Editorial

Solitary fibrous tumor: A pathological enigma and clinical dilemma

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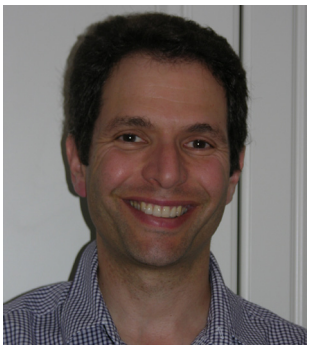

Solitary fibrous tumors are ubiquitous rare spindle cell neoplasms, most commonly arising from the pleura. Whilst now considered to be derived from mesenchymal cells, the histiogenesis has been the subject of debate. In 1931 Klemperer and Rabin first documented the occurrence of a distinctive localized pleural based tumour and proposed a submesothelial cell origin (1). Later, based on tissue culture experiments, Stout and Murray claimed derivation from mesothelial cells (2). This controversy is reflected in the variety of synonyms used for solitary fibrous tumors in the past including localized fibrous tumor, localized fibrous mesothelioma, solitary fibrous mesothelioma, fibrous mesothelioma, subserosal fibroma and submesothelial fibroma. With the advent of immunohistochemistry a fibroblastic origin, occasionally with myofibroblastic differentiation, is firmly established. This is further reinforced by the description of solitary fibrous tumors in extrathoracic sites devoid of mesothelial cells.

Spindle cell mesenchymal neoplasms represent a diverse group of benign and malignant tumors, the diagnosis of which relies on histomorphological features supported by ancillary investigations which include immunohistochemistry and, increasingly, molecular analysis. Microscopically solitary fibrous tumors are characterised by hypocellular collagen rich areas alternating with a proliferation of uniform elongated spindled cells in a haphazard distribution. Imunohistochemistry is extremely useful in establishing the diagnosis, no more so than CD34. CD34 is a myeloid progenitor cell antigen which is also positive in endothelial cells and some mesenchymal cells, including subsets of fibroblasts (3). It is no coincidence that since the description of CD34 expression in solitary fibrous tumors there has been a flurry of case reports in a wide range of sites. Cytogenetic and fluorescence in situ hybridization has shown no specific chromosomal abnormality (4) and, unlike a growing number of sarcomas, molecular tests are not utilised in confirming the diagnosis.

The pathological enigma surrounding solitary fibrous tumor is twofold. The first is identifying those tumors which have malignant potential and the second is the histological diagnosis of dedifferentiated solitary fibrous tumors. Most solitary fibrous tumors behave in a benign fashion. When arising from the pleura, 13-23% are classified as malignant in contrast to most extrapleural tumors which, with the exception of those of mediastinal origin, have a benign outcome (5). England et al used high cellularity, mitotic activity (more than four mitotic figures per 10 high-power fields), pleomorphism, hemorrhage and necrosis as criteria for distinguishing tumors with a favourable course from those that have the propensity for recurrence, local invasion and metastatic spread (6). Unfortunately biological behaviour does not always correlate with atypical histological features. De Perrot et al stratified the risk of recurrence based on histologic and morphologic

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indicators among 185 reported solitary fibrous tumors of the pleura (7). Recurrence was observed in 63% of all patients presenting with a malignant sessile lesion but 2% of the patients with a benign pedunculated tumor recurred. The proliferation marker Ki67 has been used to stratify lesions as to their clinical outcome. Positive staining is greater in malignant versus benign tumors but the overlap limits its usefulness (8). Clearly whilst the site, growth pattern and histological features correctly identify the malignant potential in the majority of cases, there still remains a small subset which behaves in an unpredictable fashion.

As sarcomas progress they may acquire additional molecular alterations which aids tumor progression. This is accompanied by transformation of the typical histological appearance to an anaplastic component, a process referred to as dedifferentiation, with frequent loss of CD34 expression (9). Frankly sarcomatous solitary fibrous tumors can only be recognized as such if they are associated with typical solitary fibrous tumors or recur at the site of a previous documented benign-looking solitary fibrous tumor (5). The largely favourable outcome of extrathoracic solitary fibrous tumors may be that only the typical ones are recognized and those showing cytomorphological atypia are diagnosed as something else.

In this issue of the Journal of Thoracic Disease, Milano et al investigate the survival of malignant solitary fibrous tumours of the pleura, lung and mediastinum in 82 patients identified from a population based dataset (10). Given the rarity of this tumor and the difficulties in identifying the malignant form, this approach has generated a large cohort of patients and provides the basis for understanding the progression of the disease and factors affecting outcome. In line with other studies, this paper confirms the positive impact of surgical excision on outcome. Univariate analysis did not support a role for adjuvant radiotherapy. The effect of chemotherapy was not analyzed but this is not surprising given that it is not effective and therefore rarely used (11).

The clinical management of malignant solitary fibrous tumors remains a dilemma, especially in cases were surgical excision is not feasible. Oncologist marvel in the success of gastrointestinal stromal tumors, a neoplasm, which like solitary fibrous tumor, is a spindle cell lesion which may behave in a benign or malignant fashion. However that is where the similarities stop. There are well defined morphological and histological parameters for defining risk of progression in gastrointestinal stromal tumors and specific molecular events have been identified which are exploited for therapy and prognosis. Indeed imatinib, a tyrosine kinase inhibitor, has revolutionised the management of patients with gastrointestinal stromal tumors. In an attempt to mirror this success, investigators have used imatinib in malignant solitary fibrous tumors overexpressing platelet-derived growth factor, both in vitro (12) and in vivo (13), with promising results.

Investigators studying solitary fibrous tumors face a number of obstacles. Its rarity, difficulty in predicating biological behaviour, occurrence in a wide range of sites and lack of a defining set of molecular events has limited attempts to fully understand the effect of standard treatment modalities and to explore different management strategies. Large population based studies, as described in this issue, and multi institutional collaborations are required to improve our understanding of this tumor, specifically with reference to identifying molecular biomarkers for disease progression and targeted treatment.

References

1. Klemperer P, Rabin CB. Primary neoplasms of the pleura. A report of five cases. Arch Pathol 1931;11:385-412.
2. Stout AP, Murray MR. Localized pleural mesothelioma: investigation of its characteristics and histogenesis by method of tissue culture. Arch Pathol 1942;34:951-64.
3. Hanau CA, Miettinen M. Solitary fibrous tumor: histological and immunohistochemical spectrum of benign and malignant variants presenting at different sites. Human Path 1995;26:440-9.
4. Swelam WM, Cheng J, Ida-Yonemochi H, Maruyama S, Saku T. Oral solitary fibrous tumor: a cytogenetic analysis of tumor cells in culture with literature review. Cancer Genet Cytogenet 2009;194:75-81.
5. Chan JKC. Solitary fibrous tumour-everywhere and a diagnosis in vogue. Histopathology 1997;31:568-76.
6. England DM, Hochholzer L, McCarthy ML. Localised benign and malignant fibrous tumors of the pleura. A clinicopathological review of 223 cases. Am J Surg Pathol 1989;13:640-58.
7. de Perrot M, Fischer S, Bründler MA, Sekine Y, Keshavjee S. Solitary fibrous tumors of the pleura. Ann Thorac Surg 2002;74:285-93.
8. Hasegawa T, Matsuno Y, Shimoda T, Hirohashi S, Hirose T, Sano T. Frequent expression of bcl-2 protein in solitary fibrous tumors. Jpn J Clin Oncol 1998;28:86-91.
9. Mosquera JM, Fletcher CD. Expanding the spectrum of malignant progression in solitary fibrous tumors: a study of cases with a discrete anaplastic component -is this dedifferentiated SFT? Am J Surg Pathol 2009;33:1314-21.
10. Milano MT, Singh DP, Zhang H. Thoracic malignant solitary fibrous tumors: a population-based study of survival. J Thorac Dis 2011;3:99-104.
11. Cardillo G, Carbone L, Carleo F, Masala N, Graziano P, Bray A, et al. Solitary fibrous tumors of the pleura: an analysis of 110 patients treated in a single institution. Ann Thorac Surg 2009;88:1632-7.
12. Prunotto M, Bosco M, Daniele L, Macri' L, Bonello L, Schirosi L, et al. Imatinib inhibits in vitro proliferation of cells derived from a pleural solitary fibrous tumor expressing platelet-derived growth factor receptor-beta. Lung Cancer 2009;64:244-6.
13. De Pas T, Toffalorio F, Colombo P, Trifirò G, Pelosi G, Vigna PD, et al. Brief report: activity of imatinib in a patient with platelet-derived-growth-factor receptor positive malignant solitary fibrous tumor of the pleura. J Thoracic Oncol 2008;3:938-41.