—Case Reports—

# A Case of Pulmonary Adenofibroma Treated by Thoracoscopic Resection

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Pulmonary adenofibroma is a rare biphasic tumor that contains epithelial and stromal components. We report a case of pulmonary adenofibroma in which the tumor was resected by thoracoscopic surgery and the diagnosis was established by histopathology. A 59-year-old woman with a past medical history of pyelonephritis visited our hospital for evaluation of an abnormal opacity on a plain chest x-ray during a comprehensive medical examination. A follow-up chest x-ray showed enlargement of the lesion, and the patient was referred to our department for further management. Chest computed tomography revealed a well-circumscribed nodule measuring 1.4 cm in diameter in the upper lobe of the left lung. The chest imaging findings suggested a benign tumor, but because of evidence of lesion enlargement and elevated serum carcinoembryonic antigen levels, we performed wide wedge resection of the left upper lobe by video-assisted thoracoscopic surgery, for diagnosis and treatment. The resected specimen was submitted for rapid pathological diagnosis during the operation, and a benign tumor, possibly sclerosing pneumocytoma, was suspected. Therefore, we completed the operation with wide wedge resection. The final histopathological diagnosis was pulmonary adenofibroma. The patient had an uneventful postoperative course, and at this writing, 6 months postoperatively, there has been no evidence of tumor recurrence. We have reported this case of pulmonary adenofibroma because the tumor is rare, has not yet been well-characterized, and has an unclear prognosis. Collection of data from a larger number of patients is necessary. (J Nippon Med Sch 2021; 88: 564–568)

**Key words:** pulmonary adenofibroma, lung tumor, video-assisted thoracoscopic surgery, immunohistochemistry

## Introduction

Pulmonary adenofibroma is a rare biphasic tumor containing epithelial and stromal components. The cause and prognosis of this tumor are unclear. We report a case of pulmonary adenofibroma in which the tumor was resected by thoracoscopic surgery and the diagnosis was established by histopathology. To our knowledge, this is the first case of pulmonary adenofibroma reported in Japan.

## Case Presentation

A 59-year-old woman with a past medical history of pyelonephritis visited our hospital for evaluation after an abnormal opacity was found on a plain chest x-ray during a comprehensive medical examination. She had no history of smoking. A follow-up chest x-ray showed evidence of lesion enlargement, and she was thus referred to our department for further management. The plain chest x-ray showed a subpleural nodule in the left middle lung field (**Fig. 1**). Chest computed tomography revealed a well-circumscribed nodule measuring 1.4 cm in diameter in the upper lobe of the left lung, and fluorodeoxyglucose positron emission tomography (FDG-PET) revealed no uptake in the lesion (**Fig. 2**).

Hematological and other laboratory examinations revealed no significant abnormalities, except for elevation of serum carcinoembryonic antigen (CEA) to 13.7 ng/mL. Chest imaging findings suggested a benign tumor, but

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because of evidence of lesion enlargement and elevation of serum CEA, we performed surgery for both diagnosis and treatment. A smooth tumor was palpable in the left upper lobe, and a wide wedge resection was performed under video-assisted thoracoscopic guidance. The resected specimen was submitted for rapid pathological diagnosis during the operation, and a benign tumor, possibly sclerosing pneumocytoma, was suspected. Therefore, we completed the operation with wide wedge resection. The operative time and estimated blood loss were 75 min and 15 mL, respectively. Histopathological examination showed a well-defined white mass (12 × 11 mm) in the left upper lobe. Cubic epithelial cells forming tubular glandular structures in a myxomatous stroma were seen (**Fig. 3**). Immunohistochemically, the epithelial component showed positive staining for cytokeratin (CK) 7, thyroid transcription factor 1 (TTF-1), and Napsin A, partially positive staining for estrogen receptor (ER), and negative staining for progesterone receptor (PR). The surrounding stromal component showed positive staining for smooth muscle actin, cluster of differentiation (CD) 34, CD 99, bcl-2, and single transducer and activator of transcription 6 (STAT6), and partially positive staining for desmin, ER, and PR (**Fig. 4**). On the basis of these findings, the tumor was diagnosed as a pulmonary adenofibroma.

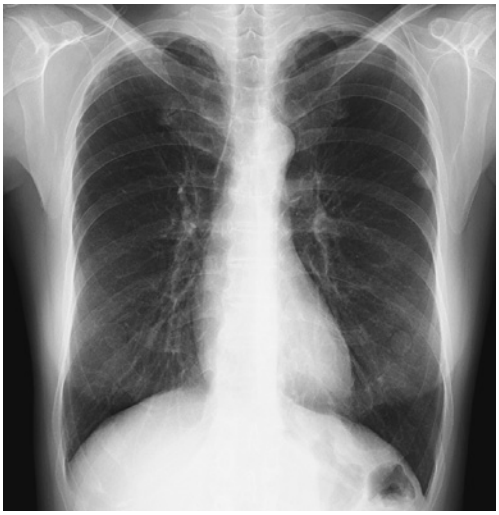

Fig. 1 Chest X-ray image showing a subpleural nodule in the left middle lung field.

The patient's postoperative course was uneventful, and she was discharged on the 4th postoperative day. At this writing, 6 months postoperatively, there has been no evidence of recurrence.

## Discussion

Pulmonary adenofibroma is a rare benign tumor, in which epithelial and stromal components proliferate with formation of lobe-like structures. The cause is unknown. Adenofibroma of the lung was reported to be morphologically similar to adenofibroma of the female genital tract and fibroadenoma of the breast[1,2].

Adenofibroma of the lung was first reported by Scarff and Gower[1], in 1944, as "fibroadenoma of the lung". Since then, there have been about 20 case reports, but the exact number of cases is unclear because the disease nomenclature is not yet established. However, it is undoubtedly extremely rare, and to our knowledge, there have been no previous case reports of adenofibroma of the lung in Japan.

A diagnosis of pulmonary adenofibroma is usually confirmed by histopathology. It is a biphasic tumor containing epithelial and stromal components. Complex, non-necrotic glandular structures are lined by simple cubic or columnar epithelium, within a stromal component

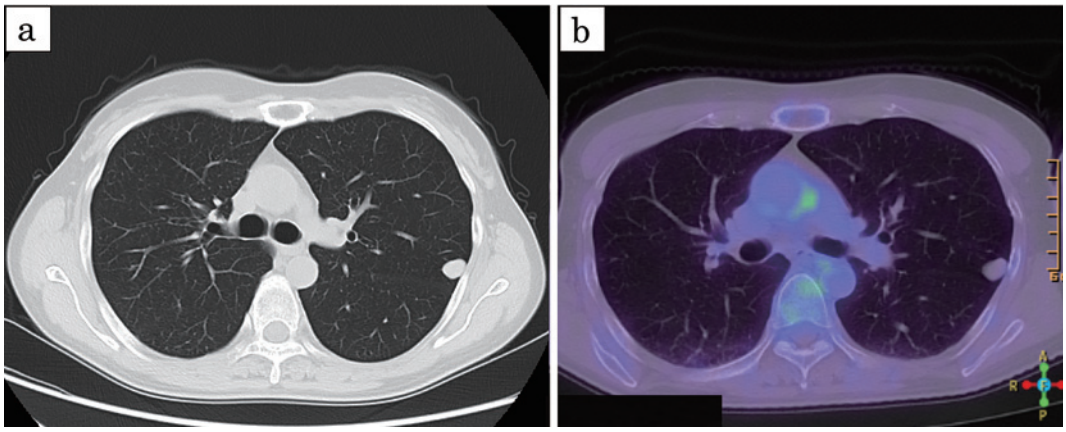


Fig. 2 Chest CT scan showing a well-circumscribed nodule in the upper lobe of the left lung (a). FDG-PET revealed no uptake in the lesion (b).

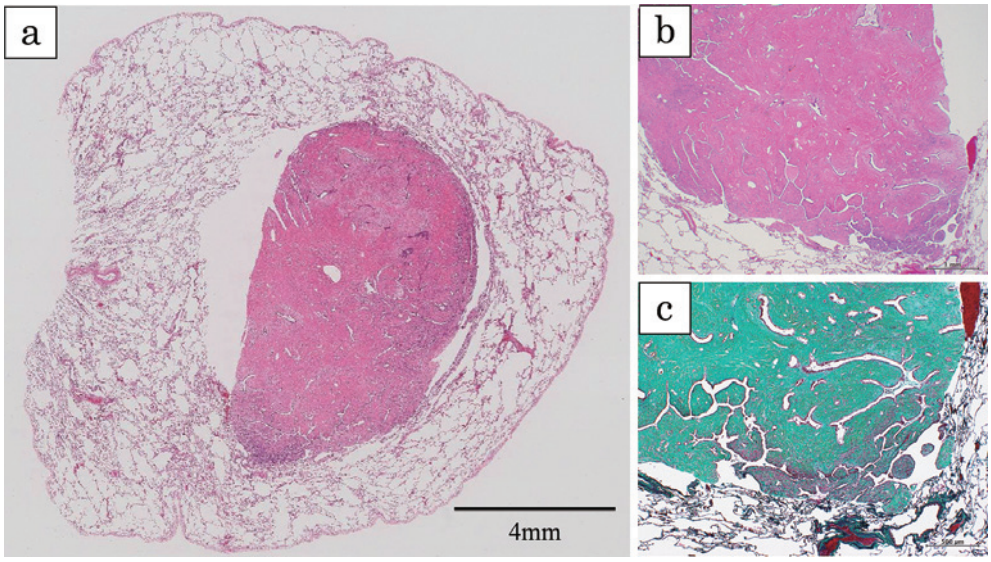


Fig. 3 Histopathological examination showed a well-defined mass measuring 12 × 11 mm (a). Cubic epithelial cells forming tubular glandular structures in a myxomatous stroma were seen (b, c).
a) Hematoxylin-eosin stain (low-power field)
b) Hematoxylin-eosin stain (high-power field)
c) Elastica Masson-Goldner stain (high-power field)

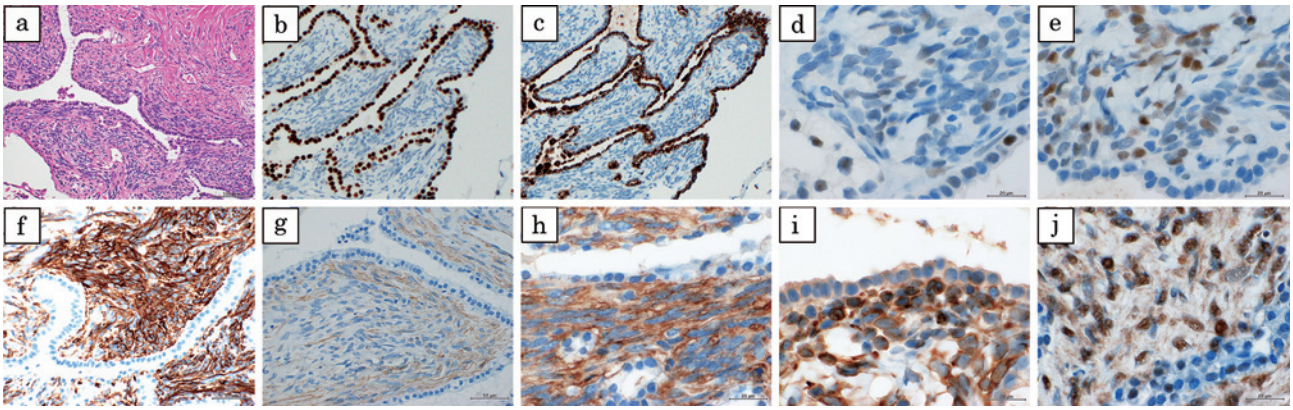


Fig. 4 Immunohistochemical findings.
Hematoxylin-eosin stain (a). The epithelial component showed positive staining for TTF-1 (b) and Napsin A (c) and partially positive staining for ER (d). The stromal component showed positive staining for CD34 (f), SMA (g), CD99 (h), bcl-2 (i) and STAT6 (j) and weak positive staining for ER (d) and PR (e).

of spindle cells. Diagnosis is based on morphologic and immunohistochemical features. We identified 14 detailed reports of cases of pulmonary adenofibroma in the English-language literature[1–14]. **Table 1** shows the results of immunostaining of 23 cases, including our case. Immunohistochemically, the epithelial component often shows positive staining for epithelial markers such as CK, TTF-1, epithelial membrane antigen, and Napsin A, and the stromal component often shows positive staining for mesenchymal markers, such as vimentin and CD34. According to Fusco et al.[11], positive staining of the stromal component for ER and PR was seen in 71% of cases (5/7), which suggests that pulmonary adenofibroma might be hormone-related. Fusco et al.[11] also proceeded with genetic studies of the stromal components and identified a fusion gene of NAB2 exon 4-STAT6 exon 2 in 71% of cases (5/7). The authors hypothesized that pulmonary adenofibroma is a histological variant of an intrapulmonary solitary fibrous tumor. The histopathological findings and immunohistochemical findings in our case, including positive staining for STAT6, were consistent with those of previous reports.

Table 1 Literature review of immunohistochemical findings of pulmonary adenofibroma

| No. | Authors | Year | Age | Sex | Immunohistochemical findings | |
|---|---|---|---|---|---|---|
| | | | | | Epithelial component | Stromal component |
| 1 | Scarff RW et al. | 1944 | 24 | M | ND | ND |
| 2 | | | 66 | M | ND | ND |
| 3 | Suster S et al. | 1993 | 54 | F | CK, EMA | Vimentin |
| 4 | | | 56 | M | CK, EMA | Vimentin |
| 5 | Vitkovski T et al. | 2013 | 29 | F | CK, TTF-1 | Vimentin, Desmin |
| 6 | Wang Y et al. | 2013 | 55 | M | CK, EMA, TTF-1 | Vimentin, CD34 |
| 7 | Kumar R et al. | 2014 | 25 | M | CK, EMA, TTF-1 | Vimentin, CD34 |
| 8 | | 2014 | 40 | F | CK7, TTF-1, Napsin A | SMA |
| 9 | | 2014 | 55 | F | CK7, TTF-1, Napsin A | SMA |
| 10 | Braham E et al. | 2014 | 56 | M | EMA, TTF-1 | Vimentin, CD34 |
| 11 | Esmaeili H et al. | 2016 | 65 | F | CK | SMA, Vimentin, CD34 |
| 12 | Hao J et al. | 2016 | 57 | F | CK7, TTF-1, Napsin A | Vimentin, Desmin, SMA, h-CALD, ER, PR, bcl-2 |
| 13 | Corzani R et al. | 2017 | 24 | M | CK, EMA, TTF-1 | Vimentin |
| 14 | Al-Amer M et al. | 2017 | 59 | M | ND | ND |
| 15 | Fusco N et al. | 2017 | 65 | F | CK7, TTF-1, Napsin A, E-cadherin, ER | Vimentin, CD34, CD 99, bcl-2, ER, PR, STAT6 |
| 16 | | | 67 | M | CK7, TTF-1, Napsin A, E-cadherin | Vimentin, CD34, CD 99, bcl-2, STAT6 |
| 17 | | | 75 | F | CK7, TTF-1, Napsin A, E-cadherin, PR | Vimentin, CD34, CD 99, bcl-2, ER, STAT6 |
| 18 | | | 63 | F | CK7, TTF-1, Napsin A, E-cadherin | Vimentin, CD34, CD 99, bcl-2, STAT6 |
| 19 | | | 63 | M | CK7, TTF-1, Napsin A, E-cadherin | Vimentin, CD34, CD 99, bcl-2, ER, PR |
| 20 | | | 48 | F | CK7, TTF-1, Napsin A, E-cadherin | Vimentin, CD34, CD 99, bcl-2, ER, PR |
| 21 | | | 74 | M | CK7, TTF-1, Napsin A, E-cadherin | Vimentin, CD34, CD 99, bcl-2, STAT6 |
| 22 | Olson NJ et al. | 2019 | 60 | M | CK AE 1/3, EMA, TTF-1, E-cadherin | CD34, ER, PR |
| 23 | Sonokawa T et al. | 2020 | 59 | F | CK7, TTF-1, Napsin A | SMA, CD34, CD99, bcl-2, ER, STAT6 |

M, Male; F, Female; ND, Not described.

**Table 2** shows the clinical findings for the cases included in **Table 1**. The patients consisted of 12 men and 11 women (median age at diagnosis, 58 years; range, 24-75 years). Eight patients presented with some symptoms and were diagnosed as having the tumor. However, no direct relationship between the clinical symptoms and the tumors has been established. A single tumor was noted in 22 cases, and multiple tumors were observed in 1 case. Single tumors were located in the left upper lobe in 8 cases, left lower lobe in 7 cases, right upper lobe in 1 case, right middle lobe in 1 case, and right lower lobe in 4 cases; the precise tumor location was not described in 1 case (left lung). The largest tumor was 9 cm in diameter. No disease recurrence or death from the disease was observed in any patient. In the patient with multiple lesions, not all of the lesions were resected; no deterioration of residual tumors was observed, and no additional treatment was required during the observation period[8]. These previous reports do not provide detailed descriptions of tumor marker levels. Serum CEA level was elevated to 13.7 ng/mL in our patient, and the possibility of malignancy could not be ruled out. Although FDG-PET revealed no uptake in the present lesion, some reports have showed FDG uptake by the lesion[2,9,11].

Pulmonary adenofibroma is a histopathologically benign tumor. However, its potential for malignant transformation and prognosis remain unknown. There have been reports of malignant transformation of adenofibroma in other organs, particularly in the biliary tract[13]. Therefore, at this time, aggressive surgical resection, such as wide wedge resection, remains the treatment of choice, as it is for other benign pulmonary tumors.

## Conclusions

We described a case of pulmonary adenofibroma requiring tumor resection by thoracoscopic surgery. This histo-

Table 2 Literature review of clinical findings of pulmonary adenofibroma

| No. | Authors | Year | Age | Sex | Symptoms | Location | Size (cm) | Procedures | Outcomes |
|---|---|---|---|---|---|---|---|---|---|
| 1 | Scarff RW et al. | 1944 | 24 | M | None | RLL | 2.5 | Autopsy | — |
| 2 | | | 66 | M | None | LUL | 1 | Autopsy | — |
| 3 | Suster S et al. | 1993 | 54 | F | ND | RUL | 1 | Lobectomy | NED (8 years) |
| 4 | | | 56 | M | ND | LUL | 2 | Lobectomy | NED (5 years) |
| 5 | Vitkovski T et al. | 2013 | 29 | F | Chest pain | Left lung | ND | Wedge resection | NED (7 months) |
| 6 | Wang Y et al. | 2013 | 55 | M | Chest discomfort | LLL | 2 | Wedge resection | NED (16 months) |
| 7 | Kumar R et al. | 2014 | 25 | M | Breathlessness | LLL | 4.5 | Lobectomy | NED (5 years) |
| 8 | | 2014 | 40 | F | Cough, hemoptysis | LLL | 5 | Lobectomy | NED (1 year) |
| 9 | | 2014 | 55 | F | Breathlessness | LUL | 2.2 | Wedge resection | NED (6 months) |
| 10 | Braham E et al. | 2014 | 56 | M | Chest pain, hemoptysis | LLL | 1.8 | Wedge resection | NED (9 months) |
| 11 | Esmaeili H et al. | 2016 | 65 | F | Abdominal pain | LLL | 9 | Lobectomy | NED (1.5 years) |
| 12 | Hao J et al. | 2016 | 57 | F | ND | Multiple | 0.2-1.5 | Wedge resection | NED (11 months) |
| 13 | Corzani R et al. | 2017 | 24 | M | None | RLL | 0.8 | Wedge resection | ND |
| 14 | Al-Amer M et al. | 2017 | 59 | M | Cough, breathlessness | LUL | 0.87 | CT-guided biopsy | ND |
| 15 | Fusco N et al. | 2017 | 65 | F | ND | LUL | 2.5 | ND | NED (9 months) |
| 16 | | | 67 | M | ND | LLL | 2 | ND | NED (17 months) |
| 17 | | | 75 | F | ND | LUL | 3 | ND | NED (12 months) |
| 18 | | | 63 | F | ND | RLL | 1.5 | ND | NED (9 months) |
| 19 | | | 63 | M | ND | LLL | 1.8 | ND | NED (22 months) |
| 20 | | | 48 | F | ND | RML | 1.9 | ND | ND |
| 21 | | | 74 | M | ND | RLL | 0.5 | ND | NED (10 months) |
| 22 | Olson NJ et al. | 2019 | 60 | M | None | LUL | 1.7 | Wedge resection | NED (2 years) |
| 23 | Sonokawa T et al. | 2020 | 59 | F | None | LUL | 1.4 | Wedge resection | NED (5 months) |

M, Male; F, Female; NED, No evidence of disease recurrence; LUL, Left upper lobe; LLL, Left lower lobe; RUL, Right upper lobe; RML, Right middle lobe; RLL, Right lower lobe; ND, Not described.

pathologically benign tumor is very rare, and additional data from future cases will necessary to elucidate the characteristics, cause, and prognosis of the tumor.

**Conflict of Interest:** The authors declare no competing interests.

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