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LETTER TO THE EDITOR

Lymphomatoid granulomatosis masquerading as pneumonia

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Dear Editor,

A 44-year-old immunocompetent Caucasian male presented with worsening dyspnea and cough for 2 months without associated fever and chills. A month ago, he was found to have bilateral pneumonia on chest x-ray and was treated with intravenous ceftriaxone and azithromycin. However, his symptoms progressively worsened, and so he was admitted for further evaluation.

Physical examination revealed multiple, painful oropharyngeal ulcers and numerous erythematous plaques on the scalp. Auscultation of lungs was significant for diffuse bilateral wheezing. Complete blood count and comprehensive metabolic panel were unremarkable. HIV screening was negative. Chest X-ray showed persistent bilateral infiltrates. Computerized tomography of chest revealed diffuse patchy parenchymal and nodular densities throughout the lungs, more prominent in lower lobes (Fig. 1). He was started empirically on intravenous vancomycin and piperacillin–tazobactam. Endobronchial biopsy with bronchoalveolar lavage (BAL) revealed "organizing pneumonia" without evidence of granuloma, hemorrhage, or eosinophilia. Cultures of blood, sputum, and BAL washings showed no growth.

The initial differential diagnosis for the oral ulcers was candidiasis, Behcet's syndrome, or other autoimmune conditions. Consulting Rheumatologist on this case felt that Behcet's syndrome was unlikely as these ulcers were more superficial in contrast to deep, well-circumscribed lesions of Behcet's. Serological tests for antinuclear antibody, antineutrophil cytoplasmic antibodies, proteinase-3, and myeloperoxidase antibodies were negative, making the diagnosis of systemic lupus erythematosus and granulomatosis with polyangiitis (Wegener's) unlikely. Oral ulcers were treated with nystatin for possible candidiasis without any response.

Video-assisted thoracic surgery-guided lung biopsy was performed, along with biopsy of tongue and scalp lesions. Lung biopsy revealed infiltrate of lymphoid cells and histiocytes with scattered atypical mononuclear cells (Fig. 2). There were also foci of necrosis within the area of infiltrate with prominent vascular infiltration. Immunohistochemistry for CD3 and CD20 as well as in situ hybridization for Epstein-Barr Virus (EBV)-encoded small nuclear RNA (EBER) were performed. Majority of the cells were CD3-positive small T cells with scattered large CD20-positive large B cells (Fig. 3) interspersed among small T cells. In situ hybridization showed scattered areas of EBER-positive cells throughout the lesions. Thus, patient was diagnosed with Grade I-II lymphomatoid granulomatosis (LYG). Histopathology of tongue and scalp lesions also confirmed LYG. Patient was started on prednisone with marked improvement. He was recently started on Rituximab.

All authors had access to the data and role in writing the manuscript.

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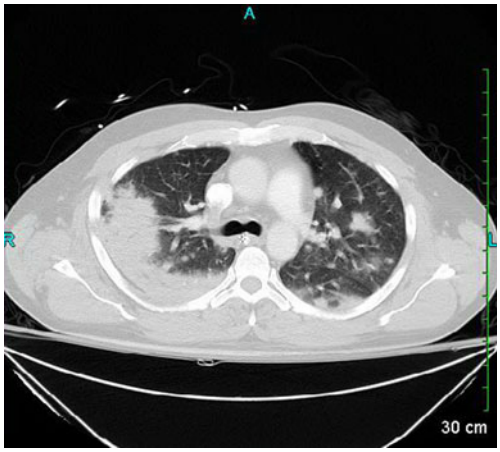

Fig. 1 CT scan of chest showing diffuse bilateral parenchymal infiltrates

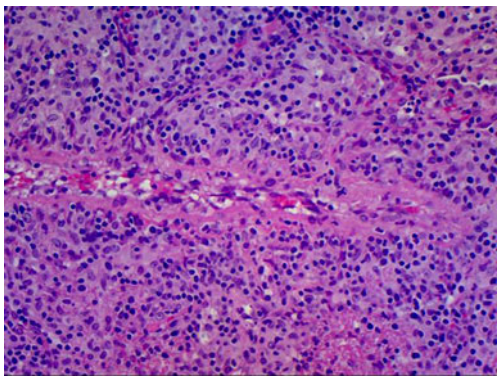

Fig. 2 Hematoxylin and eosin staining of lung biopsy showing lymphoid cell infiltrate and prominent vascular infiltration with atypical mononuclear cells

Lymphomatoid granulomatosis is an extremely rare angiodestructive lymphoproliferative disorder. It was first described by Liebow et al. in 1972 as an uncommon multiorgan systemic disease, with predilection for lungs [1]. It remained uncertain for years whether LYG is an inflammatory or a lymphoproliferative process. The World Health Organization classification in 2008 placed LYG under the category of "large B cell lymphomas" and described it as an extranodal, angiocentric, T cell-rich B cell lymphoma [2].

LYG is usually seen in middle-aged adults, with male predominance [3–5]. It is mostly EBV-associated, though a very small number of cases with no demonstrable EBV infection have been reported [3]. Lungs are most commonly involved (>90 %), while cutaneous, renal and neurological involvement may also be seen. Lymphoid organs are usually spared until the late course of disease [3, 4].

Diagnosis is often a challenge as it mimics many common pulmonary conditions [4, 6]. Histological triad of polymorphic lymphocytic infiltrate, angiitis, and granulomatosis with central necrosis is required for definitive diagnosis of LYG [3]. There is no standard therapeutic approach to this rare lymphoma. In most published cases, corticosteroids, either alone or in combination with chemotherapy are the first line of treatment [3, 4]. As in diffuse large B cell lymphomas, cyclophosphamide, doxorubicin, vincristine, and prednisone are used. Rituximab has shown improved outcome in several cases [7–9]. Interferon-alpha2b is another agent used successfully [10].

LYG is associated with a grim prognosis. In a large clinicopathological study, mortality was 63.5 % [3] and median survival was 14 months. Age less than 30 years, multiorgan involvement, and leukopenia indicate poor prognosis.

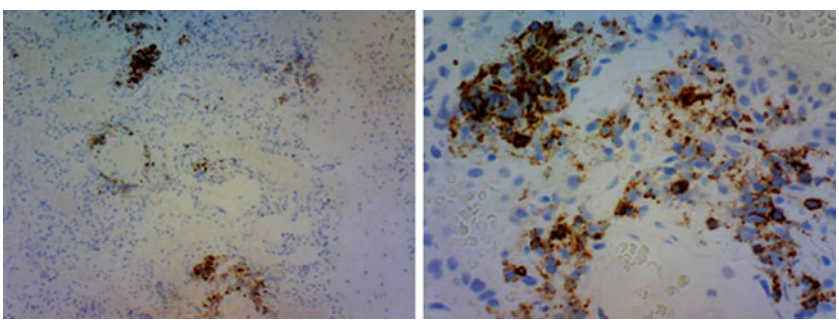

Fig. 3 Immunostaining for CD20, low-power and high-power field, respectively

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Conflict of interest All authors have no financial or other potential conflicts of interest.

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