Human Pathology (2018) 77, 175–180

ELSEVIER

Human PATHOLOGY

www.elsevier.com/locate/humpath

Case study

Solitary fibrous tumor with neuroendocrine and squamous dedifferentiation: a potential diagnostic pitfall

Chuanyong Lu MD[a,b,*], Deepu Alex MD[a], Ryma Benayed PhD[a], Marc Rosenblum MD[a], Meera Hameed MD[a]

[a]*Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY 10021*
[b]*Department of Pathology, Hospital for Special Surgery, New York, NY 10021*

Received 11 November 2017; revised 30 November 2017; accepted 14 December 2017

Keywords:
Solitary fibrous tumor;
Dedifferentiation;
Malignant transformation;
Transdifferentiation;
Neuroendocrine carcinoma;
Squamous differentiation

Summary Solitary fibrous tumor (SFT) is a ubiquitous mesenchymal neoplasm of deep soft tissue with variable and often unpredictable biological behavior. The lineage is presumed to be fibroblastic, and histological features range from benign to overtly malignant with rare tumors showing "dedifferentiation" or transformation to undifferentiated pleomorphic sarcoma. Dedifferentiation in mesenchymal neoplasms is a phenomenon of histologic progression of a well-differentiated neoplasm to a high-grade sarcoma, which can differentiate along divergent lines. It is extremely uncommon to encounter "transdifferentiation" to non-mesenchymal lineage and still maintaining the driver genetic event of the primary tumor. Herein, we report two diagnostically challenging SFTs with transformation to neuroendocrine and squamous phenotypes. The index case is a pelvic malignant SFT, which metastasized to the liver as a high-grade neuroendocrine carcinoma. The second case is a recurrent brain tumor initially presenting as a typical SFT and evolving into a dedifferentiated SFT with foci of squamous differentiation. Positive immunohistochemical stains for CD34 and STAT6 and the detection of *NAB2-STAT6* fusion supported the diagnosis of dedifferentiated SFT in both cases. In the first case, molecular study also demonstrated that both the pelvic primary and liver metastasis harbored the same *NAB2-STAT6* fusion. Dedifferentiation to a non-mesenchymal lineage/lineage infidelity can be a potential diagnostic pitfall in these tumors.

1. Introduction

Solitary fibrous tumor (SFT) is an uncommon mesenchymal neoplasm of deep soft tissue, which is classically described as a tumor composed of round to fusiform cells surrounding staghorn hyalinized vessels. The tumor shows no distinct line of differentiation microscopically and its cell of origin is presumed as fibroblastic. A classical SFT is a variably cellular tumor composed of spindle cells, which are either distributed randomly or arranged in short fascicles with areas of hyalinization in a "patternless pattern." This tumor remains a diagnostic challenge even in its classic form and ancillary studies are required for confirmation in most cases. The discovery of *NAB2-STAT6* rearrangement in nearly 100% of SFTs and as a result consistent immunohistochemical expression of STAT6 has greatly enhanced diagnostic accuracy of this

* Corresponding author at: Department of Pathology, Hospital for Special Surgery, 535 E 70th St, New York, NY 10021.
E-mail address: luc@hss.edu (C. Lu).

https://doi.org/10.1016/j.humpath.2017.12.024
0046-8177/

neoplasm in recent years [1]. While this tumor remains elusive in its biological behavior, pathological features portending malignancy include high cellularity, increased mitotic rate (>4/10HPFs), variable cytological atypia, tumor necrosis, and/or infiltrative margin [2,3]. Rarely, a well-demarcated high-grade sarcomatous component is present in an otherwise low grade typical SFT, and the tumor is then referred by some authors as dedifferentiated SFT [4]. The dedifferentiated components described thus far include undifferentiated pleomorphic sarcoma, Ewing-like small round cell tumor, and rarely rhabdomyosarcoma, osteosarcoma, or chondrosarcoma [5]. Dedifferentiated SFTs appear to have a worse prognosis compared to the typical and malignant SFTs [4,5].

Recently, we encountered two cases of SFTs where tumor transformation included a non-mesenchymal component (transdifferentiation/lineage infidelity), one showing neuroendocrine dedifferentiation and the other one with foci of squamous dedifferentiation. In both cases, CD34 and STAT6 were positive in tumor cells and molecular studies demonstrated the presence of *NAB2-STAT6* fusion, confirming the diagnosis.

2. Materials and methods

Both cases are submitted consultation cases. The clinical features are described in Table.

Immunohistochemical studies were performed on representative submitted unstained sections following routine protocols on Ventana or Bond (STAT6 only) platforms. The following antibodies (company, clone, dilution) were used: CD34 (Roche, QBend10, Ready to Use antibody), STAT6 (Santa Cruz, polyclonal, 1:2500), Ki-67 (Dako, MiB-1, 1:200), pancytokeratin (Dako, AE1/AE3, 1:1600), 34ßE12 (Roche, 34ßE12, Ready to Use antibody), CAM5.2 (Becton & Dickinson, Cam5.2, 1:50), p63 (Roche, 4A4, Ready to Use antibody), CD117 (Dako, polyclonal, 1:500), DOG-1 (Cell Marque, SP31, Ready to Use antibody), synaptophysin (BioGenex, SNP88, 1:2000), CD56 (Roche, MRQ42, Ready to Use antibody), SMA (Cell Marque, 1A4, 1:200), desmin (Roche, DER11, Ready to Use antibody), S100 (Dako, polyclonal, 1:8000), myogenin (Cell Marque, FSD, Ready to Use antibody), and TTF-1 (Roche, 8G7G3/1, Ready to Use antibody).

Molecular testing, the MSK-Solid Fusion assay, was performed on the first case on both the primary pelvic mass and the liver metastasis and on the second case on its last recurrence. The MSK-Solid Fusion assay is a targeted RNA-based panel that utilizes the Archer Anchored Multiplex PCR (AMP™) technology and next generation sequencing to detect gene fusions in solid tumor and sarcoma samples. The Archer™ custom solid panel was designed to target 62 specific genes known to be recurrently involved in rearrangements associated with these malignancies. Briefly, RNA is extracted from tumor FFPE material followed by cDNA synthesis. cDNA undergoes end repair, dA tailing and ligation with Illumina molecular barcode adapters. SPRI-cleaned ligated fragments are subject to two rounds of PCR amplifications using two sets of gene specific primers (GSP1 used in PCR1 and a nested GSP2 pool that is 3' downstream of GSP1 and used in PCR2) and a primer complementary to the Illumina adapter. At the end of two PCR steps the final targeted amplicons are fully functional and ready for sequencing on an Illumina Miseq instrument (2x150bp). The Archer™ analysis software V5.0 is used for data analysis.

3. Case summary

3.1. Case 1

The patient is a 41-year-old man who presented with abdominal discomfort. CT scan showed a large mass (14 cm) in the pelvic mesentery. The tumor and the attached rectosigmoid colon were resected. Histology showed a spindle cell neoplasm with hemangiopericytic growth pattern (Fig. 1A). In some areas, tumor cells were separated by heavily hyalinized thick bands of collagen with interspersed gaping blood vessels and perivascular hyalinization (Fig. 1B). In other areas, the tumor cells formed short fascicles with focal epithelioid

Table Clinical features of the 2 cases

Case #	Age at diagnosis	Sex	Location (primary)	Diagnosis (primary)	Treatment	Metastasis	Local recurrence	Follow up (duration after diagnosis of dSFT)	Outcome
1	41	M	Pelvic	Malignant SFT	Surgical removal	Liver, 5 months after resection of primary tumor	5 months after resection of primary tumor	8 months (2.5 months)	Alive
2	18	F	Left occipital	Typical SFT	Surgical removal	No	Multiple, first recurrence at 10 years after resection of the primary tumor	14 years (3 months)	Alive

Abbreviation: dSFT, dedifferentiated solitary fibrous tumor.