Reviewer’s report

Title: Lymphangioleiomyomatosis, multifocal micronodular pneumocyte hyperplasia, and sarcoidosis: more pathological findings in the same chest CT, or a single pathological pathway?

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Reviewer: Maneesh Bhargava

Reviewer's report:

This is a well-written and interesting case report of a middle-aged female with TSC1 mutation with cystic lung disease and PBC/ autoimmune hepatitis presenting with granulomatous inflammation. The case presented had an extensive work up to tuberous sclerosis and had cortical tubers, facial angiofibroma, periungual fibroma and renal angiomyolipoma. Chest computerized tomography demonstrated cystic lesion/nodular infiltrates and lymphadenopathy. Skin lesion showed granulomatous inflammation on biopsy.

Though the authors conclude the nodules are MMPH, these could represent nodular infiltrate due to sarcoidosis. The information available is not definitive for the conclusion made the writers.

Sarcoidosis is a diagnosis of exclusion, and several sarcoid mimics need to be considered. Granulomatous inflammation occurs in cases of primary biliary cirrhosis / autoimmune hepatitis. The workup included in the manuscript is not complete to either establish the extent of sarcoidosis nor to exclude other causes of granulomatous inflammation. What medications was the patient talking? Sirolimus-induced granulomatous inflammation has been described (PMCID: PMC3920426). Was the patient taking other medications for autoimmune hepatitis? Were other causes of granulomatous inflammation excluded such as fungal exposures, tuberculosis of GLILD associated with CVID? Was evaluation done for identifying dysregulation of Vitamin D metabolism (25 hydroxy and 1,25 dihydroxy vitamin D levels)? Was an evaluation done to determine for ocular or cardiac involvement?

The discussion is all speculative and focuses on the association of mechanisms that link TSC-LAM to granulomatous inflammation while there is more literature on the association of autoimmune hepatitis and granulomatous inflammation (OR 6.7, PMID:19520873). Case reports also exist that show a link between granulomatous hepatitis and PBC.

The reference list should include the association of autoimmune hepatitis/PBC with granulomatous inflammation to give the reader a more accurate reflection of the current status of literature.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Unable to assess

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