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Management of Pulmonary Manifestations in Tuberous Sclerosis Complex: A Case Report

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Abstract

Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem disorder resulting from mutations in the TSC1 or TSC2 genes, leading to constitutive activation of the mammalian target of rapamycin (mTOR) pathway and uncontrolled hamartomatous proliferation. Pulmonary manifestations represent an important but often under-recognized component of the disease spectrum. We report a 53-year-old male with longstanding TSC who developed radiologically evident multifocal micronodular pneumocyte hyperplasia (MMPH), a benign pulmonary lesion that may mimic more aggressive interstitial pathology. Serial high-resolution computed tomography (HRCT) over two years demonstrated stability of the nodules without cystic evolution or physiologic impairment. The patient was managed conservatively through clinical and radiologic surveillance, with favorable outcomes. This case highlights the critical distinction between MMPH and lymphangioleiomyomatosis (LAM) and emphasizes the value of accurate radiologic characterization and multidisciplinary follow-up.

Keywords: Tuberous sclerosis complex; Micronodular pneumocyte hyperplasia; Lymphangioleiomyomatosis; mTOR pathway; Pulmonary hamartoma; Case report

Introduction

Tuberous sclerosis complex is a hereditary multisystem neurocutaneous disorder with an autosomal dominant inheritance pattern, characterized by loss of function mutation in either the TCS1 or TCS2 genes, which encode tumour suppressor proteins that regulate the mammalian target of rapamycin (mTOR) pathway [1,2]. This results in constitutive mTOR activity, increased cell proliferation and the characteristic hamartoma growths in the heart, brain, skin, lungs and kidneys [3,4]. Epidemiologic studies estimate a prevalence of 1 in 6,000 to 1 in 10,000 live births, with equal sex distribution at birth but a female predominance for pulmonary disease [5,6]. Pulmonary manifestations occur in up to 40–50% of adults with TSC and are typically of two major types: lymphangioleiomyomatosis (LAM) and multifocal micronodular pneumocyte hyperplasia (MMPH) [7,8]. LAM is a progressive, cystic lung disease characterized by abnormal smooth-muscle-like cell proliferation, leading to airflow obstruction, chylous effusions, and respiratory failure [9,10]. In contrast, MMPH is a benign lesion consisting of nodular aggregates of type II pneumocytes lining alveolar septa, usually stable over time and frequently discovered incidentally on CT [11,12]. The molecular phenotype correlates with clinical severity; TSC2 mutations are associated with more extensive pulmonary involvement and systemic disease [13,14]. Although LAM is almost exclusively seen in women, MMPH can occur in both sexes and should be considered in any patient with TSC and new nodular changes on imaging [15]. This report describes a male patient with TSC and radiologically confirmed MMPH. The case illustrates the value of structured diagnostic reasoning, longitudinal surveillance, and multidisciplinary coordination in distinguishing benign pulmonary lesions from progressive cystic disease.

Case Report

A 53-year-old man with a known diagnosis of TSC was referred by his general practitioner to the respiratory outpatient clinic for

assessment of gradually progressive exertional dyspnoea and a chronic dry cough. A recent CT pulmonary angiogram (CTPA) performed prior to referral showed new bilateral ground-glass opacities and scattered pulmonary nodules, raising concern for an evolving interstitial process. The patient denied fever, hemoptysis, chest pain, or weight loss.

Past medical history

He was diagnosed with TSC at the age of 8 based on characteristic dermatologic and neurologic findings but had never undergone genetic testing to determine the specific mutation. He had well-controlled epilepsy, multiple renal angiomyolipomas, regressed cardiac rhabdomyomas, and cutaneous manifestations including facial angiofibromas and a large shagreen patch over the lumbosacral region. He also had obstructive sleep apnoea treated with continuous positive airway pressure (CPAP), though adherence was inconsistent. He had ceased smoking ten years earlier (five pack-years). There was no occupational exposure to dust, asbestos, or volatile chemicals. There was a family history of TSC affecting his mother and brother, neither of whom had pulmonary disease.

Examination

The patient appeared comfortable at rest. His oxygen saturation on room air was 97%.

Cutaneous stigmata of TSC were prominent: a large shagreen patch over the lower back (Figure 1) and numerous facial angiofibromas over the cheeks and nasal bridge (Figure 2). No oral fibromas or periungual fibromas were noted. Chest examination revealed normal bilateral air entry without adventitious sounds; cardiac and abdominal examinations were unremarkable.

Investigations

Full blood count, urea and electrolyte panel, liver function test, and inflammatory markers such as C-reactive protein were within normal ranges. Serum vascular endothelial growth factor D, used as biomarker for LAM, was not elevated. Pulmonary function testing demonstrated normal spirometry, lung volumes, and diffusing capacity, confirming preserved respiratory function. Echocardiography showed normal biventricular function without pulmonary hypertension. A repeat high-resolution CT chest (HRCT) performed three months later showed resolution of ground-glass opacities but persistence of multiple discrete, well-defined nodules (2–8 mm) scattered in both lungs. The nodules were randomly distributed without a perilymphatic pattern. There was no evidence of cystic change, fibrosis, or lymphadenopathy, and the pleural surfaces were intact. Repeat HRCT at twelve months demonstrated radiological stability, confirming a diagnosis of MMPH (Figure 3).

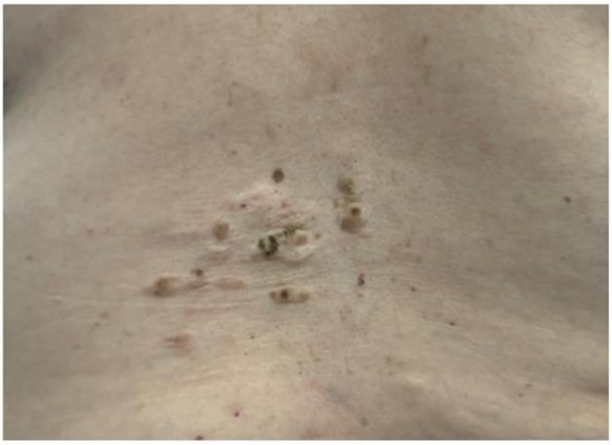

Figure 1: *Shagreen patch located over the lower back. The lesion appeared as a firm, slightly raised, irregular plaque with a leathery texture, typical of connective-tissue hamartoma associated with TSC.*

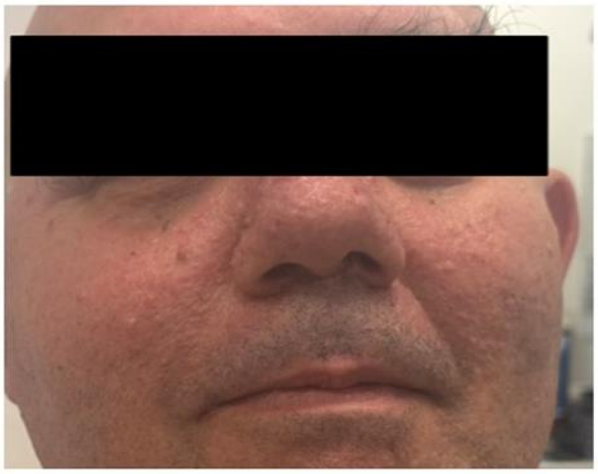

Figure 2: *Facial angiofibromas over the nasal bridge and cheeks. These presented as multiple erythematous papules consistent with fibrovascular proliferations common in TSC.*

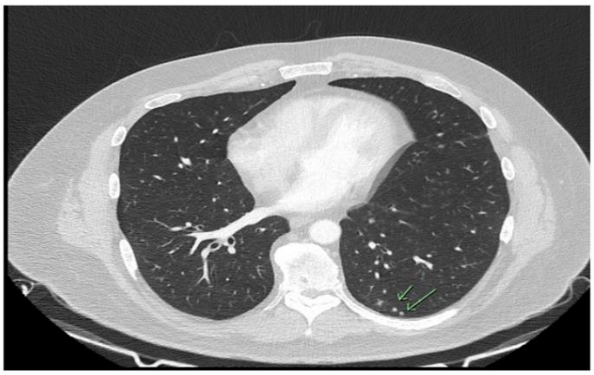

Figure 3: *Multiple micronodular opacities in a random distribution (green arrows), without cystic change or fibrosis, consistent with MMPH.*

Management and outcome

The patient was managed conservatively with annual HRCT, pulmonary function testing, and multidisciplinary follow-up. Reinforcement of CPAP compliance, renal ultrasound surveillance, and dermatologic review were undertaken. At two years, he remained clinically and radiologically stable.

Discussion

This case highlights the value of systematic evaluation and longitudinal monitoring of pulmonary manifestations in patients with tuberous sclerosis complex (TSC). Pulmonary disease in TSC encompasses a spectrum ranging from MMPH to LAM. which have different pathophysiology, disease progression and management strategies [1,2,4].

Table 1: *Differential Diagnosis of Pulmonary Findings in TSC.*

Condition	MMPH	LAM	Metastatic Nodules	Infective Granulomas
Radiological pattern	Multiple, randomly distributed 2–8 mm ground-glass or solid nodules without cysts	Diffuse thin-walled cysts of variable size throughout both lungs	Variable-sized nodules, often peripheral, may cavitate or enhance	Centrilobular nodules with tree-in-bud pattern or consolidation
Clinical course and key feature	Benign, non-progressive; often asymptomatic; normal PFTs	Progressive; may cause pneumothorax, chylothorax; responds to mTOR inhibitors	Depends on primary tumour; often accompanied by systemic symptoms	May resolve with antimicrobial therapy; positive microbiologic findings

MMPH is characterized as a benign nodular hyperplasia of type II pneumocytes in alveola septa. Histologically, lesions comprise of enlarged type II cells with ovoid nuclei and intranuclear vacuoles, as well as associated macrophages, interstitial thickening and lymphocytic infiltrates. Clinically, these lesions are stable and typically asymptomatic [4,5,7]. Conversely, LAM is a progressive cystic disease characterized by diffuse proliferation of smooth muscle-like cells infiltrating and degrading lung parenchyma [4,6]. This leads to typical presentations of worsening dyspnoea, spontaneous pneumothorax and airflow limitation [8-10]. Radiologically, differentiation is critical, and high-resolution computed tomography (HRCT) is the best modality of choice for imaging. MMPH can be identified by multiple discrete bilateral solid and ground glass nodules in a random distribution pattern without cystic changes [11,12]. LAM however, is characterized by multiple thin-walled cysts diffusely distributed bilaterally [13,14]. This patient's stable radiologic pattern, normal VEGF-D, and preserved lung function confirmed MMPH, negating the need for mTOR inhibitor therapy. Conservative management with serial imaging and functional surveillance was appropriate and consistent with current guidelines [13,14].

Genetic and Molecular Context

TSC specifically involves mutations in either the TSC1 gene on chromosome 9q34 and TSC2 gene on chromosome 16p13.3, which encode the hamartin and tuberin proteins respectively. The physiological role of these proteins involves forming a regulatory complex that inhibits the mTOR pathway as a method of tumour suppression. Consequently, loss of function mutation that result from TSC leads to hyperactivation of the mTOR pathway, causing unchecked growth and the formation of hamartomas [15,16]. Between the two variants, mutations in TSC2 are associated with more severe disease states, including pulmonary manifestations [17]. Although our patient's genetic subtype remains undetermined, his benign pulmonary course suggests either limited expression or a milder genotype. Current recommendations support offering genetic testing to all adults with TSC to refine prognostication and identify candidates for targeted therapy [18,19].

Management principles

No specific pharmacologic therapy is recommended for isolated MMPH. mTOR inhibitors (sirolimus or everolimus) have shown efficacy in halting lung function decline in LAM but have only anecdotal benefit for MMPH [20-22]. Their use should therefore be limited to cases with progressive disease or when systemic TSC manifestations warrant them. As such, only conservative follow up with serial imaging is needed for continued management. A multidisciplinary approach is of importance here, involving multiple specialists including respiratory physicians, neurologists, nephrologists, dermatologists, and genetic counsellors, to assess and manage other concurrent manifestations of TSC [23].

Prognosis

The prognosis of MMPH is generally excellent. Most cases remain radiologically and clinically stable over many years [24]. In contrast, LAM may progress to respiratory failure, occasionally requiring lung transplantation [25,26]. Our patient's two-year stability supports the benign nature of MMPH and reinforces the

appropriateness of conservative management with yearly follow-up.

Conclusion

Tuberous sclerosis complex is a heterogeneous disorder requiring lifelong, multidisciplinary management. Pulmonary involvement must be carefully characterized to distinguish benign from progressive disease. MMPH, though rare, should be recognized as a benign, stable manifestation that can be managed conservatively with imaging surveillance. This case underscores the need for tailored, evidence-based evaluation and vigilant long-term monitoring of respiratory manifestations in TSC.

Learning Points

- Pulmonary manifestations of TSC include MMPH and LAM, each with distinct clinical trajectories.
- Accurate differentiation between MMPH and LAM through imaging and functional testing is crucial to avoid overtreatment.
- MMPH generally follows a benign, stable course and does not necessitate pharmacologic therapy.
- Ongoing multidisciplinary surveillance remains the cornerstone of care for adults with TSC.

Author's Contributions

Dr Pranav Kumar: clinical diagnosis, management, conceptualization, manuscript drafting, and final approval.
Samya: literature review, data synthesis, critical manuscript revision, and final approval.
Both authors agree to be accountable for all aspects of the work.

References

1. Rout P, Thomas A. Tuberous Sclerosis. In: StatPearls. Treasure Island (FL): StatPearls Publishing. Pulmonary manifestations in tuberous sclerosis complex. PubMed. 2025.
2. De Waele L, Lagae L, Mekahli D. Tuberous sclerosis complex: the past and the future. Pediatr Nephrol. 2015; 30: 1771-1780.
3. Saxton RA, Sabatini DM. mTOR signaling in growth, metabolism, and disease. Cell. 2017; 168: 960-976.
4. Gupta N, Henske EP. Pulmonary manifestations in tuberous sclerosis complex. Am J Med Genet C Semin Med Genet. 2020; 184: 184-193.
5. Annals ATS. Pulmonary manifestations of TSC.
6. UpToDate. Tuberous sclerosis complex-associated lymphangioleiomyomatosis in adults.
7. Matsui K. Multifocal micronodular pneumocyte hyperplasia in TSC. Am J Respir Crit Care Med. 2000; 162: 1356-1360.
8. Radiopaedia.org. Multifocal micronodular pneumocyte hyperplasia.
9. McCormack FX, et al. Lymphangioleiomyomatosis: diagnosis and management. Chest. 2016; 150: 1059-1074.
10. American Thoracic Society. LAM clinical practice guideline. 2017.
11. Crino PB. Tuberous sclerosis complex: new insights into pathogenesis and treatment. Nat Rev Neurol. 2023.
12. Kingswood JC. International TSC clinical consensus guidelines update. Pediatr Neurol. 2022.
13. Johnson SR. ERS clinical practice guidelines for LAM. Eur Respir J. 2023.
14. European Respiratory Society. Guidelines for TSC-associated lung disease management. Eur Respir Rev. 2023.
15. OMIM Entry #191100 – Tuberous sclerosis 1; TSC1.
16. TSC2 gene. MedlinePlus genetics.
17. Mutations in TSC2 as a cause of tuberous sclerosis. PMC.
18. Genetics of tuberous sclerosis. Medscape reference.
19. Darling TN, Thiele EA, Moss J. TSC1 and TSC2 Genotype in tuberous sclerosis complex: Are other manifestations of this multisystem disease affected by genotype? Ann Am Thorac Soc. 2021; 18: 775-777.
20. Henske EP. mTOR signalling in TSC and LAM. J Clin Invest. 2021; 131: e150230.
21. McCormack FX, Inoue Y, Moss J, Singer LG, Strange C, Nakata K, et al. Efficacy and safety of sirolimus in LAM. N Engl J Med. 2011; 364: 1595-1606.
22. Bissler JJ. Everolimus for TSC manifestations. Lancet. 2013; 381: 817-824.
23. Cudzilo CJ. Comprehensive multidisciplinary care in TSC. Respir Med. 2020; 167: 105965.
24. Gupta N, Finlay GA, Young LR. TSC-associated pulmonary disease: clinical features and management. Respirol. 2022; 27: 183-196.
25. LAM Foundation. LAM clinical management guide. Cincinnati. 2023.
26. Crino PB, Northrup H. Tuberous sclerosis complex for the pulmonologist. Eur Respir Rev. 2024; 33: 240012.