

Sarcoid-like reaction: Hodgkin's lymphoma is a hypothesis

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Dear editor,

I, herein, present an intriguing concern of the Pathologist facing granulomas in surgical pathology routine. Inflammatory findings in surgical pathology may challenge pathologists in the setting of the diagnosis of Hodgkin's lymphoma (HL). Consequently, Pathologists' reports may also challenge Hematologists during the clinical practice due to the overlap of neoplastic and non-neoplastic diseases. In this context, we present a collection of findings from two patients diagnosed with HL, which had a sarcoid-like pattern in their morphological presentation.^{1,2}

The first case is a 53-year-old woman with mental confusion for four days, without lymph adenomegaly, hepatosplenomegaly, or palpable masses. She had pancytopenia and normal values of lactate dehydrogenase and high levels of serum ferritin (9,621 mg/dL, reference range [RR] 20-110 mg/dL). Her bone marrow biopsy has shown hemophagocytosis, non-caseating epithelioid granulomas, and some binucleated large cells with evident nucleoli that reacted positive for CD30 and CD15, confirming the diagnosis of HL (Figure 1A-1D and Figure 2).

The second patient is a 44-year-old man with cervical lymph adenomegaly, without other symptoms. Histopathological analysis of the lymph node showed several non-caseating granulomas. In the periphery of the granulomas, there were some binucleated large cells, in a typical Reed-Sternberg cell aspect. The reactions for CD30, CD15, and LMP-1 were

positive in these cells, confirming the HL diagnosis (Figure 3A-3D and 4A). The Ziehl-Neelsen and Grocott-Gomori stains were negative in both cases.

The morphology characterized by granulomas and inflammatory infiltration always leads the Pathologists to differentials as sarcoidosis, mycobacteriosis, and mycosis. The cases, presented in this letter, draw the attention to remember the possibility of lymphoid neoplasm, as HL. Epithelioid granulomas in the bone marrow or lymph nodes of patients presenting nonspecific clinical features is a diagnostic challenge to the pathologist because of the possibility of various diagnoses, namely (i) autoimmune disease, (ii) inflammatory entity, and neoplasia.^{2,3} Specific study must be performed in this morphological context, and the diagnosis of HL should ever be considered. In lymph nodes, HL may mimic sarcoidosis, like in the second case. Pathologists must observe the periphery of granulomas because the atypical cells locate in this area. Careful morphological analysis with an immunohistochemistry (IHC) study is crucial.

In the absence of typical HL morphology and IHC profile, the diagnosis will be made later.

Non-caseating granulomas strongly raise the hypothesis of sarcoidosis, a systemic disease that affects different organs and has been reported before or concomitant with carcinomas (4.4%), non-Hodgkin lymphomas (7.3%) and HL (13,8%). The presence of these granulomas in the context of an HL is called a sarcoid-like reaction. This pattern is a result from

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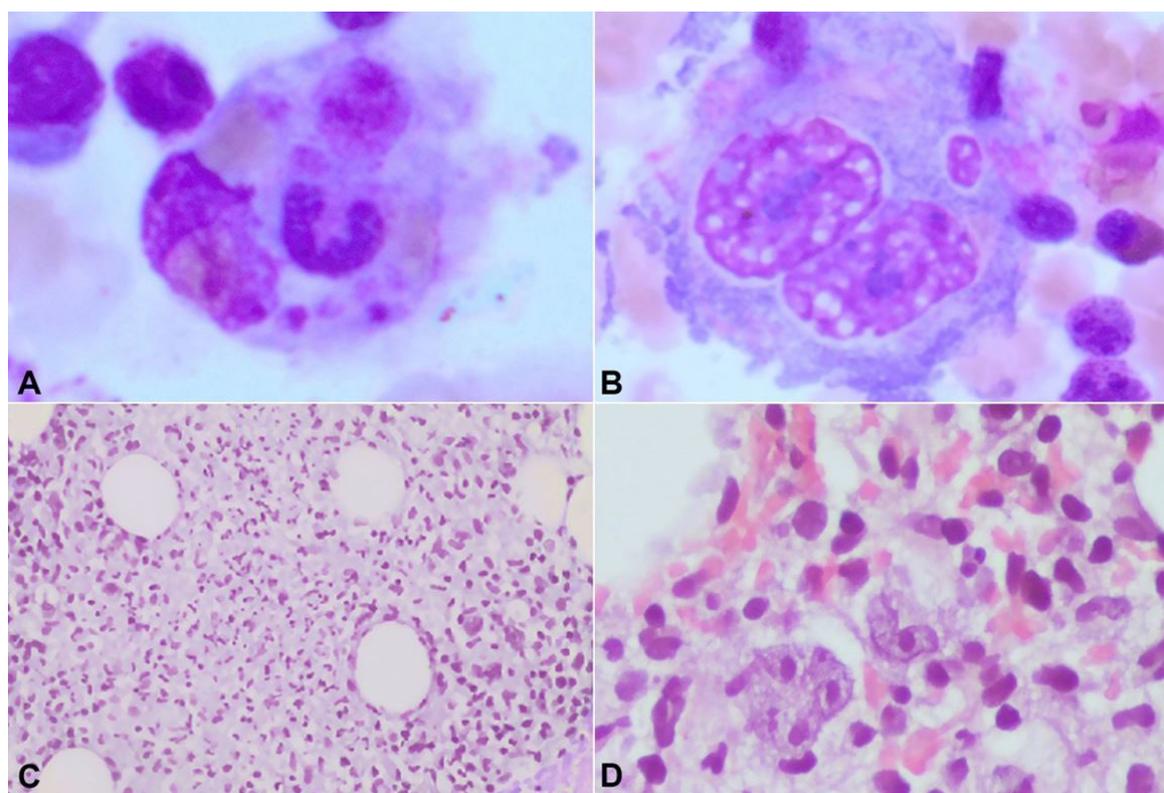


Figure 1. Photomicrograph of the bone marrow. **A** – Bone marrow aspirate demonstrated hemophagocytosis, which is compatible with the clinical aspects of the patient, and it is possible in the neoplastic context, for example, HL (Giemsa, 1000x); **B** – Cytological aspect Reed-Sternberg cell in the bone marrow aspirate (Giemsa, 1000x); **C** – there is a granulomatous aspect. **D** there are some atypical cells in the periphery of this granulomatous pattern. These atypical cells have morphological aspects of Reed-Sternberg cells and Hodgkin cells [C (H&E, 400x) and D (H&E, 400x)].

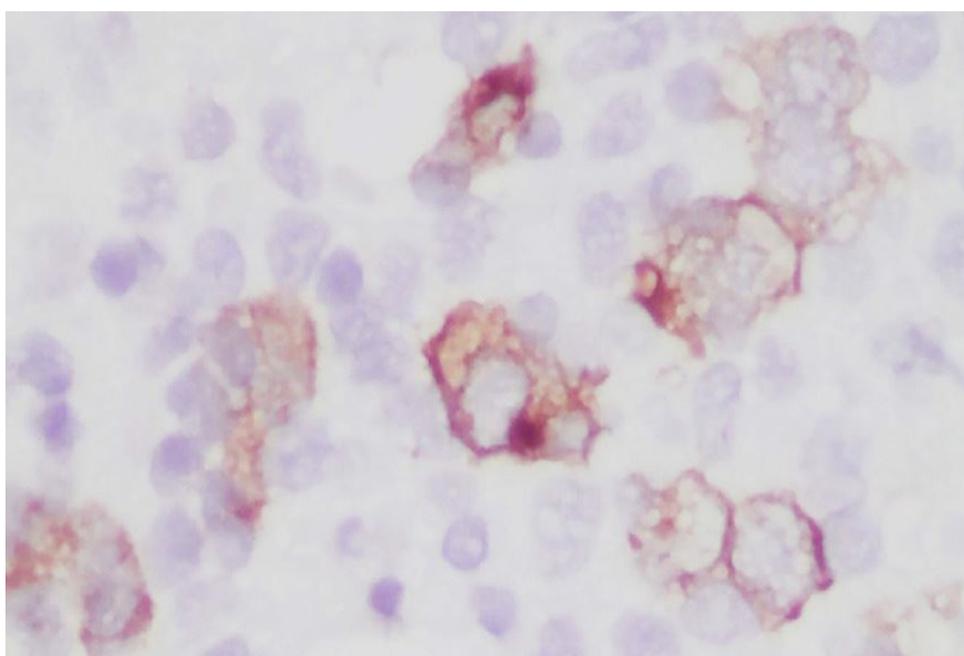


Figure 2. Photomicrograph of the bone marrow. Positivity to CD30 confirmed the diagnosis of HL (400x).

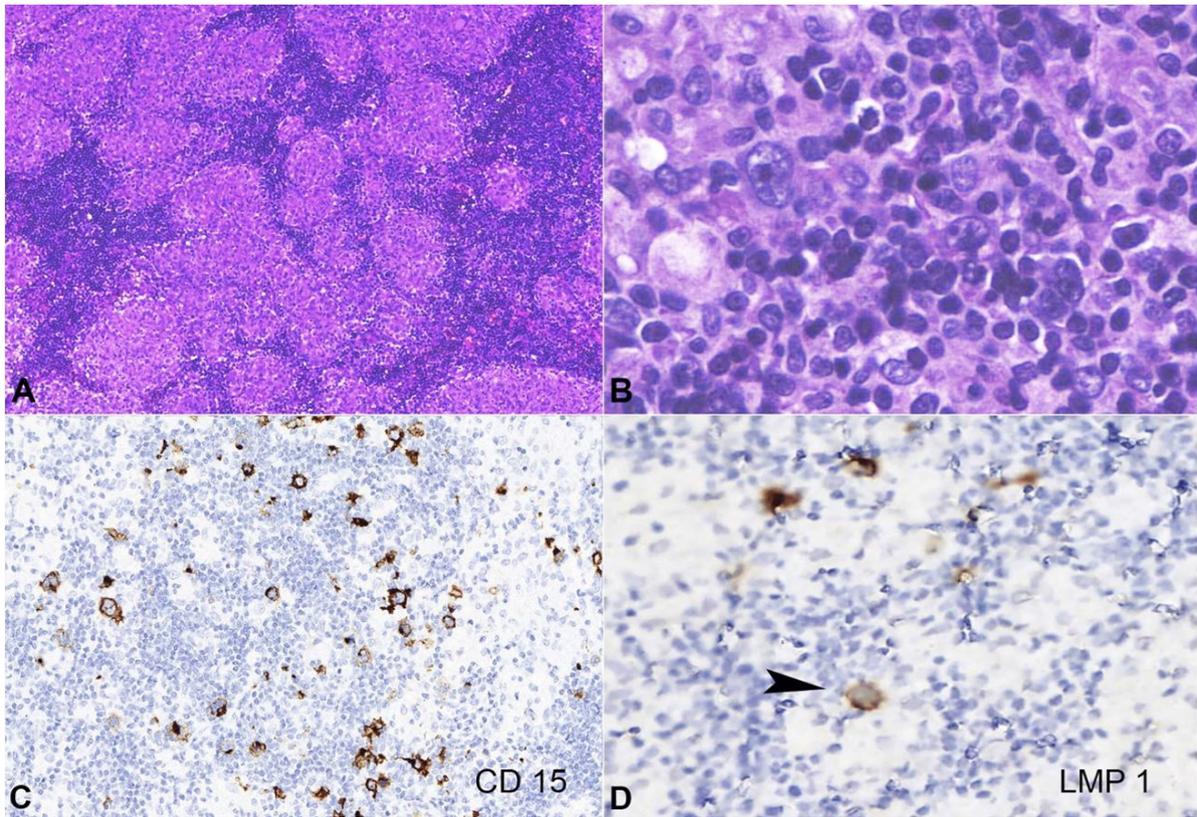


Figure 3. Photomicrograph of the lymph node. **A** – Lymph node altered architecture. There are many granulomas in a sarcoid-like aspect. However, in the granulomas’ periphery, there are some atypical cells that are presented in the image (H&E, 200x); **B** – Presence of Hodgkin cells intermingled with the lymphocytes (H&E, 400x); **C** – positive reaction to CD15 (400X); **D** – positive reaction to LMP-1/EBV (arrowhead) (400X).

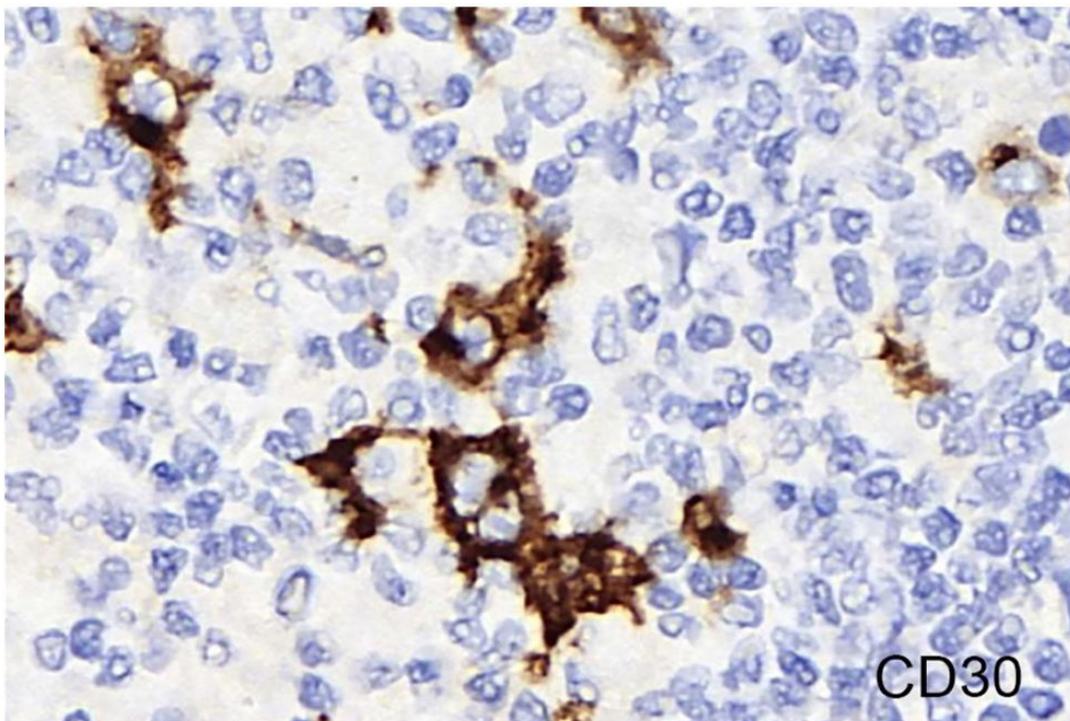


Figure 4. Photomicrograph of the lymph node. Positive reaction to CD 30 (400X).

degenerative and necrotic changes within the tumoral lesions, which leads to an increased level of inflammatory factors that cause the activation of macrophages or from an anti-neoplastic immune phenomenon, which is associated to a better prognosis.³⁻⁵ HL is a neoplasm with a marked reactive component and the presence of granulomas may be challenging for pathologists, mainly when they are plenty.

The presence of granulomas is described as a pattern of reaction that may occur in mixed cellularity classical HL (MC-cHL), a variant of this type of tumor, similar to the interfollicular subtype, and the grade 2 nodular sclerosis cHL (NS-cHL) group. The later shows a morphology characterized by intermingled fibrosis or fibro-histiocytic and more aggressive behavior.¹

Sarcoidosis, as lymphomas, activated the histiocytic system, and therefore involve the same organs. Due to their similar clinical manifestations,

the diagnosis cannot rely only on the clinical-radiological background. Clinicians should think in malignancy if there are concomitant respiratory symptoms and bilateral hilar lymphadenopathy with tomographic imaging indicating the involvement of right paratracheal and bilateral hilar lymph nodes. However, sarcoidosis may present the same clinical aspects. So, the histology is of paramount importance.^{2,5,6}

In our cases, both patients were submitted to classical chemotherapy, with a good response. These two cases teach us the approach for granulomatous lymphadenopathy: firstly, an infection investigation with special stains, close morphology analysis, and, if there is a possibility of neoplasm, perform IHC, the gold standard for diagnosis.

Keywords

Hodgkin lymphoma, bone marrow, immunohistochemistry

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