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Lack of a Common or Characteristic Cytogenetic Anomaly in Solitary Fibrous Tumor

Alireza Torabi¹, Subodh M. Lele¹, Dominick DiMaio¹, Jeffrey C. Pinnt², Michelle M. Hess², Marilu Nelson², and Julia A Bridge^{1,2,3}

¹Department of Pathology and Microbiology, University of Nebraska Medical Center, Omaha, NE 68198-3135

²Department of Pediatrics, University of Nebraska Medical Center, Omaha, NE 68198-3135

³Department of Orthopaedic Surgery, University of Nebraska Medical Center, Omaha, NE 68198-3135

Abstract

Solitary fibrous tumor is a mesenchymal tumor that was initially described as a pleural-based lesion, but later was discovered in many other locations. The light microscopic appearance of solitary fibrous tumor may overlap with other diagnostic entities; however, consistent tumor cell CD34 immunoreactivity is useful in establishing the diagnosis. Limited data suggest that solitary fibrous tumors are karyotypically diverse; a common or characteristic anomaly has not yet emerged for this entity. In this report, cytogenetic analysis of two solitary fibrous tumors, one peritoneal and the other arising in the liver, revealed predominantly structural abnormalities in the former and numerical imbalances in the latter. Clonal karyotypic abnormalities were lacking in three additional solitary fibrous tumors.

Introduction

Solitary fibrous tumor (SFT) is a mesenchymal neoplasm, which occurs most commonly in the pleura and other serosal surfaces such as pericardium and peritoneum. Extrapleural sites of SFT, including the soft tissues and visceral organs have also been reported (1-4). SFT is a slow growing mass arising predominantly in middle-aged adults with no sex preference. The majority of SFTs are benign; however, malignant behavior with metastases can occur (5). Cytogenetic reports of SFT are few and a recurrent or specific chromosomal alteration is lacking (6-8). In this study, the cytogenetic findings of two cases of SFT (one arising in the liver and the other in the peritoneum) and a review of the literature are presented.

Case histories

Case 1

A mass arising in the left lobe of the liver was detected in a 65 year old male presenting with confusion and weight loss. The patient's past medical history was significant for a cerebrovascular accident that was complicated by bleeding in 2002 and adenocarcinoma of the

Corresponding Author: Julia A. Bridge, M.D., Department of Pathology and Microbiology, 983135 Nebraska Medical Center, Omaha, NE 68198-3135, Phone: 402-559-7212, Fax: 402-559-6018, Email: jbridge@unmc.edu.

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prostate treated with total prostatectomy in 2003. Radiographic studies revealed a large, well encapsulated mass (18 × 12 cm) in the left lobe of the liver. A needle core biopsy followed by a partial hepatectomy was performed. The tan-white, well-circumscribed mass measuring 18.8 × 16.5 × 13.1 cm was composed of spindle- to oval-shaped cells with interspersed collagen and a hemangiopericytoma-like vascular pattern. The neoplastic cells were focally immunoreactive for CD34 and CD99 and diffusely positive for BCL-2. Hypercellularity was present focally with areas of necrosis and up to 3 mitoses per 10 high-power fields. A sterile, representative portion of the lesion was submitted for cytogenetic analysis.

Case 2

An 82 year old female was evaluated for an intraabdominal mass. The patient complained of weight loss in the extremities but an increase in her abdominal girth. Her past medical history was significant for total hip replacement and hysterectomy. An abdominal ultrasound and CT scan demonstrated a large mass within the left side of the abdomen, seemingly arising from the mesentery. A CT-guided needle biopsy revealed a moderately to highly spindle cell proliferation. The differential diagnosis included solitary fibrous tumor, gastrointestinal stromal tumor and leiomyoma. Subsequently, the mass was resected. The resected multilobulated mass exhibited focal areas of hemorrhage and necrosis and measured 16.2 × 10.5 × 9.2 cm. Although the tumor closely approached the pancreas, it did not involve it. The light microscopic appearance of the neoplasm was similar to that of Case 1, with uniform spindle-shaped cells separated by intervening collagen. Rare, focal areas of hypercellularity with necrosis could be appreciated but nuclear pleomorphism and atypia were absent. The neoplastic cells were diffusely immunoreactive for BCL-2 and focally for CD34 and CD99. Mitoses were less than 2 per 10 high-power field. A sterile, representative portion of this lesion was submitted for cytogenetic analysis.

Materials and Methods

The representative tumor samples were disaggregated with scalpels and collagenase and cultured in RPMI-1640 media supplemented with 20% fetal bovine serum and antibiotics for 4-6 days as previously described (9). Metaphase chromosomes were banded with Wright trypsin and karyotypes were described according to established international guidelines (10).

Results

Cytogenetic analysis of Case 1 revealed the presence of an abnormal hypotetraploid clone in all twenty metaphase cells examined: 83,XXYY,-1,-4,-6,-9,-13,-15,-17,-18,-22[20], Figure 1. An abnormal hyperdiploid stemline clone (Figure 2) and two sideline clones were identified in Case 2. The nomenclature for the abnormal clones is as follows: 47,XX,del(2)(q32q35),+5[8]/47,sl,add(X)(q22),add(18)(p11.2)[9]/46,sl,dic(9;15)(p13;p11.2)[2]. One cell was normal female.

Discussion

Solitary fibrous tumor (SFT) was first described as a pleural-based tumor with an exophytic growth pattern (11). In addition to pleural- or peritoneal-based locations, SFT has been reported in multiple organs including pancreas, liver, skin, meninges, thyroid and soft tissue [1, 3, 5]. The tumor is composed of spindle-shaped cells admixed with dense collagen and branching vasculature. Expression of CD34 and CD99 is common, BCL2 is variable, and desmin rare. It has been hypothesized that a pluripotent mesenchymal stem cell is the possible cell of origin for SFT.

Although most SFTs are benign, 10-15% may behave aggressively [3]. Hypercellularity, significant cellular pleomorphism, and more than 4 mitoses per 10 high-power fields are features suggesting aggressive or malignant behavior (12). There is no evidence of correlation between karyotype and histology, anatomic location, and clinical outcome (13). Multiple chromosomal aberrations have been detected in histopathologically benign-appearing SFTs with no evidence of recurrence or metastasis in cases with follow-up data (13).

Cytogenetic studies of SFT are relatively few, Table 1 (14). Cytogenetic abnormalities are detected in most SFTs that are larger than 10cm in diameter, but are usually undetectable in smaller SFTs (15). Of five cases analyzed by conventional cytogenetic methods at UNMC over the past 15 years, three SFTs measuring less than 10cm in diameter to include one arising in the head and neck region, one in the abdominal cavity, and another in the deep soft tissues of the lower extremity were karyotypically normal. Notably however, two of these SFTs lacking clonal karyotypic abnormalities demonstrated an identical random abnormality of trisomy 2 in one cell each. In contrast, both SFTs measuring greater than 10cm in diameter, to include a SFT of the liver (Case 1) and a peritoneal SFT (Case 2), exhibited numerical imbalances exclusively and gain of chromosome 5 in addition to structural abnormalities of chromosomes X, 2, 9, 15 and 18 respectively.

A relatively wide variety of karyotypic anomalies to include both numerical and structural abnormalities have been detected in SFT, Table 1 [13, 16]. With respect to numerical abnormalities, gains of chromosomes 5, 8, and 21 have been reported in more than one SFT. Interestingly, trisomy 5 is a shared anomaly for the two peritoneal SFTs (present in the sole previously described peritoneal SFT (16) in addition to Case 2 of the current report). Trisomy 5 has also been observed in a subclone of a SFT of unknown primary site [13]. Recently, Rossi *et al.* reported a solitary fibrous tumor of the pleura with low-grade and high-grade sarcomatous components, which both components expressed platelet derived growth factor receptor β (PDGFR β) (17). Direct-sequencing polymerase chain reaction showed a missense mutation involving exon 18 of the PDGFR β gene, only in the high-grade sarcomatous component. PDGFR β , localized to chromosome 5, encodes a cell surface tyrosine kinase receptor for members of the platelet-derived growth factor family and is expressed in undifferentiated submesothelial and perivascular mesenchymal elements of the pleura.

Trisomy 8 has previously been reported as characteristic of a subset of benign fibrous lesions of soft tissue and bone (18). Extra copies of chromosome 8 have been identified in four SFTs [2, 13, 20]. When viewed as a hypertriploid clone, numerical alterations (including excess chromosome 8 copy number) of Case 1 (SFT of the liver) are comparable with the SFT of the oral cavity, which was reported by Fletcher *et al.* (Table 1, case number 10).

Conventional cytogenetic studies have also revealed gain of chromosome 21 and complete loss or partial deletion of chromosomes 1, 6, 9, 13, 15, 17, 18, and X as occurring in more than one SFT [7, 13, 20, 21]. Similarly, chromosomal imbalances have also been detected in SFT using comparative genomic hybridization (CGH). Krismann *et al.* analyzed 12 cases of SFT by CGH (19). Seven cases were negative for imbalances. In the remaining five cases, the authors found more losses than gains of chromosomes. In particular, loss of the long arm of chromosome 13 was identified in four of these five cases. Other losses identified involved chromosomes or chromosomal arms 4q, 6, 9p, 10, 15q, 21q, and Xq. Interestingly, analogous to the conventional cytogenetic studies, gain of chromosome 8 was recurrent. Other gains involved chromosomes 5, 12, 15, and 21.

Recurrently involved breakpoints are few in SFT. Structural rearrangements of 4q13, 9p22-23, 9q22, 9q31-32, and 12q24 have each been identified in two separate SFTs suggesting there

may be SFT subgroups characterized by involvement of these breakpoints [16, 17, 20, 22, 23]. Additional cases must be studied to confirm the significance of this observation.

In summary, although a few numerical imbalances and structural breakpoints are recurrent in a subset of SFTs, the cytogenetic findings of the five cases in the current study (three karyotypically normal) and a review of the literature suggest there is a wide range of genetic changes in SFT with no consistent or specific aberration which could be of diagnostic usefulness in this entity.

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Figure 1.

Representative karyotype of Case 1 illustrating the following abnormal complement: 83,XXYY,-1,-4,-6,-9,-13,-15,-17,-18,-22. Loss of one chromosome 19 homologue seen in this metaphase cell only was a random loss.

Figure 2.
Representative karyotype of one of the abnormal sideline clones identified in Case 2 with the following nomenclature: 47,X,add(X)(q22),del(2)(q32q35),+5,add(18)(p11.2).

Table I

Conventional Cytogenetic Findings in SFT

Case Number	Age/Sex	Location	Karyotypic Finding	References
1	67/Male	Pleura	46,XY,t(4;15)(q13;q26)[18]/46,XY[2]	Dal Cin <i>et al.</i> (6)
2	49/Male	Peritoneum	47,XY,t(4;9)(q13;p23),+5	Debiec-Rychter <i>et al.</i> (16)
3	58/Male	Orbit	46,XY,t(9;22)(q31;p13)	Havlik <i>et al.</i> (20)
4	47/Male	Pleura	46,XY,t(8;12)(p11.2;q24.3)[3]/46,XY[19]	Horton <i>et al.</i> (21)
5	68/Male	Pleura	46,XY,t(6;17)(p11.2;q23),ins(9;12)(q22;q15q24.1),inv(16)(p13.1q24)	Donner <i>et al.</i> (22)
6	54/Male	Pleura	48,XY,+8,+8,del(9)(q22q32)[19]/46,XY,t(1;16)(q25;p12)[7]/46,XY[9]	De Leval <i>et al.</i> (23)
7	46/Female	Pelvic	47,XX,+21[15]	Dal Cin <i>et al.</i> (7)
8	9/Female	Shoulder	46,XX,der(4)t(4;9)(q31.1;q34),del(9)(p22p24),der(9)t(4;9)(q31.1;q34)ins(9;?)q34;?[17]/46,XX[3]	Rakheja <i>et al.</i> (24)
9	57/Male	Unknown	43-46,XY,add(17)(p11)	Fletcher <i>et al.</i> (13)
10	51/Male	Oral cavity	77,XXY,+Y,+3,+8,+10,+12,+14,+17,+21/78,idem,+19/46,XY	Fletcher <i>et al.</i> (13)
11	48/Male	Unknown	46,XY,t(6;12;19)(p22;q13;p13)/47,idem,+5/46,XY	Fletcher <i>et al.</i> (13)
12	64/Female	Upper extremity	72,X,-X,del(1)(q21),add(7)(p22),inc/46,XX	Fletcher <i>et al.</i> (13)
13	85/Male	Upper extremity	46,XY,t(2;17)(p16;q11),ins(7;11)(q36;q14q23)/46,XY	Fletcher <i>et al.</i> (13)
14	53/Female	Lower extremity	46,XX,tas(14;19)(p13;q13)/46,XX	Fletcher <i>et al.</i> (13)
15	58/Female	Pleura	46,XX,t(2;3)(p21;q26)[18]/46,XX[3]	Mertens <i>et al.</i> (8)
16	?/Male	Pleura	47,XY,+8	Hanau <i>et al.</i> (2,16)
17	?/Male	Pleura	47,XY,+8	Hanau <i>et al.</i> (2,16)
18	43/Male	Right cheek	46,XY[15]/46,XY,t(1;17;18)(p13;q11.2;q21)[5]	Manor <i>et al.</i> [21]
19*	82/Female	Lower extremity	70,XXX,+X[4],+1[2],add(1)(p36)[4],add(1)[2],+2[4],-3[4],+6[4],add(6)(p11)x2[4],+7[4],+9[3],-11[4],-12[4],-13[4],add(13)(p11)x2[4],-14[4],+15[4],-16[3],-17[4],-19[4],+20[4],+21[4],+22[2],+mar1x2[4][cp4]	Hoshino <i>et al.</i> (25)
20	65/Male	Liver	83,XXYY,-1,-4,-6,-9,-13,-15,-17,-18,-22[20]	Present case
21	82/Female	Peritoneum	47,XX,del(2)(q32,q35),+5[8]/47,sl,add(X)(q22),add(18)(p11.2)[9]/46,sl,del(9;15)(p13;p11.2)[2]	Present case

* Described as a malignant solitary fibrous tumor