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Cytogenetics of Spindle Cell/Pleomorphic Lipomas: Karyotyping and FISH Analysis of 31 Tumors

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Abstract. *Background: Spindle cell/pleomorphic lipomas are benign tumors. Here, we present our cytogenetic data on 31 such tumors. Materials and Methods: G-banding chromosome analysis and (in selected cases) fluorescence in situ hybridization (FISH) using probes for FOXO1, RB1, and HMGA2 were performed. Results: Rearrangements of chromosome 13 were found in 58% of tumors. Chromosomes 6, 1, 12, and 11 were also involved in 42%, 26%, 26%, and 23% of tumors, respectively. FISH analysis showed heterozygous deletion of RB1 in seven samples with chromosome 13 aberrations. In four of them, FOXO1 was also deleted. In two tumors with 12q15 rearrangements, FISH confirmed that HMGA2 was targeted. Conclusion: Structural rearrangements of 13q or losses of an entire chromosome 13 are the most common cytogenetic aberrations in spindle cell/pleomorphic lipomas. However, cytogenetic variation exists similarly to what is found in other lipomas, suggesting that various pathways may be responsible for tumorigenesis.*

Spindle cell lipoma was first described by Enzinger and Harvey in 1975 (1) as a benign tumor usually occurring subcutaneously in the upper back, shoulder or posterior neck of middle-aged men, after which several other studies confirmed the existence of this lipoma subgroup (2-9). Their occurrence has also been reported in other sites such as the face, limbs, oral cavity, larynx, bronchus, orbit, breast, perianal region, and spermatic cord (10). Macroscopically, spindle cell lipomas are mostly well circumscribed, round or discoid nodules. Histologically, they consist of a mixture of bland spindle cells and mature adipocytes. The matrix surrounding the cells is composed of varying amounts of mucoid material and collagen bundles haphazardly distributed throughout the lesion (1, 2, 4, 6). Spindle cell lipomas can be challenging to the radiologist, pathologist, or surgeon to diagnose, particularly when they contain little internal fat (8).

Pleomorphic lipomas were first described by Shmookler and Enzinger (11). Like spindle cell lipomas, their most common location is in subcutaneous tissue of the shoulders and posterior neck of adults, especially men. They are solitary, circumscribed, slow-growing, painless tumors. Microscopically, they show admixture of mature adipose tissue and pleomorphic multinucleated cells, so-called florette cells, and overall display histological and immunophenotypic features similar to those of spindle cell lipomas (3, 4, 12). Thus, this tumor type is now accepted as an extremely pleomorphic variant of spindle cell lipomas and the two are lumped together as spindle cell/pleomorphic lipoma (13).

In 1994, Mandahl *et al.* (14) reported the cytogenetic findings in six spindle cell lipomas and two pleomorphic lipomas. One spindle cell lipoma had a supernumerary ring chromosome as the sole anomaly. The other five spindle cell lipomas and both pleomorphic lipomas had hypodiploid stemlines with monosomy 16 or unbalanced aberrations leading to loss of 16q13-qter. Unbalanced aberrations of chromosomes 13 and 10 were also found. In addition, both pleomorphic lipomas, but none of the spindle cell lipomas, had hypotetraploid sidelines, multiple nonclonal aberrations, and telomeric associations (14).

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Key Words: Spindle cell lipomas, pleomorphic lipomas, cytogenetics, chromosome 13, chromosome 12, *RB1* gene, *FOXO1* gene, *HMGA2* gene.

Table I. *Clinicopathological and cytogenetic data of the 31 spindle cell/pleomorphic lipomas.*

Case	Gender/ Age	Location	Depth	Largest diameter (cm)	Diagnosis	Material for cytogenetic analysis	Karyotype
1	M/46	Upper arm	Subcutaneous	5	Spindle cell lipoma	Resection	38~46,XY,-10,der(11)add(11)(p15)add(11)(q21),inc[cp14]
2	M/58	Neck	Not available	6.5	Spindle cell lipoma	Resection	45,XY,del(2)(q33),del(6)(q15),inv(11)(p15q23),-13[cp15]
3	M/59	Knee	Subcutaneous	1	Spindle cell lipoma	Resection	45~46,XY,del(1)(p32),add(2)(p25),inc[cp4]
4	M/66	Thenar	Intramuscular	3	Spindle cell lipoma	Resection	46,XY,t(13;14)(q12;q24)[15]
5	F/62	Back	Subcutaneous	8.5	Pleomorphic lipoma	Resection	45~46,XX,del(2)(q11),der(2)t(2;13)(?;q14),del(6)(q13q23),del(13)(q21),der(?13)t(8;?13)(p11;q11),der(17)(17qter->17q21::17p13->17q21::8q11->8qter)[cp6]/44~45,idem,-X[cp5]/86~95,idemx2[cp5]
6	M/51	Scalp	Subcutaneous	8.5	Spindle cell lipoma	Resection	57~59<2n>,XY,+X,+5,+8,+12,+der(12)t(12;17)(q15;q23),+15,+18+18,+20,+21+21,+mar[cp11]
7	M/66	Leg	Intramuscular	9.5	Spindle cell lipoma	Resection	46,XY,t(16;19)(q13;p13)[16]/46,XY,del(1)(q32),inc[2]/46,XY[2]
8	M/75	Back	Subcutaneous		Spindle cell lipoma	Tumor biopsy	45,XY,-13,-22,+mar[cp6]
9a	M/58	Neck	Subcutaneous	9	Spindle cell lipoma	Tumor biopsy	42~46,XY,add(5)(p15),del(7)(q22),del(10)(q22),add(19)(q13)[cp6]/46,XY[8]
9b			Subcutaneous	9	Spindle cell lipoma	Resection	44,Y,t(X;14)(p22;q13),der(1)t(1;18)(p13;q11),-6,-9,der(10)t(6;10)(p11;p11),t(11;17)(p11;p13),der(13)t(1;13)(p13;q14)ins(13;?)(q14;?),add(18)(q11)[15]
10	M/69	Neck	Subcutaneous	14	Spindle cell lipoma	Resection	45,XY,-3,der(6)t(3;6)(q12;q13),del(13)(q14q22)[15]
11	M/44	Flank	Subcutaneous	4	Spindle cell lipoma	Resection	46,XY,t(1;12)(p32;q15)[15]
12	M/80	Shoulder	Subcutaneous	4	Spindle cell lipoma	Resection	45,XY,-6,der(13)t(6;13)(q13;q14),der(14)t(6;14)(p21;q32)[cp8]/46,XY[2]
13	M/53	Shoulder	Subcutaneous	19	Spindle cell lipoma	Resection	46,XY,t(1;13)(p36;q22),der(4)t(4;6)(q21;q21),der(6)del(6)(p21)t(4;6),t(15;22)(q21;q12)[14]/46,XY[2]
14	F/67	Neck	Subcutaneous	4	Pleomorphic lipoma	Tumor biopsy	46,XX,t(1;7;5)(p36;p15;q11)[9]/46,XX[16]
15	M/69	Back	Intramuscular	9	Spindle cell lipoma	Resection	46,XY,der(1)t(1;12)(q23;q15),der(12)t(1;12)(q23;q11),-13,-21,+2mar[17]
16	F/58	Wrist	Not available	3.5	Spindle cell lipoma	Resection	46,XX,t(12;14)(q15;q24)[15]
17	M/32	Thoracic wall	Intramuscular	4.5	Spindle cell lipoma, myxoid	Tumor biopsy	48~49,XY,+8,+8,+12[cp5]/46,XY[4]
18a	M/57	Neck	Subcutaneous	9	Pleomorphic lipoma	Tumor biopsy	46,XY,t(5;13)(p15;q14)[22]
18b		Neck	Subcutaneous	9	Pleomorphic lipoma	Resection	46,XY,t(5;13)(p15;q14)[5]/46,XY[2]
19	F/64	Upper arm	Subcutaneous		Spindle cell lipoma	Tumor biopsy	46,X,inv(X)(p22q26),der(4)t(4;11)(p16;q22),del(10)(p13),t(12;12)(q15;q21)[12]/47,idem,+10[cp3]
20	F/58	Neck	Subcutaneous	7.0	Spindle cell lipoma	Resection	46,X,t(X;22)(p21~22;q11),del(13)(q14)[15]
21	M/42	Shoulder	Subcutaneous	5.6	Spindle cell lipoma, myxoid	Resection	47,XY,+4,-6,+8,der(12)del(12)(q14q14)inv(12)(q12q14),-13,-14,-16,+18,+2mar[14]/46,XY[2]
22	M/56	Neck	Not available	5	Spindle cell lipoma	Tumor biopsy	46,XY,t(7;17)(q22;p13)[3]/46,XY[10]
23	M/51	Thoracic wall	Intramuscular	6	Spindle cell lipoma	Resection	69,XXY,+Y,-6,-8,-10,-13,+15,-16,+18,+19,+20,+21,-22[11]/46,XY[2]
24	M/71	Thigh	Not available	8	Pleomorphic lipoma	Resection	65~72,XXY,-1,i(11)(q10),ins(12;?)(q13;?)x2,add(15)(p13),add(17)(p13)x2,add(19)(p13),add(19)(p13),add(21)(p11),der(22)t(1;22)(p13;q13),+1~2r,inc[cp7]/46,XY[2]
25	M/55	Neck	Subcutaneous	3	Spindle cell lipoma	Resection	45,XY,-13,-14,+mar[10]
26	M/68	Back	Subcutaneous	5.2	Spindle cell lipoma	Resection	44~45,XY,add(6)(q23),-10,-13,der(16)t(10;16)(q11;q13),+mar[cp5]/44~45,idem,del(11)(q23)[cp5]
27	M/58	Thigh	Not available	5.5	Spindle cell lipoma	Resection	45,XY,-6,der(13)t(6;13)(p21;q14)[10]
28	M/51	Instep	Not available	4.3	Spindle cell lipoma	Resection	46,XY,der(6)t(6;11)(p21;q13),der(8)t(6;8)(p21;p21),der(11)t(8;11)(p21;p15)del(11)(q13)[11]
29	M/58	Back	Not available	4.8	Pleomorphic lipoma	Resection	47,XY,del(13)(q11q14),der(16)add(16)(p11)del(16)(q22),add(17)(p13),der(17)t(17;18)(q23;q12),add(18)(q12),+r[2]/45~46,idem,-2[cp6]/46,XY[7]

Table I. *Continued*

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Case	Gender/ Age	Location	Depth	Largest diameter (cm)	Diagnosis	Material for cytogenetic analysis	Karyotype
30	F/53	Neck	Not available	4.2	Spindle cell lipoma	Resection	46,XX,der(4)inv(4)(p14q31)t(4;6)(q31;p21),t(5;21)(q33;q22),der(6)t(4;6)(p14;p21),del(13)(q12q22)[10]
31	F/63	Neck	Not available	7	Spindle cell lipoma	Resection	45,XX,-6,der(22)t(6;22)(p21;q13)[5]/46,idem,+mar[7]

Current cytogenetic knowledge about these tumors is scant. According to the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer (http://cgap.nci.nih.gov/Chromosomes/Mitelman, Database last updated on August 23, 2017), only 28 spindle cell/pleomorphic lipomas (only two of them were pleomorphic) with abnormal karyotypes have been reported in seven English-language articles (14-20). In addition, another two cases of spindle cell lipoma were reported in a French-language report (21). By way of comparison, the same database contains information on altogether 490 karyotypically abnormal ordinary lipomas reported in 57 articles. The cytogenetic knowledge about spindle cell/pleomorphic lipomas based on these reports can be summarized as follows: in the majority of cases, the chromosome number is 44-46 and monosomies or partial chromosome losses are the dominating abnormalities. Chromosomes 13 and 16 are the most frequently affected with monosomy for or partial loss of chromosome 13 and deletion of 16q13-qter coming across as the most common aberrations (22). We wanted to add to the cytogenetic knowledge on spindle cell/pleomorphic lipoma and for this reason present our data on another 31 tumors of this type.

Materials and Methods

Materials. Information about the patients' sex and age and the tumors' location, depth, and size is given in Table I. The patients were 25 males and 6 females. The age range was from 32 to 80 years, with a median of 58. In 26 patients, the diagnosis was spindle cell lipoma (Figure 1A), in one of them with a myxoid component, whereas the diagnosis was pleomorphic lipoma in 5 tumors (Figure 1B). Eleven of the tumors were located in the neck, five in the back, three in the shoulders, two in the thoracic wall, and two in the upper arm. Other tumors were found in the leg, flank, instep, knee, wrist, hand, and scalp.

The material for cytogenetic analysis consisted of 26 tumor resections and 7 tumor biopsies from 31 patients (2 tumors were examined first on biopsy material, later on resectates). They were diagnosed as spindle cell or pleomorphic lipoma at the Department of Pathology and cytogenetically analyzed at the Section for Cancer Cytogenetics, both at The Norwegian Radium Hospital, Oslo University Hospital, between 2002 and 2016. The study was approved by the regional ethics committee (Regional komité for medisinsk forskningsetikk Sør-Øst, Norge, http://helseforskning.etikkom.no). All patient information has been de-identified.

G-banding and karyotyping. Fresh tissues from a representative area of resected tumors (n=26) or core needle biopsies (n=7; two tumors were examined both as biopsies and resectates) were received and analyzed cytogenetically as part of our diagnostic routine. The samples were disaggregated mechanically and enzymatically with collagenase II (Worthington, Freehold, NJ, USA). The resulting cells were cultured and harvested using standard techniques (23). Chromosome preparations were G-banded with Wright's stain (Sigma-Aldrich; St. Louis, MO, USA) and examined. Metaphases were analyzed and karyograms were prepared using the CytoVision computer assisted karyotyping system (Leica Biosystems, Newcastle, UK). The karyotypes were described according to the International System for Human Cytogenomic Nomenclature (24).

Fluorescence in situ hybridization (FISH). The following probes were used for FISH analysis: i) *FOXO1* break apart rearrangement probe purchased from Cytocell (Cytocell, Cambridge, UK). This probe hybridizes to a 1.5 Mbp sequence on 13q14.11 which contains the *FOXO1* gene. According to the company's information, it consists of two probes (405 kb and 183 kb), labelled in green, situated proximal to the *FOXO1* gene and covering markers D13S765 and SHGC-111293, and four probes (123 kb, 142 kb, 95kb, and 253kb), labelled in red, situated distal to the *FOXO1* gene and covering markers D13S638 and SHGC-16596. ii) RB1 deletion probe, purchased from Cytocell (Cytocell, Cambridge, UK) and used to detect deletion of the *RB1* locus in 13q14.2. It consists of a 318 kb red probe spanning *RB1* and a 13qter green probe acting as a control for chromosome 13. iii) A homemade break apart *HMGA2* probe (25). The 5'-end of the probe (red signal) was constructed from a pool of the clones RP11-185K16, RP11-30I11, and RP11-662G15. The 3'-end of the probe (green signal) was constructed from a pool of the clones RP118B13, RP11-745O10, and RP11-263A04. All of them map to chromosome subband 12q14.3 and cover the *HMGA2* locus. Detailed information on the *HMGA2* BAC clones is given elsewhere (25). Fluorescent signals were captured and analyzed using the CytoVision system (Leica Biosystems, Newcastle, UK).

Results

Karyotyping. All the samples had cells carrying cytogenetic aberrations; during the same time period, only one other tumor with this diagnosis was subjected to cytogenetic

analysis but was found to have a normal karyotype (data not shown). Most of the tumors had pseudo- or near-diploid karyotypes, although two were near-triploid (cases 23 and 24) (Table I). In two tumors (cases 17 and 23), only numerical changes were found whereas the rest had structural only or both structural and numerical aberrations. In cases 9 and 18, cytogenetic analysis was performed on both a tumor biopsy (a) and material from the resected tumor (b). In case 9, cytogenetically-different structural aberrations were found in the biopsy and the resection (Table I, 9a and 9b), whereas the two samples in case 18 had the same karyotypes (Table I, 18a and 18b).

The most frequent aberrations (over 20%) involved numerical and/or structural changes of chromosomes 13, 6, 1, 12, and 11 (in decreasing order; Table I). Abnormalities of chromosome 13 were found in 18 tumors (58%). Loss of the entire chromosome (cases 2, 8, 15, 21, 23, 25, and 26) or partial losses of the long arm (cases 5, 9b, 10, 12, 20, 27, 29, and 30) occurred in 15 tumors, whereas balanced translocations were seen in 3 cases (4, 13, 18a, and 18b). Partial karyotypes, showing the rearrangements of chromosome 13, for samples 9b, 12, 18b are presented in Figure 2.

Changes of chromosome 6 were found in 13 tumors (42%). Seven of them had either loss of the entire copy (cases 21 and 23) or deletions in or of 6q (cases 2, 5, 9b, 10, 12, 26, and 27), while 6 tumors had structural aberrations targeting 6p21 (cases 12, 13, 27, 28, 30, and 31).

Chromosome 1 aberrations were seen in 8 tumors (26%), either as losses in the p-arm (case 3) or q-arm (cases 7 and 24) or as balanced rearrangements (cases 9b, 11, and 13-15). Changes of chromosome 12 were also found in 8 tumors; in the majority of them (cases 6, 11, 15, 16, 19, 21, and 24), structural aberrations affected region 12q13~15, whereas 2 tumors (cases 6 and 17) had an extra copy of the chromosome. The partial karyotype showing the t(1;12)(p32;q15) for sample 1 is presented in Figure 2. The arms of chromosome 11 were affected by structural aberrations in a total of 7 tumors (23%) (cases 1, 2, 9b, 19, 24, 26, and 28).

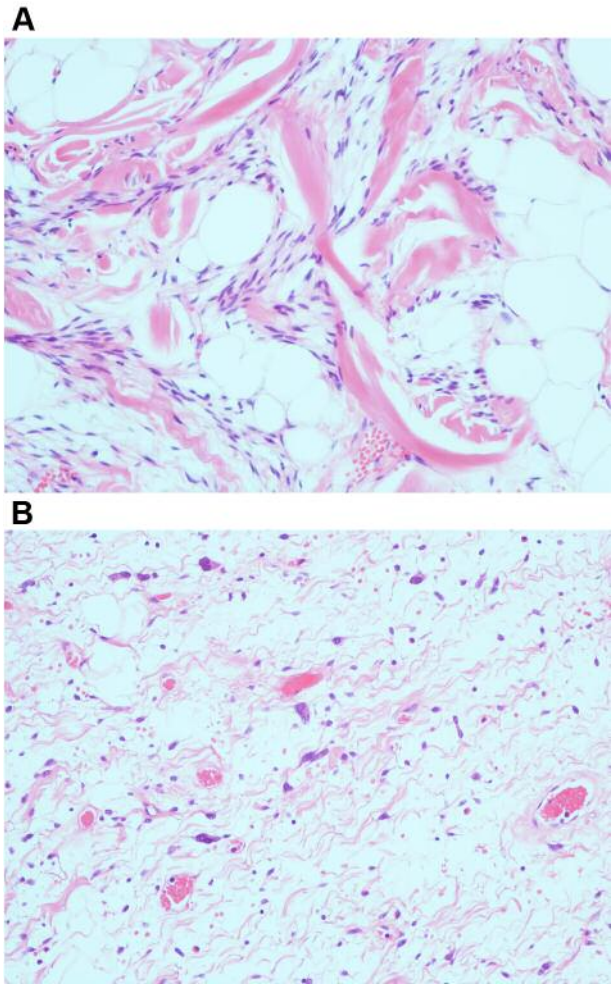

Figure 1. *Histological examination of spindle cell and pleomorphic lipomas. A) Typical features of spindle cell lipoma with admixed ropy collagen, bland spindle cells, and elements of mature fat. B) Typical features of pleomorphic lipoma with easily identifiable large atypical cells with hyperchromatic nuclei, admixed with bland spindle cells, collagen, and mature adipocytes. Hematoxylin and eosin (H&E) staining, magnification ×200).*

FISH. The results of interphase FISH analyses with *RB1* (13q14.2), 13qter, *FOXO1* (13q14.11), and *HMGA2* (12q14) probes are presented in Table II. The analyses could be performed on 13 samples (12 cases): eight cases with chromosome 13q aberrations (4, 9b, 12, 18a, 18b, 27, 29, and 30), one tumor with chromosome 13 and 12q changes (case 15), one tumor with 12q rearrangement (case 11), and three cases without aberrations of chromosomes 12 and 13 (14, 22, and 28).

Heterozygous deletion of the *RB1* probe was observed in seven cases: 9b, 12, 18a and 18b, 27, 29, and 30. In cases 9b and 27, heterozygous deletion of the 13qter probe was also found. Furthermore, in cases 9b, 12, 29, and 30, heterozygous deletion of *FOXO1* was observed; in case 29, the deletion was partial. In contrast, cases 18a and 18b did not show deletions of *FOXO1*. Rearrangements of the *HMGA2* gene were detected in cases 11 and 15. Cases 4, 14, 22, and 28 did not show any changes by FISH with the probes used. In Figure 2 FISH analyses are shown with *FOXO1* break apart and *RB1* deletion probes for samples 9b, 12, and 18b, and with an *HMGA2* probe for sample 11.

Discussion

To the best of our knowledge, the present study describes the largest series of cytogenetically-abnormal spindle cell/pleomorphic lipomas. Our findings show that structural

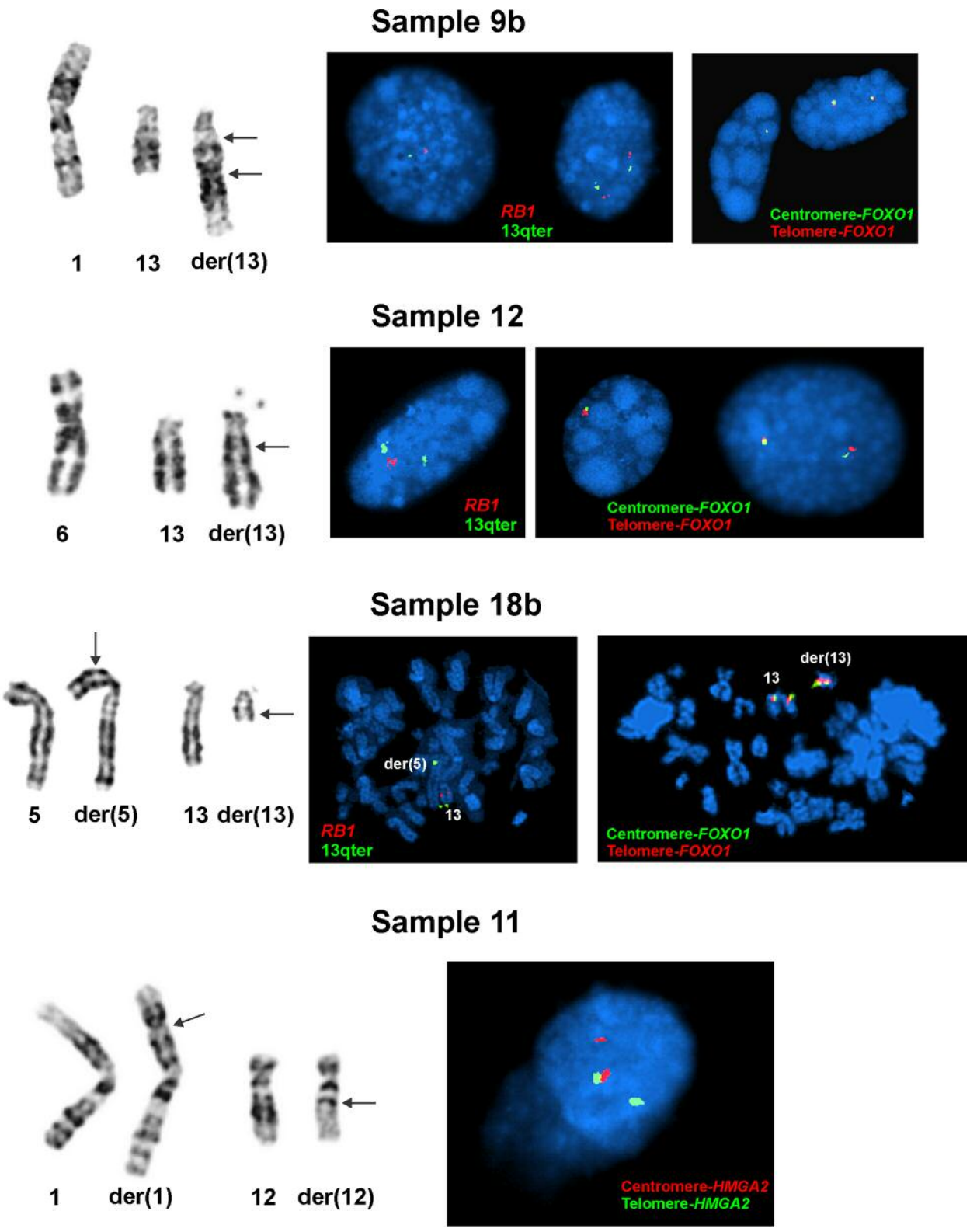

Figure 2. *Cytogenetic and FISH analyses of spindle cell/pleomorphic lipomas. Results for samples 9b, 12, 18b, and 11 are shown. Left: partial karyotype. Arrows indicate breakpoints. Right: FISH analyses with FOXO1 break apart and RB1 deletion probes for samples 9b, 12, and18b, and with an HMGA2 probe for sample 11.*

Table II. *Summary of FISH analyses of 13 samples of spindle cell/pleomorphic lipoma.*

Case	Heterozygous deletion of		No of nuclei studied	Heterozygous deletion of *FOXO1* (%)	No of nuclei studied	Rearrangement of *HMGA2* (%)	No of nuclei studied
	RB1 (%)	13qter (%)					
4	0	0	50	fail	fail	0	100
9b	93	93	107	96	104	0	100
11	0	0	100	0	100	100	100
12	87	0	94	31	103	0	75
14	0	0	100	0	100	0	100
15	0	0	100	0	107	50	200
18a	100	0	100	0	100	0	70
18b	100	0	100	0	100	0	90
22	0	0	50	0	30	Fail	Fail
27	96	96	99	Not done	Not done	Not done	Not done
28	0	0	96	Not done	Not done	Not done	Not done
29	82	0	114	(partial) 83	104	Not done	Not done
30	98	0	203	98	205	Not done	Not done

aberrations, mainly deletions, of chromosome arm 13q or loss of the entire chromosome 13 are frequent in this tumor type inasmuch as they were found in 58 % (18/31) of the tumors. This aspect of our data is in agreement with previously published reports in which deletion of 13q/-13 was also found in spindle cell lipomas (14, 16-18, 20, 21, 26). Mandahl *et al.* (14) reported unbalanced aberrations leading to partial 13q-loss in 5 out of 8 examined spindle cell/pleomorphic lipomas (14). Dahlén *et al.* (17) presented 11 spindle cell lipomas with deletions of chromosome arm 13q or losses of the whole chromosome. In two articles, Bartuma *et al.* (16, 26) presented altogether 16 spindle cell lipomas, all of which had changes of chromosome 13. Dumollard *et al.* (21) reported two cases of spindle cell lipomas with chromosome 13 abnormalities. Dal Cin *et al.* (18) reported one spindle cell lipoma with loss of chromosome 13 and a second with 13q deletion. Finally, Welther *et al.* (20) reported a spindle cell lipoma with structural rearrangement of 13q.

Deletions of 13q or loss of chromosome 13 were also reported in ordinary lipomas with karyotypic aberrations, albeit less frequently (16, 17, 27, 28). In the Mitelman Database of Chromosome Aberrations and Gene Fusions in Cancer, 12 lipomas with -13 and 35 lipomas with del(13q) are listed (29). Involvement of chromosome 13 was also found in cellular angiofibroma, extramammary myofibroblastoma, and recently in angiolipoma (30-32). The morphologic similarities among cellular angiofibroma, extramammary myofibroblastoma, and spindle cell lipoma together with their cytogenetic similarities, in particular loss of material from the long arm of chromosome 13, suggest that these tumors arise through largely identical pathogenetic mechanisms from a common connective tissue precursor cell which then undergoes (myo)fibroblastic or adipocytic differentiation (30, 31, 33, 34).

The results of interphase FISH analysis with *RB1* and/or *FOXO1* probes were in good overall agreement with the results of G-banding analysis (Tables I and II). In four tumors without chromosome 13 changes (cases 11, 14, 22, and 28), no deletions of any probe were found. Neither was deletion of *RB1* nor deletion of 13qter detected in case 4 which had a balanced t(13;14) involving 13q12. On the other hand, heterozygous deletion of the *RB1* locus was observed in seven samples with 13q rearrangements or loss detected by G-banding (cases 9b, 12, 18a, 18b, 27, 29, and 30); in five of these cases, the 13qter probe was retained. In the four cases (9b, 12, 29, and 30) with structural unbalanced aberrations involving 13q14, both *RB1* and *FOXO1* were deleted.

In the two samples of case 18, with a seemingly balanced t(5;13)(p15;q14) as the sole anomaly, heterozygous deletion of *RB1* but not of *FOXO1* and 13qter was found. The data indicate the presence of a submicroscopic deletion of the *RB1* locus which in its turn suggests that *RB1*, or another gene very close, may be important in spindle cell/pleomorphic lipoma pathogenesis.

The fact is that the molecular target of chromosome 13 aberrations in spindle cell/pleomorphic lipomas, typical lipomas, cellular angiofibromas, extramammary myofibroblastoma, and angiolipoma remains unknown. Bartuma *et al.* (16) identified two minimal deleted regions (MDR) in 13q14 for spindle cell lipoma and one for typical lipomas. These deletions were associated with down-regulated expression of several genes. Because the expression levels of *RB1* were not significantly reduced and because no mutations were seen by sequencing, the authors concluded that there is no decisive

support for *RB1* as the main target for the13q-deletions in spindle cell lipomas (16). Instead, their data implicated miR-16-1 as a potential target for the 13q deletions (16). On the other hand, FISH analyses of cellular angiofibromas, extramammary myofibroblastoma, and angiolipoma detected monoallelic (and sometimes biallelic) loss of *RB1* (30-32, 35, 36). Furthermore, using immunohistochemical staining for RB1, Chen *et al*. (37) showed that nuclear RB1 expression was deficient in all examined spindle cell lipomas, pleomorphic lipomas, and cellular angiofibromas examined by them, as well as in 17 of 19 (89%) mammary-type myofibroblastomas.

In our series, involvement of chromosome 12 was found in 26% of the tumors. Rearrangements of the bands 12q13-15 are the most common change in ordinary lipomas where they are found in two-thirds of all tumors with an abnormal karyotype (22). The translocation t(1;12)(p32;q15), found in case 11 as the sole anomaly, has also been described in ordinary lipomas (29), whereas the t(12;14)(q15;q24) found in case 16 is often found in uterine leiomyomas and chondroid hamartomas (29). The target gene of the 12q13-15 rearrangements in benign connective tumors is *HMGA2* (22). Our FISH experiments confirmed the involvement of *HMGA2* in cases 11 and 15 with 12q15 rearrangements; neither deletion of *RB1* nor deletion of *FOXO1* was found in these tumors.

Chromosome 16 was in the past reported as being frequently rearranged in spindle cell/pleomorphic lipomas (22). Mandahl *et al*. (14) found unbalanced aberrations of chromosome 16 in 7 out of 8 examined spindle cell/pleomorphic lipomas. Bartuma *et al*. (16) reported chromosome 16 rearrangements in 9 out of 11 tumors and Dahlén *et al*. (17) found similar changes in 4 of 11 tumors. In our series, only 5 out of 31 tumors had a visible aberration of chromosome 16, and in four of them the aberration was seen together with changes of chromosome 13. In comparison, chromosomes 6, 1, 12, and 11 were involved more frequently (40-20% in decreasing order). Our data indicate that alternative genetic pathways exist for the development of spindle cell/pleomorphic lipomas, many of which are shared by other benign connective tissue tumors. However, the presence of submicroscopic deletions within 13q14 or rearrangements targeting the *HMGA2* locus cannot be excluded as pathogenetically important in tumors without any microscopically visible changes of chromosomes 12 and 13.

Conflicts of Interest

The Authors declare that they have no competing interests.

Acknowledgements

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