Sir,

A 15-year-old asymptomatic female patient with apparently abnormal chest radiograph underwent high-resolution computed tomography (HRCT) chest – both of which were sent to our department for reporting. The chest radiograph was misinterpreted due to rotation of the patient. The HRCT chest, however, demonstrated multiple, tiny randomly distributed nodules of solid and ground glass attenuation and a single cyst noted in the medial segment of the right middle lobe [Figure 1]. The sections through the upper abdomen revealed numerous fat attenuation lesions present in both the kidneys [Figure 2]. Besides, a few hypodense lesions were noted in the liver and pancreas. The bone windows depicted patchy sclerosis throughout the visualized vertebral bodies. On inquiry, the patient had a poor scholastic performance and was on medication for a seizure disorder. On examination, she had adenoma sebaceum on the face and a few ash-leaf macules on the neck. A CT brain was performed which showed multiple calcified subependymal nodules. Hence, the final diagnosis was tuberous sclerosis complex (TSC) with possible multifocal micronodular pneumocyte hyperplasia (MMPH) in the lungs and adenoma/leiomyoma in the liver and pancreas. The patient denied biopsy of the lesions, but she is on regular follow-up. At a follow-up visit after 1 year, neither the pulmonary nodules nor the hepatic or pancreatic lesions have increased in number or size, thus establishing the diagnosis of MMPH.

Pulmonary involvement in TSC was formerly reported to be as low as 0.1%–1% (Dwyer, Jao) to 1%–2.3% (Castro), with the majority of lesions being lymphangioleiomyomatosis (LAM). Recent studies, however, report an incidence of 26%–39% of pulmonary involvement in females with TSC. This is presumably due to the wide availability of CT as well as high-resolution algorithms. Similarly, MMPH in TSC was previously thought to be a rare entity; however, works of Moss et al., Franz et al., Muzykewicz et al., and Wataya-Kaneda et al. reported an incidence of 28%, 43%, 58%, and 71%, respectively. Notably, all the case series mentioned above were based on CT findings. Furthermore, the pulmonary nodules in these above mentioned studies were considered to be MMPH in the given clinical setting of TSC without a biopsy. Franz et al. believe MMPH to be far more common than what the radiologic data suggests since the nodules of MMPH may be beyond the resolution of HRCT chest.

MMPH, first described by Popper (1991), is a hamartomatous proliferation of type 2 pneumocytes along the alveolar septa that exhibits fibrous thickening. Furthermore, there is an increase in elastic fibers and alveolar macrophages in these nodules. These nodules exhibit positivity to cytokeratin and apoprotein A and B in contradistinction to LAM. LAM may, however, often coexist with MMPH. In fact, this coexistence with LAM is what makes pneumothorax

---

**Figure 1:** Axial section high-resolution CT lung reveals multiple, tiny, randomly distributed nodules. The nodules are either ground glass in attenuation with a solid peripheral halo (arrow in a) or are solid (arrows in b and c). In addition, a small lung cyst is seen in medial segment of the right middle lobe (arrow in d). Follow-up imaging did not show any change in morphology or number of the lesions

**Figure 2:** Coronal CT images of the chest with upper abdomen (a) shows multiple fat attenuation lesions in the left kidney. An abdominal sonogram was performed, which demonstrated multiple, randomly distributed hyperechoic lesions in both kidneys (b and c)
the most common presenting feature of MMPH as well. The biological behavior of MMPH is characterized by the absence of cellular and nuclear atypia.\textsuperscript{[6]} There is neither a tendency to invade the adjacent structures nor of progression.\textsuperscript{[6]}

MMPH is usually described in association with LAM in TSC patients, both males and females.\textsuperscript{[7]} The lesions of MMPH, however, may be seen in the absence of LAM in premenopausal or postmenopausal women with TSC or women with sporadic LAM. Rarely, MMPH may be seen in patients without TSC.\textsuperscript{[7]} The common clinical features include a dry cough, moderate exertional dyspnea, and asymptomatic to moderate hypoxemia.\textsuperscript{[8]}

Radiologically, the nodules of MMPH are diffusely and randomly (with respect to secondary pulmonary nodule) distributed.\textsuperscript{[8]} However, there is a slight predilection for periphery and upper lobes, but these nodules do not spare the bases, unlike Langerhans cell histiocytosis. MMPH is present bilaterally, and lesions are well-defined, noncalcified, and generally measure 1–8 mm.\textsuperscript{[8]} They may present with ground glass attenuation or may be solid or may even show a reversed halo configuration.\textsuperscript{[2]}

Common differentials include miliary tuberculosis (has presence of constitutional symptoms and lymphadenopathy), sarcoïd (skin manifestations and mediastinal lymphadenopathy), nodular stage of Langerhans cell histiocytosis (centrilobular nodules which progress to cystic change from apex downward, nodules present on inferior margins of affected lung), miliary metastasis (presence of a primary malignancy), and atypical adenomatoid hyperplasia (coexists with adenocarcinoma of lung, multicentricity is uncommon).\textsuperscript{[9]}

Diagnosis of MMPH in the numerous case series is based on the consideration of clinical findings of TSC; however, case reports describe video-assisted lung biopsy for the diagnosis.\textsuperscript{[6,8,9]} In our case, biopsy was denied by the patient. The diagnosis of MMPH in our case was thus based on the presence of clinical and imaging features of TSC along with no change on follow-up imaging. This approach may thus obviate the need for biopsy.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Yashant Aswani, Bhakti Gavai
Department of Radiology TNMC and BYL Nair Charitable Hospital, Mumbai, Maharashtra, India
E-mail: aswanyashant@gmail.com

REFERENCES

1. Franz DN, Brody A, Meyer C, Leonard J, Chuck G, Dabora S, et al. Mutational and radiographic analysis of pulmonary disease consistent with lymphangioleiomyomatosis and micronodular pneumocyte hyperplasia in women with tuberous sclerosis. Am J Respir Crit Care Med 2001;164:661-8.
2. Suzuki K, Seyama K, Hayashi T, Yamashiro Y, Shiraishi A, Kuwatsuru R, et al. Reversed halo sign in tuberous sclerosis complex. Case Rep Radiol 2013;2013:428501.
3. Moss J, Avila NA, Barnes PM, Litzenberger RA, Bechtle J, Brooks PG, et al. Prevalence and clinical characteristics of lymphangioleiomyomatosis (LAM) in patients with tuberous sclerosis complex. Am J Respir Crit Care Med 2001;164:669-71.
4. Muzykewicz DA, Black ME, Muse V, Numis AL, Rajagopal J, Thiele EA, et al. Multifocal micronodular pneumocyte hyperplasia: Computed tomographic appearance and follow-up in tuberous sclerosis complex. J Comput Assist Tomogr 2012;36:518-22.
5. Wataya-Kaneda M, Tanaka M, Hamasaki T, Katayama I. Trends in the prevalence of tuberous sclerosis complex manifestations: An epidemiological study of 166 Japanese patients. PLoS One 2013;8:e63910.
6. Kobashi Y, Yoshida K, Miyashita N, Niki Y, Matsushima T, Iriy T, et al. Multifocal micronodular pneumocyte hyperplasia in a man with tuberous sclerosis. Intern Med 2005;44:462-6.
7. Miravet Sorribes L, Mancheño Franch N, Batalla Bautista L. Multifocal micronodular pneumocyte hyperplasia in a patient with tuberous sclerosis. Arch Bronconeumol 2013;49:36-7.
8. Ristagno RL, Biddinger PW, Pina EM, Meyer CA. Multifocal micronodular pneumocyte hyperplasia in tuberous sclerosis. AJR Am J Roentgenol 2005;184:537-9.
9. Sun Q, Cai HR, Mark EJ, Miao LY, Wu HY, Zhou Q, et al. Multifocal micronodular pneumocyte hyperplasia in a Chinese man masquerading as miliary tuberculosis. Int J Clin Exp Pathol 2015;8:2165-70.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Access this article online

Quick Response Code:  
Website: www.lungindia.com  
DOI: 10.4103/lungindia.lungindia_398_17

How to cite this article: Aswani Y, Gavai B. Multifocal micronodular pneumocyte hyperplasia: A “touch-me-not” pulmonary lesion in tuberous sclerosis complex. Lung India 2018;35:445-6.