1 day and urine studies and exam consistent with SIADH secondary to hematologic illness. Legionella and rickettsial disease panel were negative. MRI Brain was unremarkable, but lumbar puncture demonstrated an increased LGL population. Further workup revealed low fibrinogen of 124 mg/dl, elevated triglycerides of 296 mg/dl, extremely elevated IL-2 receptor alpha level (CD25) of 4667 U/ml (expected 223-710), and hepatosplenomegaly on abdominal CT. Bone marrow biopsy was normal. As patient met six of eight diagnostic criteria for HLH, she was started on treatment with dexamethasone along with hypertonic saline for acute SIADH with marked improvement of her clinical status over the next 3 days. The patient was subsequently discharged with prednisone with plans for outpatient hematology follow-up.

### **Discussion**

HLH was historically described as a rare familial disorder of the young, but has increasingly been also recognized as an aggressive and potentially fatal syndrome in adults. Its presentation necessitates prompt hematologic evaluation and management. Limited literature has discussed the rare association of secondary HLH with LGL (<1% of cases), with our case demonstrating rapid and drastic improvement with treatment of this unusual combination. Given its life-threatening nature, it is important for clinicians to consider HLH when dealing with a similar clinical scenario.