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CASE REPORT

Multifocal micronodular pneumocyte hyperplasia: A rare pulmonary manifestation of tuberous sclerosis

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Abstract

Multifocal micronodular pneumocyte hyperplasia (MMPH) is a rare pulmonary manifestation of tuberous sclerosis complex (TSC). Based on thoracic computed tomography (CT) findings, this pulmonary condition was suspected in a 50-year-old patient who presented without respiratory symptoms. The diagnosis was supported by the presence of characteristic ground-glass nodules and strong multisystemic extra-thoracic features suggestive of tuberous sclerosis complex. MMPH is a recently described entity characterized by benign hamartomatous proliferation of type II pneumocytes with no malignant potential. Imaging plays a crucial role in both the positive and differential diagnosis. Histological examination was not performed in this case, underscoring the efficacy of diagnostic imaging as a reliable tool for diagnosis. The aim of this report is to enhance the existing knowledge surrounding MMPH and its association with TSC, offering valuable insights for clinicians and researchers in the field.

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Introduction

Multifocal micronodular pneumocyte hyperplasia (MMPH) is a rare and under-recognized pulmonary manifestation of tuberous sclerosis complex (TSC). It involves benign hamartomatous proliferation of type II pneumocytes and is often associated with lymphangioleiomyomatosis (LAM) [1,2]. This report describes a case of MMPH, emphasizing the radiological features that facilitated diagnosis and discussing its implications in the broader context of TSC.

Case Report

A 50-year-old woman presented with multiple periungual fibromas over the past year. Biopsy of these lesions confirmed fibrokeratomas without malignancy (Fig. 1). Her medical history included refractory partial seizures, but no prior radiological or functional neurological evaluation had been conducted due to limited access to healthcare and neurological diagnostic resources. She exhibited no respiratory symptoms.

A thoracic computed tomography (CT) scan performed to investigate a potential phakomatosis, revealed multiple, well-circumscribed bilateral ground-glass nodular opacities (3–8 mm) predominantly in the upper lobes. Some lesions exhibited cavitation (Fig. 2).

Additionally, a well-defined, fatty-density lesion (-30 HU) in the right mid-basal parenchyma was consistent with a hamartoma (Fig. 3). No cystic involvement was found in our patient.

A diffuse osteosclerotic involvement affecting the axial and peripheral skeleton was also observed, characterized by multiple sclerotic foci of varying sizes, predominantly in the vertebral, costal, and sternal regions (Fig. 4).

High abdominal sections revealed the presence of an exophytic, lobulated, soft tissue mass in the mid-left kidney, without a fatty component, measuring 20 mm in diameter, and enhancing after contrast injection, suggesting an oncocytoma (Fig. 5).

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Figure 1. Periungual fibromas associated with keratotic lesions of the nail matrix.

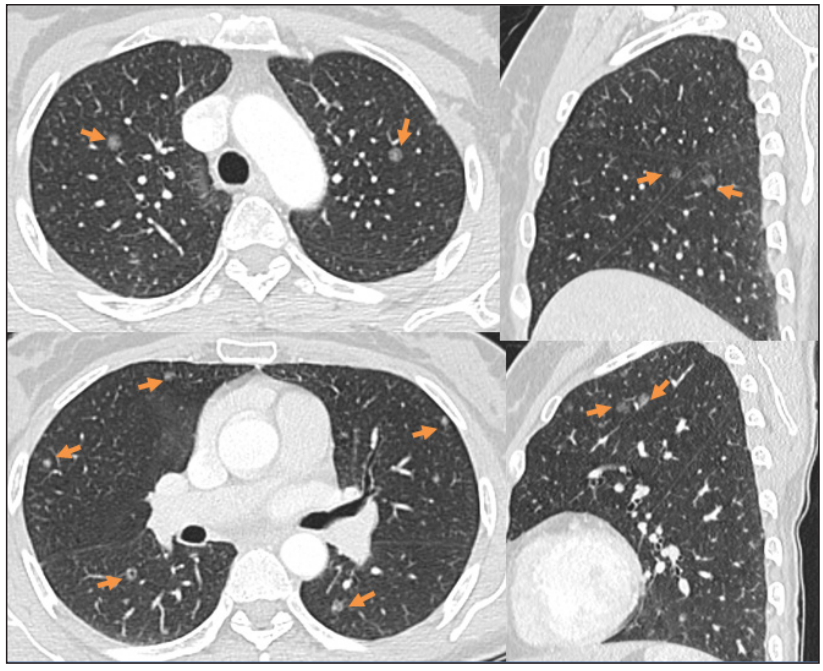


Figure 2. Thoracic CT scan in parenchymal window with axial and sagittal sections showing multiple bilateral intraparenchymal ground-glass nodules predominantly in the peripheral upper lobes (arrows).

Given the polymorphism and heterogeneity of the lesions, along with the history of refractory epilepsy, TSC was suspected. A brain MRI was performed to search for neurological involvement supporting the diagnosis. The MRI revealed multiple subependymal nodules showing signal void on susceptibility-weighted imaging and intense enhancement after gadolinium injection, along with supratentorial cortical and subcortical lesions that appeared hyperintense on T2 and FLAIR sequences, suggestive of cortical tubers (Fig. 6).

The combination of nodular pulmonary, ungual, renal, osseous, and neurological lesions is consistent with a diagnosis of tuberous sclerosis complex. This diagnosis was confirmed by the presence of major criteria in our patient, including ungual fibromas, cortical dysplasias, and subependymal nodules.

Considering the context, the ground-glass parenchymal nodular involvement was attributed to MMPH without requiring histological proof. A follow-up thoracic CT scan performed after six months showed stability in the size and number of nodules.

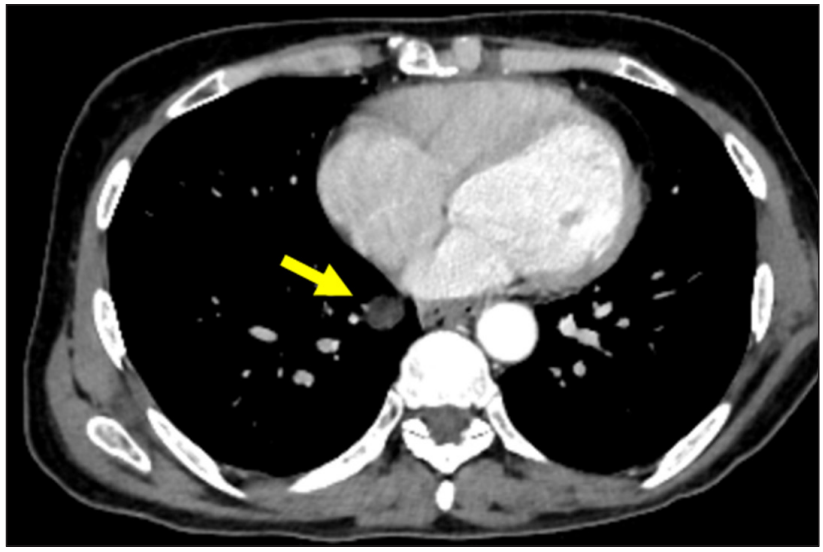


Figure 3. Thoracic CT scan with contrast in mediastinal window showing a well-defined, fatty-density lesion in the right mid-basal region consistent with a hamartoma (arrow).

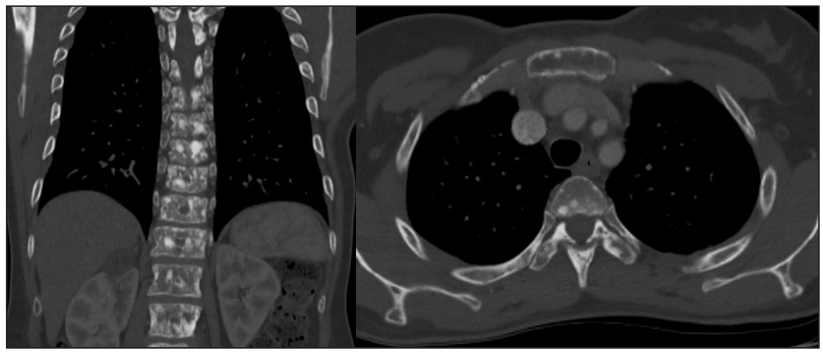


Figure 4. Thoracic CT scan in bone window with coronal and axial sections showing diffuse sclerotic involvement (vertebral, sternal, and costal).

Discussion

First described by Popper in 1991, MMPH represents one of the rarest manifestations of TSC. Unlike LAM, which features cystic smooth muscle proliferation, MMPH involves type II pneumocyte proliferation along the alveolar septa. Most patients with MMPH are asymptomatic or exhibit mild respiratory symptoms, such as a dry cough or exertional dyspnea.

MMPH is generally described in association with LAM in patients with TSC. However, this condition can also be observed in the absence of LAM in premenopausal or postmenopausal women with TSC [3]. Isolated involvement has also been reported in patients who do not have TSC or LAM. Clinically, patients are often pauci-symptomatic, with the most common signs, including a dry cough, moderate exertional dyspnea, and sometimes asymptomatic to moderate hypoxemia [4,5].

High-resolution thoracic CT reveals multiple bilateral pulmonary nodules, mostly ground-glass opacities, well-defined, noncalcified, and measuring 1–8 mm in diameter. These nodules have a predilection for the upper and peripheral lobes without sparing the bases. The nodules may exhibit a solid component, a reversed halo sign, and cavitations [1,4]. In the literature, cases of MMPH without respiratory symptoms have indeed been documented, often showing similar CT findings characterized by bilateral ground-glass nodules [2].

The main differential diagnosis is atypical adenomatous hyperplasia (AAH); however, AAH tends to coexist with pulmonary adenocarcinoma and does not exhibit multicentricity [6]. The diagnosis is

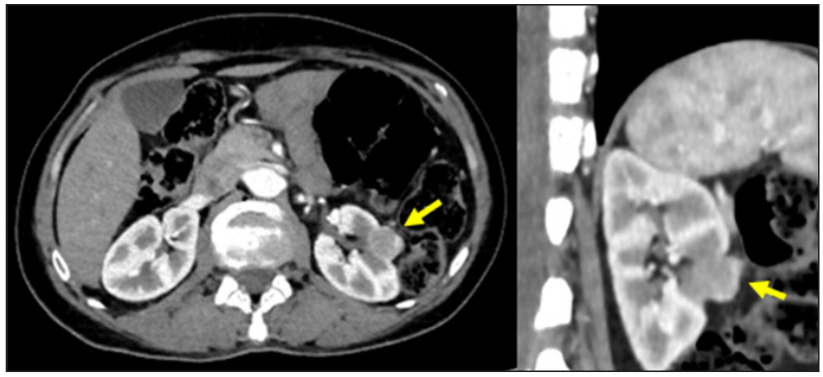


Figure 5. Axial and sagittal abdominal sections from thoracic CT scan showing an exophytic, contrast-enhanced mass in the mid-left kidney, consistent with an oncocytoma (arrow).

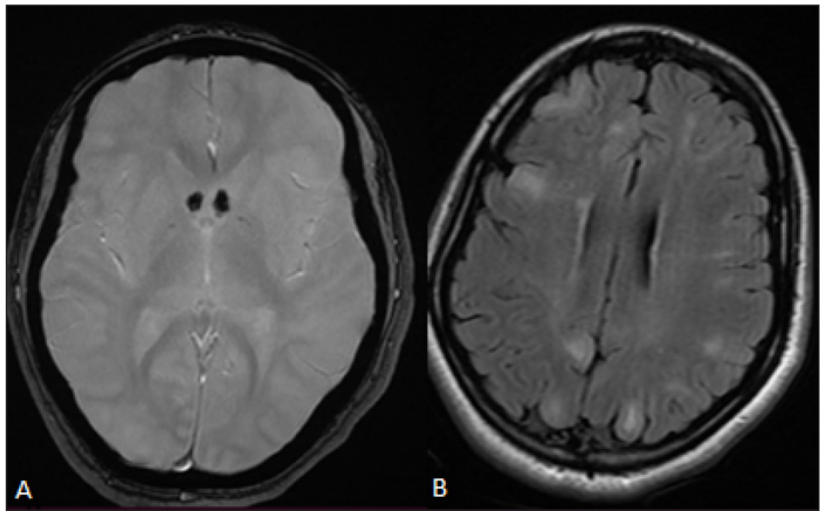


Figure 6. Brain MRI with T2*-weighted sequence (A) and T2 FLAIR (B) showing subependymal nodules with T2 signal voids indicative of calcifications, along with triangular peripheral-based cortical–subcortical FLAIR hyperintensities consistent with cortical tubers.

based on clinical, radiological, and histological data. Thoracoscopic lung biopsy confirms pneumocyte proliferation and fibrous thickening of the septa [4].

In the literature, there are documented cases of MMPH occurring alongside renal oncocytoma. This association is particularly relevant in the context of TSC, where both conditions can manifest due to the underlying genetic mutations affecting cellular proliferation[2].

Additionally, the absence of respiratory symptoms despite multiple pulmonary nodules emphasizes the importance of considering asymptomatic presentations of MMPH.

The role of hamartomas in this case underscores the diagnostic value of imaging in identifying benign proliferative processes associated with TSC.

The performance of a brain MRI in this case was crucial for evaluating potential neurological involvement associated with TSC. The MRI revealed multiple subependymal nodules, which are indicative of TSC, along with supratentorial cortical and subcortical lesions that appeared hyperintense on T2 and FLAIR sequences, suggestive of cortical tubers. These findings are significant as they correlate with the patient's history of refractory partial seizures.

The presence of multiple periungual fibromas in conjunction with seizures further supports the diagnosis of TSC. In such cases, performing a brain MRI can help ascertain the extent of neurological involvement and guide management strategies.

The diagnosis of MMPH in this patient was established based on characteristic imaging findings,

clinical context, and the stability of the pulmonary nodules observed on follow-up imaging, thereby obviating the need for invasive procedures such as a pulmonary biopsy. Avoiding a pulmonary biopsy not only reduces patient risk associated with invasive procedures but also streamlines the diagnostic process. This case illustrates that in certain clinical scenarios, especially with benign conditions like MMPH, imaging can serve as a reliable diagnostic tool.

Conclusion

This case highlights the diagnostic significance of imaging in identifying MMPH, particularly in the context of TSC. The avoidance of invasive diagnostic procedures, such as biopsy, underscores the potential for imaging to serve as a definitive diagnostic tool. Clinicians should consider MMPH in asymptomatic patients presenting with characteristic radiological findings and features of TSC.

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