Primary soft tissue tumours of the lung

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Abstract

Although primary mesenchymal tumours of the lung are rare, a working knowledge of the morphology, clinical features, genetic abnormalities, and appropriate ancillary studies applicable to these lesions will be very helpful to practising pathologists who review pulmonary material. This is especially important since mesenchymal neoplasms frequently enter the differential diagnosis of other more common pulmonary tumours with sarcomatoid appearance, including sarcomatoid carcinoma and mesothelioma. This review will cover the key morphologic and clinicopathologic features of primary soft tissue tumours of the lung, including solitary fibrous tumour, synovial sarcoma, inflammatory myofibroblastic tumour, pleuropulmonary blastoma, vascular lesions, and others. A practical approach to the differential diagnosis and appropriate use of relevant immunohistochemical markers and ancillary genetic studies will be discussed.

Keywords lung; mesenchymal; nerve sheath; sarcoma; vascular

Introduction

The incidence of primary mesenchymal neoplasms arising in the lung pales in comparison to the commonplace occurrence of lung carcinoma. The rarity of primary pulmonary mesenchymal tumours is further complicated by site-specific morphologic mimics, including sarcomatoid carcinoma and mesothelioma. In addition, most true sarcomas encountered in the lung are likely to be metastatic from extrapulmonary sites. All these factors contribute to the diagnostic difficulty of mesenchymal neoplasms in the lung, especially on small biopsies. However, most of these diagnostic problems can be resolved with a thoughtful histologic exam, appropriate immunohistochemical stains, ancillary genetic testing as needed, and consideration of the overall clinical and radiographic context. This review will cover selected mesenchymal neoplasms that arise in the lung, with a practical discussion of important considerations for the practising pathologist.

Solitary fibrous tumour

Solitary fibrous tumour (SFT) is one of the more commonly encountered mesenchymal tumours in the lung, which frequently arises as a visceral pleural based mass showing a very wide size range.[1] Most patients are adults, and many tumours are discovered incidentally, although some may present with cough, pain, pleural effusion, or other localizing complaints.[1,2] The tumours are often circumscribed and attached to the pleural surface by a pedicle, but may also grow down into the lung parenchyma or involve the pleura in a sessile fashion.[1] The histology of SFT can be quite variable. The classic appearance is the "patternless pattern" of ovoid to spindle-shaped cells showing bland nuclear features in a background of dense intercellular collagen, which is often eosinophilic, wiry, and refractile (Figure 1). However, the morphologic spectrum of SFT also includes tumours historically classified as "hemangiopericytoma", with more plump ovoid cells, higher tumour cellularity, and less collagen deposition.[1] This morphologic pattern often shows short fascicles or storiform growth, and may be more difficult to recognize as SFT. These two patterns are often mixed within the same tumour, and share a hemangiopericytoma-like vascular pattern (Figure 1). While classic examples are often straight forward, cellular examples or tumours occurring in the lung parenchyma without obvious pleural attachment may prove difficult to diagnose on small biopsies. The immunohistochemical marker CD34 is often very useful, as most cases of SFT (>90%) are strongly and diffusely positive.[3] It has recently been shown that most SFTs harbour a recurrent translocation resulting in the *NAB2-STAT6* fusion gene.[4] Nuclear STAT6 protein can be detected by immunohistochemistry, which is a useful diagnostic marker.[5] Cytoplasmic background staining (sometimes combined with weak nuclear staining) is not specific and should be disregarded.[5] While most SFTs behave in a benign fashion and are cured by complete resection, a minority will follow an aggressive clinical course with potential for local recurrence and distant metastases.[6] Prognostic risk stratification of SFT is helpful to predict likelihood of aggressive behaviour, and the recently proposed scoring system consists of six variables: parietal (vs. visceral) pleural origin, sessile (vs. pedunculated) morphology, size ≥10 cm (vs. <10 cm), the presence of hypercellularity, necrosis and mitotic activity ≥4/HPF (vs. <4/HPF).[6] Because of the inherent histopathologic heterogeneity in these tumours, risk stratification is best performed upon examination of the complete

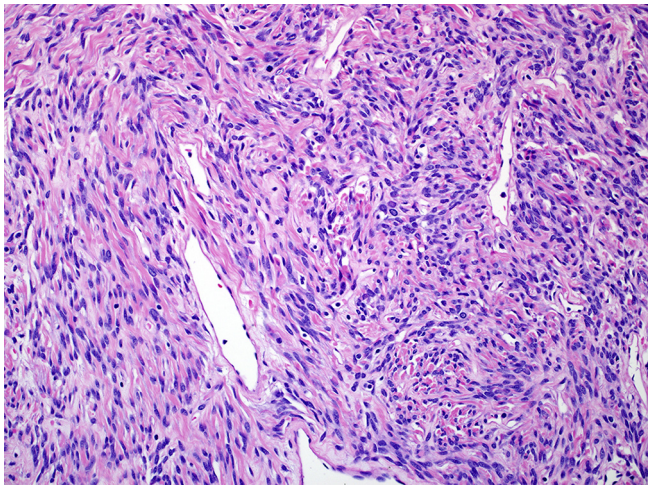

Figure 1 Solitary fibrous tumour, showing bland short spindled to ovoid cells, wiry collagen, hemangiopericytoma-like vessels, and rare mitoses.

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surgical resection specimen. However, if atypical features (high mitotic rate, necrosis, etc.) are noted on small biopsy, these features should be mentioned in the pathology report, alerting clinicians to the possibility of a high-risk tumour.

Synovial sarcoma

Although quite rare, synovial sarcoma (SS) is one of the most commonly encountered primary sarcomas in the lung. SS tends to occur in young to middle aged adults, but the age range in pulmonary SS is wide.[7–9] Patients often present with local symptoms including haemoptysis, cough, and pain.[2,7] Pulmonary SS are typically parenchymal or pleural based masses of variable size,[7–9] although they may rarely be endobronchial.[9] In the lung, monophasic SS are much more common than their biphasic counterparts,[7–9] and are characterized by densely cellular monomorphic ovoid to elongate spindle cells (Figure 2), often growing in well-formed fascicles. One of the hallmark histologic features of synovial sarcoma is nuclear monotony, as is the case with other translocation-associated sarcomas. SS generally does not show marked nuclear pleomorphism, which would be a strong indication to consider an alternative diagnosis, particularly sarcomatoid carcinoma or mesothelioma. Monophasic SS can often entrap benign bronchioles lined by ciliated epithelium, which should not be confused with true biphasic morphology.[2] Pulmonary SS tend to have well-circumscribed appearance, and often show a hemangiopericytoma-like vascular pattern (Figure 2).[7] They frequently demonstrate brisk mitotic rate and regions of necrosis.[2] SS occurring in the lung have a tendency to be "poorly differentiated",[7,8] which may be characterized by small round blue cells (small cell morphology), large/epithelioid cells, or high grade spindle cell morphology. Even poorly differentiated examples usually retain some degree of nuclear monotony. SS typically show focal expression of keratins and EMA.[7,8] Molecular testing is often very useful to confirm the diagnosis of SS, and exclude other monomorphic spindle cell sarcomas with similar morphology such as malignant peripheral nerve sheath tumour and fibrosarcoma. SS has a recurrent t(X; 18) (p11.2; q11.2) translocation, resulting in *SYT-SSX1* or *SYT-SSX2* fusion genes in >95% of cases.[7] This can be tested by RT-PCR for the specific fusion genes, or florescence in situ hybridization (FISH) using a break-apart probe for *SYT*. SS is categorically a high grade sarcoma, with high risk of aggressive behaviour and distant metastasis. Pulmonary SS seems to have a worse prognosis than their soft tissue counterparts, with 5-year disease-specific survival around 30%.[7,8] The poor prognosis likely relates to several site-specific factors, including late detection, large tumour size, older patient age, high incidence of poorly differentiated tumours, and proximity to critical anatomic structures.[7,8]

Inflammatory myofibroblastic tumour

Inflammatory myofibroblastic tumour (IMT) is a neoplasm of myofibroblastic/fibroblastic cells with a rich inflammatory background.[3,10] While many IMTs occur in the abdominal cavity/retroperitoneum, the lung is also a preferred site.[3,11] Historically, pulmonary IMT had been grouped under the umbrella term "inflammatory pseudotumour" ("plasma cell granuloma"), which encompassed IMT as well as a number of non-neoplastic entities, including IgG4-related disease, non-specific fibroinflammatory processes, and other entities. The distinction of IMT from these other processes is important, since IMT is a neoplasm with potential for locally aggressive behaviour and distant metastases in rare cases.[10,11] Pulmonary IMTs occur mostly in children and young adults, but may also occur in older patients.[3,11] A subset of patients with IMT will present with inflammatory systemic symptoms, including fever, weight loss, anaemia, and hyergammaglobulinemia.[3,11] Patients with pulmonary tumours may also present with localizing symptoms, including cough, dyspnoea, and haemoptysis. IMTs are typically lobulated/circumscribed masses that vary widely in size, and may be endobronchial or parenchymal. Histologically, IMT is composed of myofibroblastic/fibroblastic cells, usually plump and spindle shaped, with mixed chronic inflammatory cells including plasma cells, lymphocytes, and eosinophils (Figure 3). However, the morphology may be variable depending on the

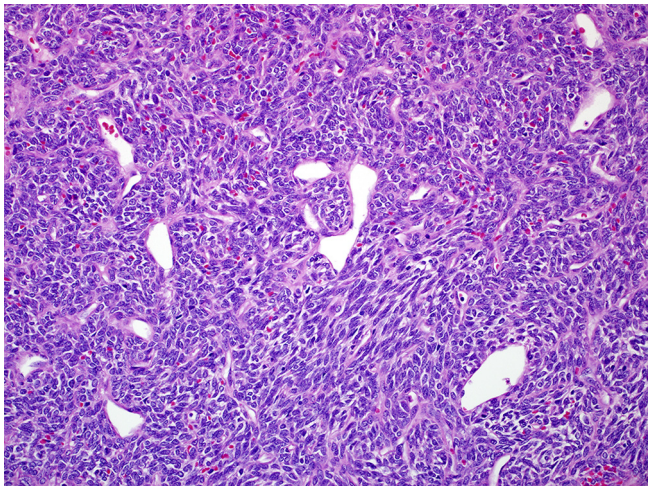

Figure 2 Pulmonary monophasic synovial sarcoma, characterized by monotonous spindled cells with focal fascicular growth, high cellularity, and hemangiopericytoma-like vessels.

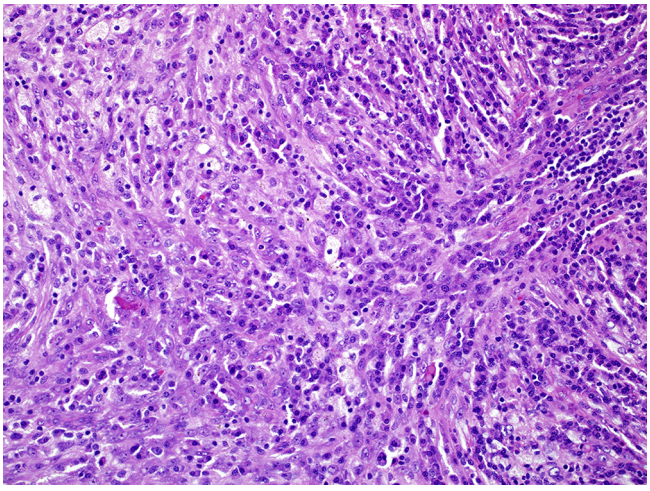

Figure 3 Inflammatory myofibroblastic tumour, with plump myofibroblastic cells showing vesicular chromatin and occasional prominent nucleoli, and a chronic inflammatory infiltrate with abundant plasma cells and lymphocytes.