Case Report

A Case of Micronodular Pneumocyte Hyperplasia Diagnosed through Surgical Resection

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Micronodular pneumocyte hyperplasia (MNPH) is often associated with tuberous sclerosis complex and/or lymphangioleiomyomatosis. We present the case of a 45-year-old woman with MNPH without evidence of either. A preoperative high-resolution chest computed topographic scan demonstrated a ground-glass opacity 8 mm in diameter that revealed the possibility of atypical adenomatous hyperplasia (AAH) or bronchioloalveolar carcinoma (BAC). Therefore an S3 segmentectomy of the right lung was performed, and the specimens revealed the characteristic histological and immunohistological features of MNPH. Solitary MNPH is extremely rare and requires to be distinguished from AAH or BAC on a computed tomographic scan; therefore surgical resection may be required to definitely rule out malignancy. (Ann Thorac Cardiovasc Surg 2010; 16: 45–47)

Key words: micronodular pneumocyte hyperplasia, atypical adenomatous hyperplasia, ground-glass opacity

Introduction

Micronodular pneumocyte hyperplasia (MNPH) is described as an extremely rare pulmonary manifestation of tuberous sclerosis complex (TSC).[1,2] Furthermore, most patients with MNPH in TSC is associated with lymphangioleiomyomatosis (LAM).[3,4] In this report we describe a case of MNPH without association with them whose resected specimen showed the characteristic histological and immunohistological features of MNPH.

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Case Report

A 45-year-old female was incidentally discovered to have a solitary right lung nodule during a computed tomographic (CT) scan of the chest for medical checkup. A high-resolution CT scan demonstrated a ground-glass opacity (GGO) 8 mm in diameter, which revealed the possibility of atypical adenomatous hyperplasia (AAH) or bronchioloalveolar carcinoma (BAC) (Fig. 1). She had no history of other diseases. Hematological and biochemical tests were unremarkable. To rule out malignancy, we performed a video-assisted thoracotomy. Because the tumor was not palpable, an S3-segmentectomy of the right lung was performed.

The specimens showed that a separate yellow-white nodule, 5 mm in diameter, was identified in the right upper lobe of the lung (Fig. 2). Histologically, the nodule had a comparatively clear margin and was composed of a proliferation of benign type II pneumocytes with fibrous thickening of alveolar septa and aggregations of macrophages in the alveolar lumens (Fig. 3). Immunohistochemical stains showed reactivity for epithelial membrane antigen

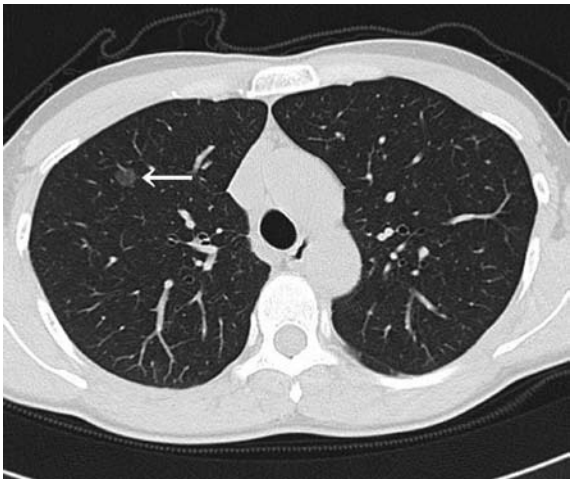


Fig. 1. Computed tomographic scan of chest showing a ground-glass opacity 8 mm in diameter (arrow).

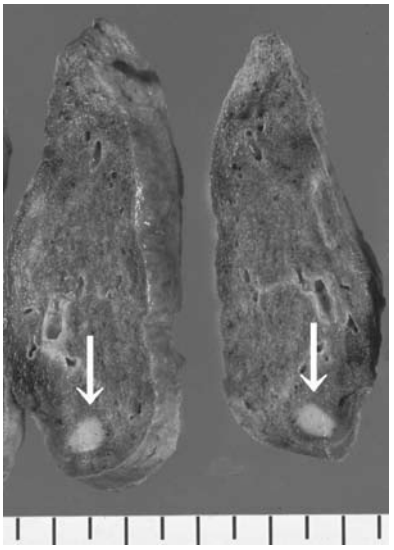


Fig. 2. The cut surface of the removed specimens shows separate yellow-white nodules 5 mm in diameter (arrows).

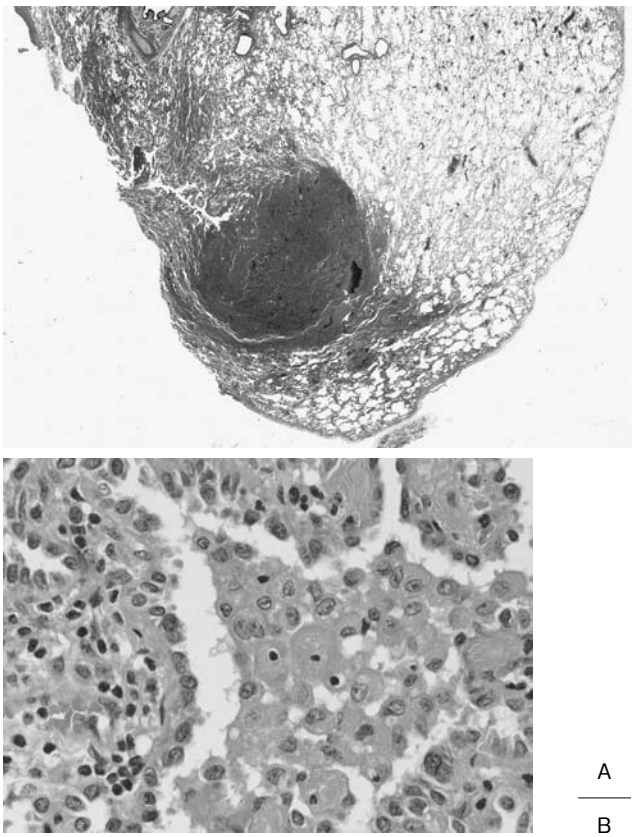
(EMA), cytokeratin, and surfactant apoprotein A, but not homatropine methylbromide 45 (HMB-45), carcinoembryonic antigen (CEA), p53, or desmin, which were characteristic features of MNPH. The background of the lung revealed no significant change.

Postoperative systemic screening examinations for TSC revealed no abnormalities. She is doing well 12 months postoperatively.

Discussion

We present here a case of MNPH that could definitely be diagnosed after surgical resection. MNPH has been reported to be a pulmonary manifestation of TSC, which presents with multiple, diffuse pulmonary nodules on chest roentgenogram or high-resolution CT scan because of multifocal nodular proliferation of alveolar type II cells.[5] Solitary MNPH is rare; therefore our patient was initially suspected to be a case of AAH or BAC, which may present with solitary GGO. In our case, immunohistological analysis revealed no features of LAM. Although MNPH in patients with TSC is reported to be associated with LAM, Muir et al. reported that 2 of 14 patients with MNPH had neither TSC nor LAM, indicating that MNPH can occur outside of TSC.[1]

For a pathological differential diagnosis, AAH, so-called sclerosing hemangioma, BAC should be included.[6] In our case, the diagnosis of MNPH was confirmed by a proliferation of type II pneumocytes without the typical nuclear atypia and aggregations of macrophages in the alveolar lumens. AAH typically consists of epithelial cells with



A

B

Fig. 3. Histopathological findings of the nodule consist of a proliferation of benign type II pneumocytes with fibrous thickening of alveolar septa and aggregations of macrophages in the alveolar lumens. (hematoxilin and eosin stain, magnification; **A**: ×10, **B**: ×600)

nuclear atypia and a high nuclear-to-cytoplasmic ratio, and it shows alveolar structure with no intra-alveolar macrophages other than MNPH. Furthermore, MNPH shows no invasion into the blood or lymphatic vessels.[7] Whereas MNPH cells show no immunoreactivity for CEA, desmin, or HMB-45, AAH shows immunoreactivity for CEA and p53.[8] Therefore we could clearly distinguish MNPH from AAH in our case.

TSC is an autosomal dominant genetic disease characterized by the triad of mental retardation, seizures, and facial angiofibroma.[1] This case had none of them. Because the central nervous system, kidney, heart, and lung are often involved in patients with TSC, we performed systemic screening examinations such as magnetic resonance imaging (MRI) of the head and CT of the abdomen postoperatively to rule out TSC or LAM, which revealed no abnormalities. Although there is no evidence that MNPH is preneoplastic,[9] we will follow up this patient to find other pulmonary tiny nodules that MNPH often develops on high-resolution CT scans of the chest every year for several years.

In conclusion, we report a case of MNPH without evidence of TSC and LAM, diagnosed after surgical resection. Solitary MNPH requires to be distinguished from AAH or BAC on a CT scan; therefore the surgical resection may have an important role in the diagnosis of the pulmonary nodule, including rare diseases the same as or similar to the one our patient has.

References

1. Muir TE, Leslie KO, Popper H, Kitaichi M, Gagné E, et al. Micronodular pneumocyte hyperplasia. *Am J Surg Pathol* 1998; **22**: 465–72.
2. Maruyama H, Ohbayashi C, Hino O, Tsutsumi M, Konishi Y. Pathogenesis of multifocal micronodular pneumocyte hyperplasia and lymphangioleiomyomatosis in tuberous sclerosis and association with tuberous sclerosis genes TSC1 and TSC2. *Pathol Int* 2001; **51**: 585–94.
3. Wu K, Tazelaar HD. Pulmonary angiomyolipoma and multifocal micronodular pneumocyte hyperplasia associated with tuberous sclerosis. *Hum Pathol* 1999; **30**: 1266–8.
4. Flieder DB, Travis WD. Clear cell "sugar" tumor of the lung: association with lymphangioleiomyomatosis and multifocal micronodular pneumocyte hyperplasia in a patient with tuberous sclerosis. *Am J Surg Pathol* 1997; **21**: 1242–7.
5. Franz DN, Brody A, Meyer C, Leonard J, Chuck G, et al. Mutational and radiographic analysis of pulmonary disease consistent with lymphangioleiomyomatosis and micronodular pneumocyte hyperplasia in woman with tuberous sclerosis. *Am J Respir Crit Care Med* 2001; **164**: 661–8.
6. Yamanaka A, Kitaichi M, Fujimoto T, Hirai T, Hori H, et al. Multifocal micronodular pneumocyte hyperplasia in a postmenopausal woman with tuberous sclerosis. *Virchows Arch* 2000; **436**: 389–92.
7. Lantuejoul S, Ferretti G, Negoescu A, Parent B, Brambilla E. Multifocal alveolar hyperplasia associated with lymphangioleiomyomatosis in tuberous sclerosis. *Histopathology* 1997; **30**: 570–5.
8. Popper HH, Juettner-Smolle FM, Pongratz MG. Micronodular hyperplasia of type II pneumocytes—a new lung lesion associated with tuberous sclerosis. *Histopathology* 1991; **18**: 347–54.
9. Kobashi Y, Yoshida K, Miyashita N, Niki Y, Matsushima T, et al. Multifocal micronodular pneumocyte hyperplasia in a man with tuberous sclerosis. *Intern Med* 2005; **44**: 462–6.