

Pulmonary adenofibroma: a rare biphasic lung tumour in a young male

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Abstract

We report a very unusual case of benign pulmonary adenofibroma (PAF) in a young man who presented with intermittent chest pain and was found to have a lung mass. PAF is extremely rare and is poorly characterized but thought to be benign based on the limited available literature. Indolent PAF may be misdiagnosed as solitary fibrous tumour (SFT), due to similar histological features. We review the morphological histopathological features and the relevant panel of immunohistochemical stains and molecular tests that can help, to prevent misdiagnosis and overtreatment.

Keywords Benign adenofibroma of the lung; biphasic tumour; fibroadenoma; low grade sarcoma; pulmonary hamartoma; solitary fibrous tumour; STAT6

Case report

A non-smoking South Asian man in his twenties with no significant past medical history presented with intermittent left chest pain over a period of months.

A chest X ray showed a 4 cm well-defined rounded mass lesion in the left hemithorax (Figure 1a). This left lower lobe well-circumscribed soft tissue density showed low fluorodeoxyglucose (FDG) uptake on PET CT (Figure 1b).

Core biopsy was reported as a pulmonary hamartoma. Immunohistochemistry was diffusely positive for SMA, and negative for MNF116, CK7, S100, AE1/AE3, CD34 and TTF-1. MDT discussion offered a differential diagnosis of an atypical hamartoma, low-grade sarcoma and less likely primary lung carcinoma.

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The lesion progressively enlarged and a few years later, he underwent a left utility thoracotomy open excision of the lesion from the left lower lobe.

Macroscopically, a 50 mm well defined multilobulated tan nodule with focal cystic change and haemorrhage of the cut surface was seen.

Microscopically, sections show a biphasic lesion comprising whorled short fascicles interspersed with regularly spaced fine capillaries (Figures 2 and 3). The stroma consists of short, spindle cells with pale, microcystic cytoplasm, ovoid nuclei and finely granular chromatin, without mitoses or necrosis. Stroma is condensed beneath irregularly spaced epithelial elements of canalicular patterns, lined by bland cuboidal epithelium. No other mesenchymal differentiation is seen.

Stroma is immunonegative for STAT6 (Figure 4), CD34, AE1/3, p40 and TTF-1 with only weak positivity for CD99 and bcl2. Epithelial elements stain for AE1/3 and TTF-1, highlighting entrapped lung glandular tissue (Figure 5). RNA extraction and screening for gene fusion transcripts associated with a range of cancer types (Illumina TruSight RNA Fusion Panel) detected no gene fusions.

Overall, features confirm the rare diagnosis of pulmonary adenofibroma (PAF).

Discussion

PAF is an uncommon tumour initially described by Scarff in 1944¹ and named in 1993 by Suster and Moran² after the resemblance to breast and gynaecological adenofibromas. PAF is considered benign and indolent based on the limited literature, however it can mimic intrapulmonary solitary fibrous tumour (SFT), which is a fibroblastic neoplasm of variable prognosis dependent on histological features. PAF is more common in females and occurs more frequently in the left lung.³ Due to low incidence, PAF has not yet been included within the latest WHO Classification of Tumours of the Lung, Pleura, Thymus and Heart.

Lindholm et al.⁴ described a series of 13 cases of PAF, helping identify it as distinct from SFT. PAF occurs as an asymptomatic, well circumscribed solid or partially cystic lesion with fibrous and glandular components and a dense fibrous capsule. However, symptoms as in this case may include chest pain, cough and breathlessness. Cytologically, PAF has bland spindle-shaped cells with uniform nuclei, minimal pleomorphism and low

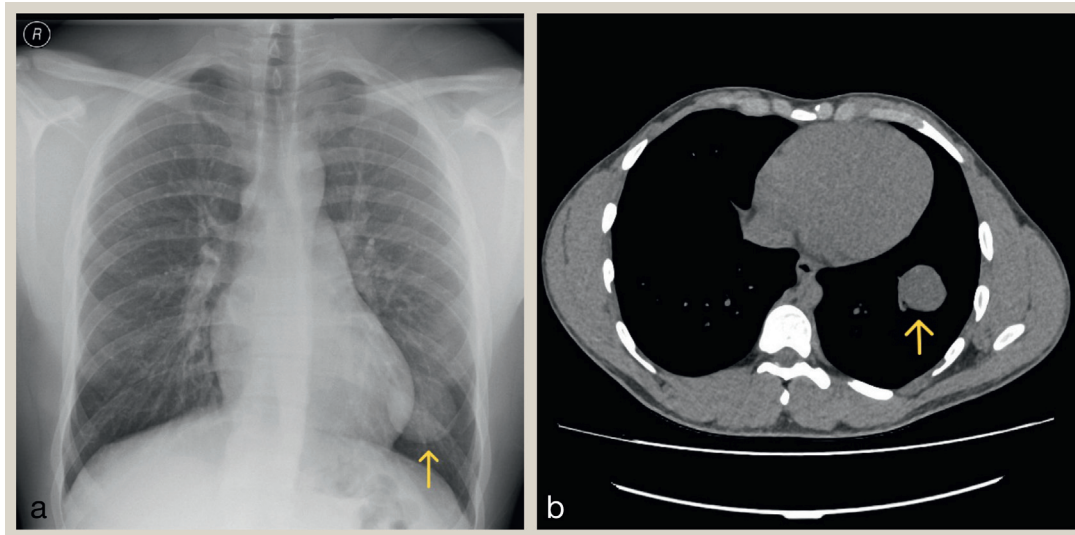


Figure 1 Radiological appearances of the lung lesion. Chest X ray (a) and CT scan (b). Arrows pointing to the lesion.

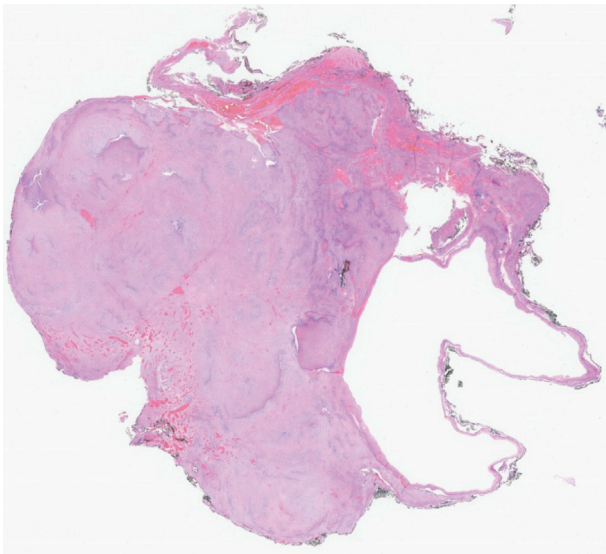


Figure 2 Low power view of the pulmonary adenofibroma excised (H&E, 0.5x).

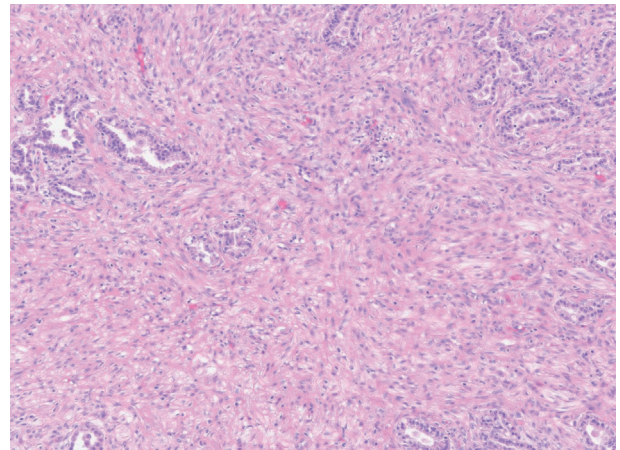


Figure 3 Pulmonary adenofibroma showing the biphasic components and predominant whorled short fascicles interspersed with regularly spaced fine capillaries (H&E, 10x).

nuclear-to-cytoplasmic ratio, consistent with benign appearance. PAF usually lacks haemorrhage, necrosis and mitotic activity. Prognosis is excellent with rare recurrence post-excision.³

Immunohistochemistry of the stroma typically reveals negative staining for STAT6, S100, and keratins with variable CD34 and Bcl-2 positivity. Desmin, SMA and oestrogen/progesterone receptors may also be positive.³ The epithelium may express Cytokeratin, EMA and TTF-1.³ No significant molecular alterations or gene fusions have been reported.³

SFT most commonly occurs in the pleura. SFT is characterized by a highly specific NAB2-STAT6 fusion, resulting in STAT6 overexpression.⁵ Intrapulmonary SFTs are rare and based on patient age, tumour size, mitotic activity and necrosis stratified into low risk, intermediate risk and high risk.⁶

Intrapulmonary SFT has been reported as a well-circumscribed, unencapsulated tumour with mean size around

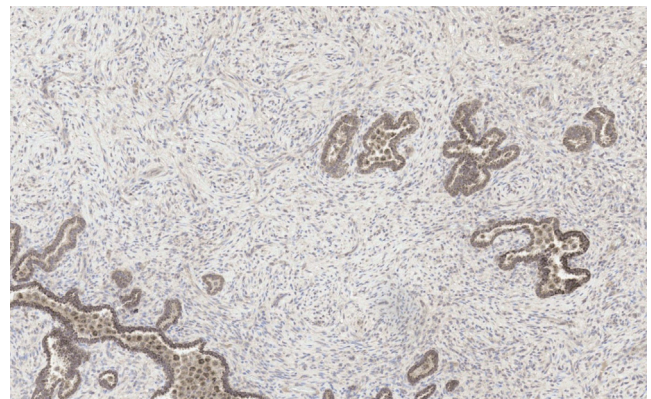


Figure 4 STAT6 staining of the pulmonary adenofibroma showing positivity in the glands but immunonegative stroma (10x).

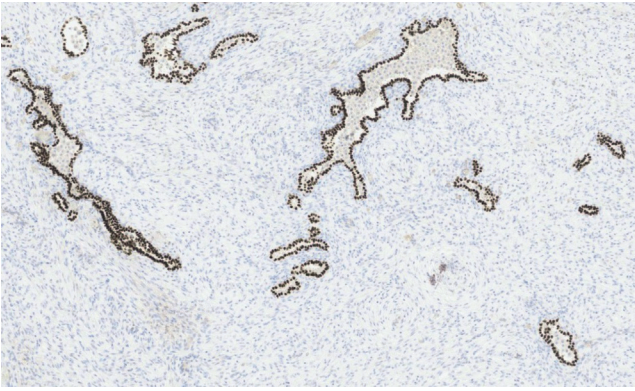


Figure 5 TTF-1 immunostaining of pulmonary adenofibroma showing immunonegative stroma and positive entrapped glands within the stroma (5x).

8 cm.⁶ Intrapulmonary SFTs show conventional SFT microscopic features, including storiform or patternless arrangement with thick collagen bundles and occasional branched (haemangiopericytoma-like) vessels. The spindle cells have hyperchromatic variably pleomorphic nuclei and occasional mitoses with abundant pale cytoplasm. Immunohistochemically, STAT 6 and CD34 expression is characteristically strong and diffuse, with CD99 and bcl-2 positivity seen in the majority.⁶ PAFs may be distinguished from hamartomatous lesions with stromal and glandular elements, sclerosing pneumocytoma, papillary adenoma, sarcomatoid carcinoma, metastatic breast phyllodes tumour and mesothelioma if near the pleura.

These appearances can present diagnostic challenges for those unfamiliar with PAF and risk misdiagnosis.

Conclusion

Overall, PAF is a rare biphasic tumour with excellent prognosis that can be misdiagnosed as SFT and potentially more aggressive entities. Pathologists should be aware of the entity to prevent overtreatment. ◆

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Practice points

- Pulmonary adenofibroma (PAF) is extremely rare and not well characterized
- PAF appears as a biphasic tumour with glandular epithelial and fibrous stromal components with well-circumscribed solid or solid cystic morphology. The stromal component comprises bland spindle-shaped cells with no significant mitoses
- PAF can mimic solitary fibrous tumour (SFT), which has potentially worse prognosis with increased recurrence risk, and may result in overtreatment
- PAF is negative for STAT6, unlike SFT which has a characteristic NAB2-STAT6 gene fusion leading to STAT6 overexpression

Self-assessment multiple choice questions

1. What is a key histological feature of pulmonary adenofibroma?

- A. Necrosis
- B. Biphasic differentiation
- C. Hyperchromatic nuclei with frequent mitotic activity
- D. Predominantly pleural involvement
- E. Storiform pattern

Correct answer: b

2. Which finding is characteristically associated with solitary fibrous tumour but not pulmonary adenofibroma?

- A. NAB2-STAT6 gene fusion
- B. BRAF V600E mutation
- C. Variable CD34 staining
- D. Diffuse S100 positivity
- E. High oestrogen receptor expression positivity

Correct answer: a

3. What is the typical prognosis of pulmonary adenofibroma following surgical excision?

- A. High risk of local recurrence with poor prognosis
- B. Low recurrence and excellent prognosis
- C. Frequent malignant transformation
- D. Requires adjuvant chemotherapy for a good prognosis
- E. Distant recurrence is commonly seen

Correct answer: b