

Sarcoidosis, the Great Imitator: An Unusual Finding on Bone Marrow Pathology.

Grace Berlin DO

Lehigh Valley Health Network, grace.berlin@lvhn.org

Carolyn Casey

Lehigh Valley Health Network, Carolyn.Casey@lvhn.org

Susan Kim MD

Lehigh Valley Health Network, Susan.Kim@lvhn.org

Marie O'Brien

Lehigh Valley Health Network

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Sarcoidosis, the Great Imitator: An Unusual Finding on Bone Marrow Pathology

Berlin G, Casey C, Kim SS, O'Brien M
Lehigh Valley Health Network, Allentown, Pennsylvania

INTRODUCTION

The multi-system nature of sarcoidosis can make it difficult to ascertain the extent of disease in affected patients, especially once disease becomes advanced. As sarcoidosis may involve any system, determination of this disease during a flare versus another coexisting disease causing similar findings is particularly challenging⁴. A comparable diagnostic dilemma emerges with determining the presence of hemophagocytic lymphohistiocytosis (HLH) as this disease manifests in those with pervasive illness^{1,2}.

CLINICAL CASE

A 72 year old male with significant history of sarcoidosis with biopsy-proven bone marrow and prostate involvement as well as limited systemic sclerosis (positive centromere antibody with Raynauds, telangiectasias, and puffy hands) admitted with fever and pancytopenia. He was found to have streptococcal mitis/oralis bacteremia of uncertain primary source. Empiric prednisone therapy was initiated for pancytopenia along with intravenous (IV) antibiotics for presumed active sarcoid involvement of his bone marrow. The patient's fevers resolved after addition of high dose steroid therapy. The patient was discharged home on oral steroids and completion of IV antibiotics.

The patient was readmitted three days after discharge with symptomatic hypercalcemia, recurrent fevers, and persistent pancytopenia. He underwent a bone marrow biopsy which indicated presence of hemophagocytosis, supportive of HLH, in the background of mildly hypercellular bone marrow aspirate and features of sarcoid involvement, specifically lobular disarray with scattered epithelioid granulomas. HLH diagnosis was ultimately supported with criteria used in the HLH 2004 trial by findings of hemophagocytosis on bone marrow biopsy, elevated soluble CD 25 (soluble IL-2 receptor alpha), peripheral blood cytopenia, hypofibrinogenemia, and splenomegaly. He was empirically treated with three doses of Etoposide as well as Dexamethasone per HLH treatment protocol. His pancytopenia failed to improve on the induction therapy and repeat bone marrow biopsy was completed. Second bone marrow biopsy results yielded post-chemotherapy hypo cellular bone marrow aspirate with stromal changes, residual sarcoid granulomas, and no evidence of hemophagocytosis. Due to the incongruence of hemophagocytosis resolution without appropriate improvement in the patient's pancytopenia, the patient was transferred to an academic center for further reassessment where review supported extensive sarcoid involvement of the bone marrow rather than de-novo HLH. During this hospitalization, the patient developed progressive hepatic failure and was found to have cirrhosis suspected to be related to infiltrative sarcoid process.

CONCLUSION

This case highlights the clinical quandary of determining the true presence of HLH with active sarcoid involvement in the bone marrow¹. Upon reflection, factors outside the marrow such as cirrhosis likely played a role in misinterpretation of factors that would typically be supportive of HLH diagnosis, such as hypofibrinogenemia, normal triglycerides, and normal ferritin. Hemophagocytosis seen on the patient's bone marrow biopsy demonstrated initially excessive macrophage activation, therefore can be supportive of an HLH disease process, however this finding neither is pathognomonic nor needs to be present for HLH diagnosis^{2,3}. Prompt treatment of HLH if highly suspected is imperative given the life-threatening nature of the disease¹, although treatment of suspected HLH in this case was of no clinical benefit. Lack of response should and did require reevaluation of the initial diagnosis. Means of early and correct diagnosis of alternative disease processes in cases of advanced sarcoidosis is imperative.

Table 1. HLH Diagnostic Criteria

Features of HLH	Presence in our Patient
Fever >38.5 degrees Celsius	No
Splenomegaly	Yes
Peripheral blood cytopenia (two of the following: Hgb <9, PLT<100K, ANC<1000)	Yes
Hypertriglyceridemia (fasting triglycerides>256) and/or hypofibrinogenemia (fibrinogen<150)	Yes
Hemophagocytosis in bone marrow aspirate, spleen, lymph node, or liver	Yes
Ferritin >500 (> 3000 more indicative of HLH)	No
Low or absent NK cell activity	Uncertain
Elevated soluble CD25 (soluble IL-2 receptor alpha) two standard deviations above age-adjusted normal range	Yes

Comment: At least five out of the above eight features should be present for HLH diagnosis based on diagnostic criteria used in the HLH 2004 trial for those without molecular identification of an HLH-associated gene mutation^{1,2}.

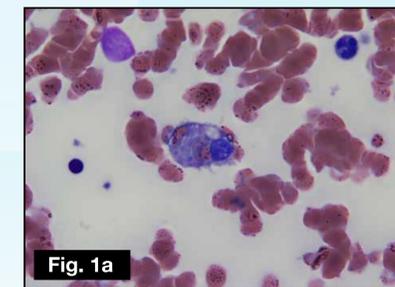


Fig. 1a

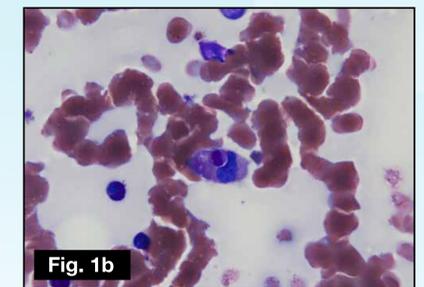


Fig. 1b

Comment: Both photos from initial bone marrow biopsy sample collected 4/24/17 demonstrating hemophagocytosis.

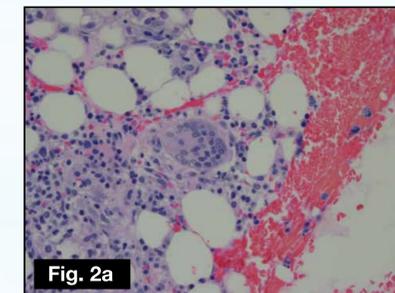


Fig. 2a

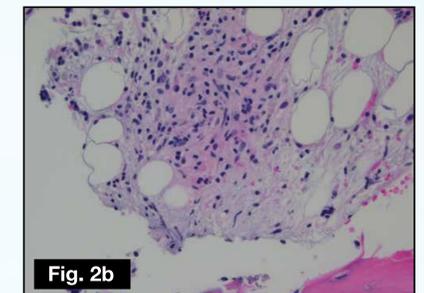


Fig. 2b

Comment: Both of the above photos are bone marrow biopsy aspirates from the second sample 5/19/17 status post treatment for HLH demonstrating granulomas (no hemophagocytosis identified).

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