A Rare Pulmonary Myoepithelial Tumor With Novel *TRPS1-PLAG1* Fusions

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Case Report

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Abstract

Background: Little is known about the morphological and molecular features of intra-thoracic myoepithelial tumors. Here, we describe a rare pulmonary myoepithelial tumor with novel *TRPS1-PLAG1* fusions.

Case presentation: A 30-year-old male presented with multiple lung nodules that detected by routine computed tomography (CT) scan 3 years ago. Positron emission tomography-computed tomography (PET-CT) demonstrated a well-circumscribed mass with a diameter of 3cm in the left pulmonary hilum and multiple nodules in bilateral lungs. No other extra-thoracic primary lesion and distant metastasis was found. The clinical history was not other specified. Microscopically, these lesions were well-defined, showed nodular growth pattern filling the bronchioles and alveoli. The tumor cells were epithelioid to plasmacytoid with slightly eosinophilic cytoplasm, arranged in aggregates, nests and cords. Myxoid background presented in some foci. Nuclear pleomorphism was mild and mitotic activity was not prominent. No distinct gland formation was identified. Immunostains demonstrated that the tumor cells were diffusely positive for pan-cytokeratin (AE1/AE3), CK5/6, S100, SOX10, and negative for calponin. Noticeably, a *TRPS1-PLAG1* gene fusion was identified in this tumor by targeted RNA sequencing involved *TRPS1* exon1 and *PLAG1* exon2, this rare rearrangement was validated by fluorescence in situ hybridization (FISH) for *PLAG1* break-apart probe, and 30% tumor cells showed break apart signals.

Conclusions: Here we present the first case of a disseminated thoracic myoepithelial tumor with novel *TRPS1-PLAG1* fusions. Targeted RNA sequencing strongly facilitates precise classification and providing opportunities for unknown fusion partner discovery, which is significant for risk stratification and development of potential therapeutic targets.

1. Introduction

Primary salivary gland-type tumors of the lungs are very rare, most of which occur in the central large bronchus, among them mucoepidermoid carcinoma (MEC) and adenoid cystic carcinoma (AdCC) are relatively common. The incidence of pulmonary myoepithelial neoplasms is extremely low and little is known about its morphological and genetic profile. Here, we present a rare pulmonary myoepithelial tumor with novel *TRPS1-PLAG1* fusions that detected by targeted RNA sequencing.

2. Case Presentation

A 30-year-old male presented with multiple lung nodules that detected by routine CT scan 3 years ago. During this period, regular CT follow-up showed no obvious progression of these lesions. PET-CT demonstrated a well-circumscribed mass with a diameter of 3 cm in the left pulmonary hilum and multiple nodules in bilateral lungs, F¹⁸ – FDG metabolism was increased in some lesions (Fig. 1). No other extra-thoracic primary lesion and distant metastasis was found by PET-CT. The clinical history was

not other specified. Due to the difficulty of complete removal of hilar mass, a diagnostic wedge resection of nodules in right middle and lower lobes was performed in May 2020.

2.1 Pathologic findings

Microscopically, these lesions were well-defined, showed nodular growth pattern filling the bronchioles and alveoli. Spreading into surrounding air spaces was occasionally seen. The tumor cells were epithelioid to plasmacytoid with slightly eosinophilic cytoplasm, arranged in aggregates, nests and cords. Myxoid background presented in some foci. Prominent lymphoplasmacytic infiltration was found in some nodules. Nuclear pleomorphism was mild and mitotic activity was not prominent. No distinct gland formation was identified (Fig. 2). Immunostains demonstrated that the tumor cells were diffusely positive for pan-cytokeratin (AE1/AE3), CK5/6, S100, SOX10, and negative for calponin. INI-1 (SMARCB1) nuclear expression in the tumor cells was intact.

2.2 Molecular findings

Noticeably, a *TRPS1-PLAG1* gene fusion was identified in this tumor by targeted RNA sequencing involved *TRPS1* exon1 and *PLAG1* exon2 (Fig. 3), this rare rearrangement was further validated by fluorescence in situ hybridization (FISH) for *PLAG1* break-apart probe, and 30% tumor cells showed break apart signals.

3. Discussion

TRPS1-PLAG1 gene fusion is a recently found novel fusion type in soft tissue myoepithelioma¹, uterine myxoid leiomyosarcoma^{2, 3}, and chondroid syringoma⁴. Leduc et al summarized 8 primary thoracic myoepithelial tumor, *EWSR1-PBX1*, *EWSR1-ZNF444*, and *FUS-KLF17* fusions were found in half of the cases, while no cases were found to harbor *HMGA2* or *PLAG1* abnormalities⁵. To the best of our knowledge, this case may represent the first thoracic myoepithelial tumor with *TRPS1-PLAG1* fusions.

As is known to us, *PLAG1* is one of the most common partners involved in pleomorphic adenoma/mixed tumor arising in salivary glands and skin. The detection of *TRPS1-PLAG1* fusions may be more favor the diagnosis of pleomorphic adenoma rather myepithelioma. While in this case, the young patient lack of the history of previous salivary pleomorphic adenoma or cutaneous chondroid syringoma. What is more, the resected specimen showed purely myoepithelial components without gland formation. Thus, this lesion may be pulmonary primary with intrathoracic dissemination, though metastasis of unknown primary origin could not be totally excluded. Clinically, this lesion disseminated into surrounding lung parenchyma, which showed more aggressive behavior than common myoepithelioma. The definitive relationship between the biology and this novel fusion partner is needed to be further investigated in additional cases.

In summary, here we present the first case of a disseminated thoracic myoepithelial tumor with novel *TRPS1-PLAG1* fusions. Integration of morphological, immunohistochemical and molecular investigations is necessary for the precise diagnosis and optimal clinical management of rare lung tumors. Targeted RNA sequencing strongly facilitates precise classification and providing opportunities for unknown fusion partner discovery, which is significant for risk stratification and development of potential therapeutic targets.

List Of Abbreviations

CT, computed tomography

PET-CT, Positron emission tomography-computed tomography

FISH, fluorescence in situ hybridization

MEC, mucoepidermoid carcinoma

AdCC, adenoid cystic carcinoma

PLAG1, pleiomorphic adenoma gene 1

TRPS1, tricho-rhinophalangeal syndrome gene 1

Declarations

Ethics approval and consent to participate

This study has been approved by institutional board of fudan university shanghai cancer center.

Consent for publication

Consent for publication has been obtained from the patient.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

SLL performed primary pathological analysis and immunostainings for this case. QZ and YL performed the pathological consultation and histological analysis of this case, and QZ was major contributor in writing the manuscript. QMB and XYZ performed molecular examination and explained the results. YW collected clinicopathological data and histological figures. All authors read and approved the final manuscript.

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Authors' information (optional)

Not applicable

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Figures

Figure 1

PET-CT showed a well-circumscribed mass in the left pulmonary hilum, with a diameter of 3cm (A). Multiple nodules were also found scattered in bilateral lungs with increased F18 –FDG metabolism (B).

Figure 2

Microscopically, the tumors showed nodular growth pattern extended into the bronchioles and alveoli (A). Spreading into surrounding air spaces was occasionally seen (B). The tumor cells were epithelioid to plasmacytoid with slightly eosinophilic cytoplasm, myxoid background presented in some foci (C and D). The tumor cells were positive for S100 (E) and SOX10 (F).