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Small Supernumerary Marker Chromosomes (sSMC) in Patients with a 45,X/46,X,+mar Karyotype – 17 New Cases and a Review of the Literature

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Key Words
Fluorescence in situ hybridization (FISH) · Gonadoblastoma · Incidence · Small supernumerary marker chromosome (sSMC) · Turner syndrome

Abstract
Small supernumerary marker chromosomes (sSMC) can appear in a numerically normal 'basic karyotype', but also in a numerically abnormal one like a Turner syndrome karyotype (= sSMC^T). Here we present 17 new cases with such a mos 45,X/46,X,+mar karyotype. Moreover we reviewed all 512 cytogenetically similar cases available from the literature and supply for the first time data on occurrence, shapes and subgroups of this rare cytogenetic entity. sSMC^T are very rare in the common population (1:100,000) – however, they can be observed with a 45- and even 60-times higher frequency in infertile and (develop)mentally retarded patients, respectively. Even though sSMC^T derive from one of the gonosomes in >99% of the cases, there are also exceptional reports on sSMC^T derived from one of the autosomes. The majority of sSMC^T(X) form ring chromosomes, while most sSMC^T(Y) are inverted duplicated/isodicentric chromosomes. Although >500 sSMC^T are reported, a detailed characterization of the chromosomal breakpoints is only given for a minority. Thus, more cases with detailed (molecular) cytogenetic marker chromosome characterization are needed to provide information on formation and effects of an sSMC^T.

Small supernumerary marker chromosomes (sSMC) are defined as structurally abnormal chromosomes that cannot be identified or characterized unambiguously by conventional banding cytogenetics alone; they are generally equal in size or smaller than a chromosome 20 of the same metaphase spread. sSMC can be present (1) in a karyotype of 46 normal chromosomes, (2) in a numerically abnormal karyotype (like Turner or Down syndrome) or (3) in a structurally abnormal but balanced

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karyotype (e.g. Robertsonian translocation or ring chromosome formation) [Liehr et al., 2004].

Recently, we reviewed all reported sSMC present additionally in a normal 'basic karyotype' of 46 chromosomes [Liehr et al., 2006; Liehr, 2007]. We also determined sSMC frequencies in different clinical subgroups: 0.075% in prenatal diagnoses, 0.044% in consecutively studied postnatal cases, 0.125% in infertile and 0.288 in (develop)mentally retarded patients [Liehr and Weise, 2007]. However, in the literature no special attention was ever given to sSMC present in a Turner karyotype of mos 45,X/46,X,+mar. sSMC in a Turner karyotype are abbreviated in the following as sSMC^T.

There are reviews on clinical aspects of mos 45,X/46,X,+mar karyotypes leading to female [Mittwoch, 1992; Ramos, 2007] or male phenotypes [Egozcue et al., 2000]. The question whether the karyotype was mos 45,X/46,XX(/47,XXX) or mos 45,X/46,XY(/47,XXY) [Hsu, 1994; Ogata and Matsuo, 1995] was also addressed and variation of mosaicism in different tissues was analyzed [Park et al., 1999]. Furthermore, in a mos 45,X/46,X,der(X) karyotype it is important to test for the ability of the der(X) to be inactivated, i.e. for the presence of the *XIST* gene [Sagi et al., 2007]. Contrary, when a mos 45,X/46,X,der(Y) or 45,X/46,XY karyotype is characterized, it is important to counsel the patient concerning a possible gonadoblastoma and a preventive removement of gonadal tissue [Bianco et al., 2006]. In this context, the necessity of applying molecular approaches for detection of cryptic 45,X/46,XY mosaicism is discussed [Medlej et al., 1992; Nagafuchi et al., 1992; Binder et al., 1995; Nishi et al., 2002; Semerci et al., 2007], as a direct relationship between percentage of cells exhibiting a 45,X karyotype and the patient's phenotype does not exist [Alvarez-Nava et al., 2003].

Here we report on 17 new cases with an sSMC^T. Moreover, we review similar cases and provide for the first time data on the frequency and subgroups of the rare cytogenetic entity 'cases with an sSMC^T'.

Materials and Methods

Cytogenetics and Molecular Cytogenetics

Seventeen cases with an sSMC^T (table 1) were studied by cytogenetics and molecular cytogenetics.

GTG-banding was done according to standard procedures. Fluorescence in situ hybridization (FISH) was performed using commercially available centromeric probes for chromosomes X and Y according to the manufacturer's instruction (Abbott/Vysis). When indicated LSI SRY, a subtelomeric probe for X/Ypter (Abbott/Vysis), or probes adjacent to the *XIST* region, RP11-372C14 and RP11-183A17, were applied. Moreover, subcentromere-specific multicolor FISH (subcenM-FISH), using probe sets for the X and the Y chromosome, was done as previously reported [Starke et al., 2003]. In some cases also the multicolor banding (MCB) probe set for the X chromosome was applied [Liehr et al., 2002].

Data Mining in the Literature

Frequency of 46,X,+mar Cases. Recently we determined the sSMC frequency (for karyotypes 47,+mar) in different prenatal and postnatal entities [Liehr and Weise, 2007]. Here we did the same for sSMC^T (see tables 2–4). The same literature as previously described was used, however, references reporting only sSMC frequencies were excluded here. For details on references and way of data mining see Liehr and Weise [2007]. For comparison, the frequencies of the karyotype (mos) 45,X without presence of an sSMC^T were also determined in the corresponding clinical subgroups.

sSMC Homepage [Liehr, 2007]. We recently collected all literature on sSMC and made it available on the sSMC homepage [Liehr, 2007]. For this paper we assembled all presently available 512 sSMC^T [(mos) 46,X,+mar – see sub page of Liehr, 2007: http://www.med.uni-jena.de/fish/sSMC/sturner.htm]. According to the cytogenetic definition of an sSMC [Liehr et al., 2004] only marker chromosomes smaller in size than a chromosome 20 are included. Thus, larger structurally aberrant X chromosomes, like i(Xq), i(Xp), etc. are not considered here. On the other hand, due to the small size of the male gonosome, practically all derivatives of the Y chromosome were taken into account. Only derivatives reported as del(Y) or del(Yq) were excluded, as they are easily characterized as shortened Y chromosomes and not as unidentified markers. Accordingly, 371 cases with an sSMC(Y) in contrast to only 139 sSMC(X) were included in Liehr [2007] – the 17 new cases reported here are already incorporated in this dataset.

All aforementioned published cases with an sSMC^T were analyzed in detail for the quality of their cytogenetic description, shape of the sSMC^T and their clinical outcome.

Results and Discussion

17 New Cases with sSMC^T

In 17 cases with a 46,X,+mar karyotype the origin, shape and genetic content of the sSMC^T were characterized. Apart from three cases, all cases were mosaic containing at least an additional cell line with 45 chromosomes (45,X). Two of the cases were male (cases m-urY-18 and m-iY-q11.22/1-3), the remaining 15 cases female. The sSMC^T were derived from the X chromosome in the majority (12 cases) of the cases tested here. The different shapes of the sSMC^T are specified in table 1. Ring, centric minute and inverted duplication shape were characterized. An exemplary FISH result is depicted in figure 1. In case m-urY-18 the exact breakpoint in Yq could not be determined due to lack of cytogenetic material.

Table 1. Results of 17 new cases with an $sSMC^T$

Case No. [acc. to Liehr, 2007]	45,X (%) in peripheral blood	sSMC karyotype	Lack of puberty	(Develop) mental delay	Short stature	Others
rX-p11.3∼11.4/ 1-1	79	r(X)(p11.3∼11.4q13.3)[19%]/ r(X;X)(p11.3∼11.4q13.3::p11.3∼11.4q13.3)[2%]	n.a.	+	+	+
rX-p11.2∼11.3/ 1-1	11	r(X)(p11.2∼p11.3q21)[66%]/ min(X)(p11.2∼p11.3q21)[23%]	n.a.	n.a.	+	+
rX-p11.21/ 2-1	40	r(X)(::p11.21q21.2∼q21.2::)	n.a.	n.a.	+	+
rX-p11.2/ 1-1	16	r(X)(p11.2q13)	+	–	+	+
rX-p11.2/ 2-1	80	r(X)(p11.2q13.1)	n.a.	+	+	+
iX-p11.1/ 1-1	30	idic(X)(p11.1q12::q12q11.1)[54%]/ XX[16%]	+	–	+	+
minX-p11.2/ 1-1	–	min(X)(p11.21q10)[12%]/ min(X)(p11.21q10::q10p11.21)[3%]/ XX[85%]	n.a.	–	–	–
minX-p11.2/ 2-1	9	min(X)(p11.2q12)[18%]/ min(X)(:q12→p11.2::p11.2→q12:)[6%]/ XXX[5%]/XX[62%]	n.a.	n.a.	n.a.	+
minX-p11.1/ 2-1	60	min(p11.1q11::q11p11.1 or q11p11.1::p11.1q11 or : q11p11.1::q11p11.1)	n.a.	n.a.	+	+
minX-p11.1/ 3-1	46	min(X)(p11.1q13.2∼13.3)	n.a.	+	–	+
minX-p11.1/ 4-1	32 (amnion)	mar1a = min(X)(p11.1q11.21:)[9]/ mar1b = min(q11.21p11.1::p11.1q11.21)[4]/ mar1c = r(X)(q11.21p11.1::p11.1q11.21: :q11.21p11.1:: p11.1q11.21)[1]/ mar2 = min(X)(:p11.1→q11.1:)[10] complex mosaic: mar1a+mar2[6]/ mar1b+mar2[3]/ mar1c+mar2[1]/ mar1a[3]/mar1b[1]/mar2[1]	n.a.	n.a.	n.a.	+
minX-p11.1/ 3-2	+ (% n.a.)	min(X)(p11.1q13.1)	n.a.	n.a.	n.a.	top
f-iY-q11.1/ 2-1	97	idic(Y)(q11.1)[1.3]/ min(Y)(p11.2q11.1)[1.7]	n.a.	–	–	+
f-iY-q11.2/ 1-18	+ (% n.a.)	idic(Y)(q11.2)	n.a.	n.a.	n.a.	prenatal
f-minY-p11.1/ 1-1	–	min(Y)(:p11.1→q11.1:)	n.a.	n.a.	+	+
m-urY-18	–	r(Y)(p11.2→q?)	n.a.	–	+	+
m-iY-q11.22/ 1-3	14	idic(Y)(q11.22)	+	+	+	–

n.a. = Not available.

Frequency of 46,X,+mar Cases

$sSMC^T$ in general are extremely rare findings: approximately 1 $sSMC^T$/100,000 newborn cases and 7/100,000 prenatal diagnoses are reported. No such cases were detected in 4,269 prenatal diagnoses with ultrasound abnormalities or 4,562 ICSI cases (table 2). In developmentally and/or mentally retarded patients $sSMC^T$ were present in 9/19,170 cases (0.060%) (table 3) and in patients with fertility problems in 12/26,938 cases (0.045%) (table 4).

Table 2. Twenty studies on consecutively collected prenatal cases are summarized, detecting $sSMC^T$ in 0.004% and (mos) 45,X in 0.139% of cases. Moreover, 19 studies on two pre-selected subpopulations of prenatal diagnostics are listed, detecting only $sSMC^T$ or Turner karyotypes in ICSI or in ultrasound abnormal prenatal cases.

No. of study [acc. to Liehr and Weise, 2007]	Studied cases		
	Overall	45,X	45,X/46,X,+mar
Consecutively collected prenatal cases			
1	551	6	0
3	2,500	1	0
4	2,975	11	0
6	5,484	0	0
7	6,515	5	0
8	5,501	9	0
11	2,264	2	0
13	1,687	1	0
14	7,800	19	0
15	7,415	14	2
16	5,165	1	0
17	1,687	10	0
18	52,965	24	0
22	3,000	1	0
23	15,109	5	0
24	2,699	1	0
26	11,436	14	0
31	15,781	n.a.	5
35	12,454	81	0
37	2,888	4	0
Total	165,876	209 (0.139%)	7 (0.004%)
Only in ultrasound aberrant cases			
7	875	19	0
43	151	7	0
44	147	7	0
45	288	4	0
46	428	4	0
47	2,143	42	0
48	237	8	0
Total	4,269	91 (2.132%)	0 (0%)
ICSI cases			
50	43	0	0
51	56	1	0
53	71	4	0
54	108	0	0
55	142	1	0
56	146	0	0
57	149	0	0
58	209	0	0
59	1,136	3	0
60	1,586	1	0
61	486	0	0
62	430	1	0
Total	4,562	11 (0.241%)	0 (0%)

n.a. = Not available.

Table 3. Eight studies on consecutive newborns detecting $sSMC^T$ and Turner karyotypes. 18 studies each provided data for Turner karyotype and $sSMC^T$ frequency in (develop)mentally retarded patients.

No. of study [acc. to Liehr and Weise, 2007]	Studied cases		
	Total	45,X	45,X/46,X,+mar
Consecutive newborn cases			
63	930	0	0
64	2,079	0	0
65	14,835	8	0
66	56,952	11	0
67	3,993	0	0
69	3,665	0	1
70	23,762	9	0
72	1,830	0	0
Total	108,046	28 (0.026%)	1 (0.001%)
Developmentally and/or mentally retarded patients			
21	1,443	n.a.	4
74	120	0	0
76	324	0	0
77	337	6	0
78	455	1	0
80	1,905	2	1
81	1,586	8	0
82	972	56	1
83	470	0	0
84	4,485	6	0
85	611	0	0
86	600	2	0
88	604	2	0
89	4,117	114	n.a.
90	504	0	0
92	161	14	1
93	154	2	2
94	120	0	0
95	202	0	0
Total	19,170	213 (1.202%)	9 (0.060%)

n.a. = Not available.

The frequency of the (mos) 45,X karyotype in the corresponding clinical subgroups was determined (tables 2–4, fig. 2) as well. The data from Liehr and Weise [2007] concerning the frequency of sSMC was also included in figure 2.

$sSMC^T$ were detected more frequently in prenatal than in postnatal cases, however, the same observation was made for cases with a karyotype 45,X or an sSMC (fig. 2). This is mainly due to the fact that the postnatal studies are based on consecutive, unselected collectives, while in

Table 4. In patients with fertility problems Turner karyotypes with or without sSMC^T were found with frequencies of 0.045% and 0.969%, respectively. Differences were detected between males and females.

No. of study [acc. to Liehr and Weise, 2007]	Studied cases								
	Number			45,X			45,X/46,X,+mar		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
52	301	301	602	0	0	0	0	0	0
54	261	261	522	0	0	0	0	0	0
77	128	129	57	0	0	0	0	0	0
97	n.a.	15	15	n.a.	0	0	n.a.	0	0
98	32	n.a.	32	0	n.a.	0	0	n.a.	0
99	72	n.a.	72	0	n.a.	0	0	n.a.	0
100	84	n.a.	84	1	n.a.	1	0	n.a.	0
101	103	n.a.	103	0	n.a.	0	3	n.a.	3
103	65	65	130	0	2	2	0	0	0
104	137	n.a.	137	0	n.a.	0	0	n.a.	0
105	72	72	144	0	10	10	0	0	0
106	n.a.	163	163	n.a.	2	2	n.a.	0	0
107	128	122	250	0	0	0	0	0	0
109	392	n.a.	392	0	n.a.	0	1	n.a.	1
110	820	n.a.	820	0	n.a.	0	0	n.a.	0
111	554	n.a.	554	0	n.a.	0	1	n.a.	1
112	305	305	610	0	0	0	0	0	0
113	1,007	n.a.	1,007	2	n.a.	2	3	n.a.	3
114	639	639	1,278	0	1	1	0	0	0
115	645	645	1,290	1	0	1	0	0	0
117	781	781	1,562	18	4	22	1	0	1
118	676	624	1,300	3	24	27	0	0	0
119	2,196	1,012	3,208	9	25	34	0	1	1
120	500	500	1,000	0	4	4	0	0	0
121	432	436	868	1	16	17	0	0	0
122	1,116	1,164	2,280	3	77	80	0	1	1
123	335	370	705	0	40	40	0	0	0
125	1,792	n.a.	1,792	7	n.a.	7	0	n.a.	0
126	1,599	966	2,565	0	1	1	0	0	0
127	1,210	n.a.	1,210	0	n.a.	0	1	n.a.	1
128	150	150	300	3	6	9	0	0	0
129	952	n.a.	952	1	n.a.	1	0	n.a.	0
130	150	n.a.	150	0	n.a.	0	0	n.a.	0
131	496	n.a.	496	0	n.a.	0	0	n.a.	0
132	88	n.a.	88	0	n.a.	0	0	n.a.	0
Total	18,218	8,720	26,938	49 (0.269%)	212 (2.431%)	261 (0.969%)	10 (0.055%)	2 (0.023%)	12 (0.045%)

n.a.: Not available.

prenatal diagnosis indications like advanced maternal age or ultrasound abnormalities are the reason for amniocentesis. Thus, there is no unselected collective available for the prenatal human population [see as well Liehr and Weise, 2007]. Considering the data for prenatal cases with ultrasound aberrations and those of prenatal cases after ICSI it has to be concluded that ~4,500 cases each were not sufficient to detect sSMC^T.

Figure 2 clearly shows that in all three groups (mos) 45,X, sSMC^T and sSMC, the corresponding aberrant karyotype is markedly enhanced in (develop)mentally retarded and infertile patients. For sSMC^T the detection rate is ~60-fold higher in (develop)mentally retarded and ~45-fold enhanced in infertile individuals as compared to the general population. Interestingly, the karyotype (mos) 45,X was predominantly found in female patients

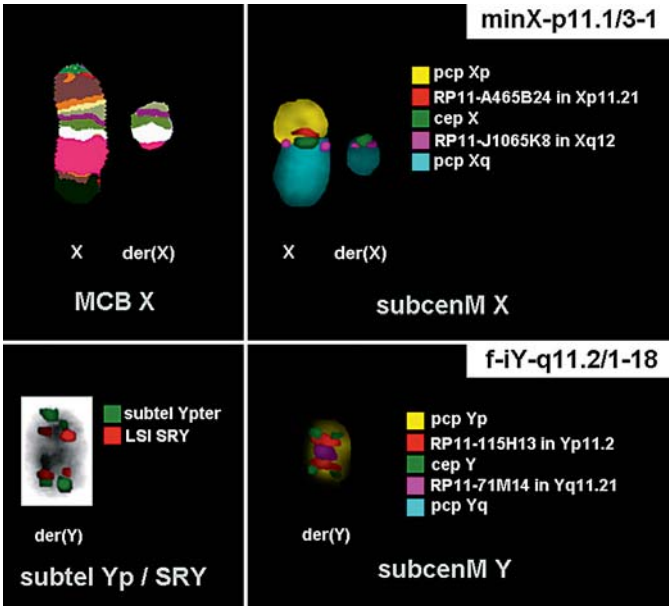

Fig. 1. Different multicolor FISH approaches led to the characterization of the sSMC^T karyotypes as listed in table 1. Here two examples of corresponding FISH experiments are shown. In case minX-p11.1/3-1 a min(X)(p11.1q13.2~13.3) was characterized after application of MCB and subcenM-FISH. Case f-iY-q11.2/1-18: an idic(Y)(q11.2) was characterized by subcenM-FISH probe set Y and two-color FISH using a subtelomeric probe for Ypter and *SRY* (Abbott/Vysis).

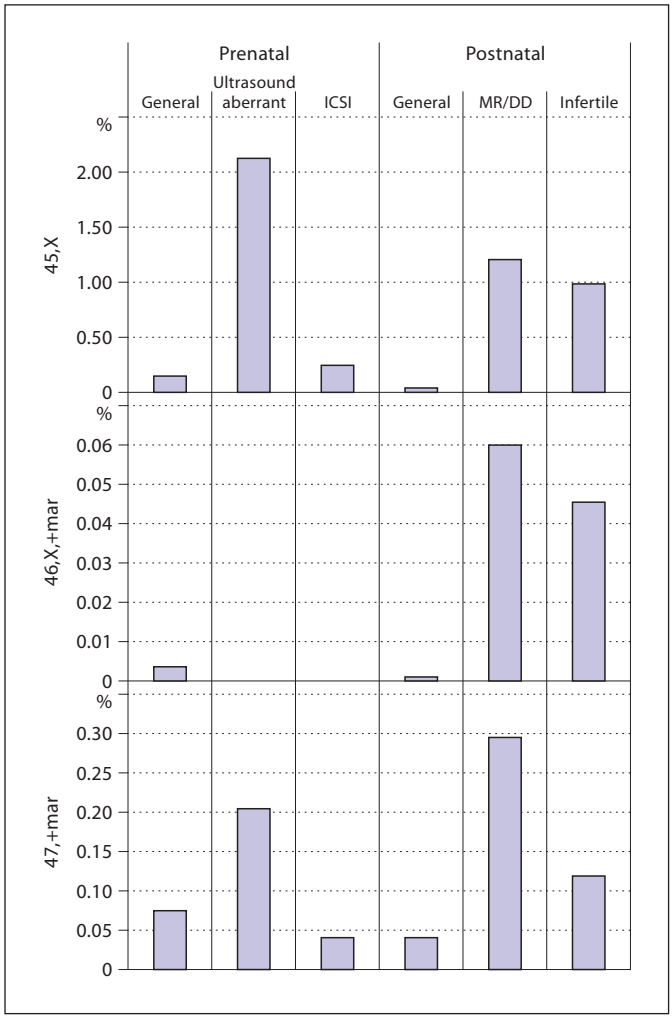

Fig. 2. Frequency of karyotype (mos) 45,X, 46,X,+mar (= sSMC^T) and 47,+mar (= sSMC) in pre- and postnatal cases.

(81% of patients with fertility problems), while an sSMC^T was present mainly in males (83%).

Origin of sSMC^T

The collection of 512 published sSMC^T cases [Liehr, 2007], allowed to distinguish three different sSMC^T groups according to their origin. Most sSMC^T originate from the Y chromosome (371/512 cases = 72.6%). The second largest group is formed by sSMC^T derived from the X chromosome (139/512 cases = 27%). Surprisingly, there is a third possibility – two sSMC^T (0.4%) that were not derived from one of the gonosomes, but from an autosome are reported in the literature. Wiktor and Van Dyke [2004] report on one case in which the sSMC^T did not stain with centromeric probes for the X or Y chromosome, and Gray et al. [2001] identified an sSMC^T derived from chromosome 20. Thus, this third subgroup might be an underestimated entity among sSMC^T cases.

Other sSMC^T 'special cases' not considered in this review are those with further additional chromosome aberrations. E.g. there are reports on a mos 46,X,+21/47,X, min(X)(p11.1q11.1),+21 [Li et al., 2000 – case 6], a microdeletion in 15q12 present additionally to a 45,X/46,X,r(Y) [Kurosawa et al., 2004], a karyotype mos 45,dup(X)(p22.2)/46,X,idic(Y)(q11) [Stuppia et al., 1996], a case of a 47,XX,r(Y)pat [Arnedo et al., 2005] and two cases of 46,X,r(X;Y) [Grass et al., 2000; Shago et al., 2002]. Thus, clinical features not necessarily fitting to a 46,X,+mar karyotype strongly indicate further studies in each individual case.

Shapes of sSMC^T

sSMC^T can have isodicentric/inverted duplicated (idic), ring (r), or centric minute (min) shapes. The abbreviation 'min' is used according to Crolla [1998] for centric minute sSMC – see also Liehr et al. [2004]. As summa-

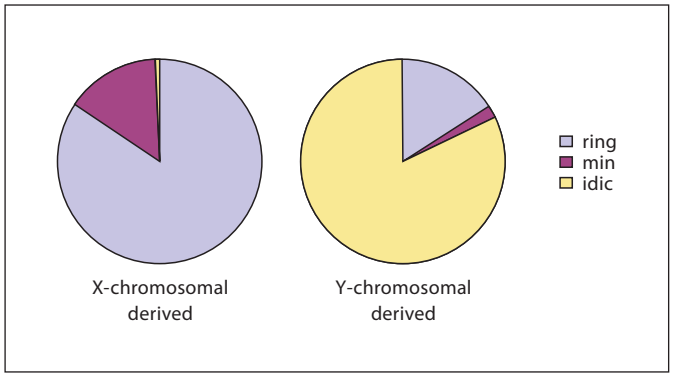

Fig. 3. Distribution of ring-, centric minute (min) and inverted duplication/isodicentric (idic) morphology in X and Y chromosome derived sSMC^T cases.

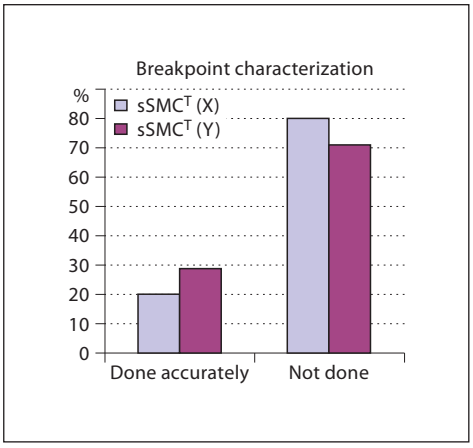

Fig. 4. An accurate breakpoint characterization was done in 20% and 29% of sSMC^T cases derived from the X and the Y chromosome, respectively.

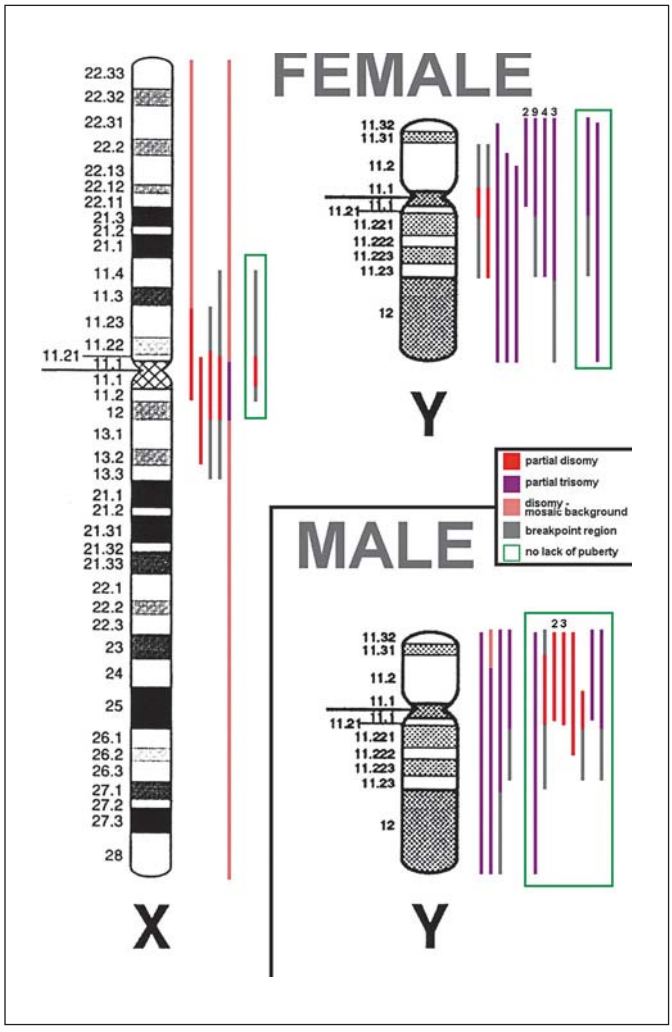

Fig. 5. Imbalances induced by the cytogenetically characterized sSMC^T(X) and sSMC^T(Y). Male and female cases are listed separately. Cases with no lack of puberty are marked by green frames. It is obvious, that similar imbalances of the Y chromosome can lead to male or female habitus. Also male development or lack of puberty may be present or absent independently of the chromosomal breakpoints.

rized in figure 3 the shapes of sSMC^T differ significantly according to their origin. Ring formation is predominant in sSMC^T(X), while sSMC^T(Y) are mostly isodicentric/inverted duplicated chromosomes. The biological basis for this fact is currently still unknown. It is also striking that no direct influence of sSMC^T shape on the clinical outcome is obvious yet.

Characterization of sSMC^T Breakpoints

In only 28 of 139 sSMC^T(X) and in 107 of 371 sSMC^T(Y) (i.e. in ~25% of the published cases) the chromosomal breakpoints were characterized on a sound cytogenetic level – i.e. more detailed than Yp1, Yq1, Yp11, Yq11, Xp or Xq [Liehr, 2007] (fig. 4). Here further research may be fruitful. Comprehensively characterized breakpoints in sSMC^T would contribute to a better understanding of formation and karyotypic evolution of these special marker chromosomes.

Availability of Clinical Data in Cases with an sSMC^T

In most published sSMC^T cases the available clinical data is very limited, especially concerning sexual development. This is mainly due to the fact that ~50% of such

Table 5. All sSMC^T patients in whom chromosomal breakpoints were characterized in more detail, with information on gender and pubertal state

Case no.	Cells with 45,X (%)	sSMC karyotype	Lack of puberty/ amenorrhea
X-chromosomal origin			
rX-p11.23/1-1	82	r(X)(p11.23q11.2)[16%]/dic(X)(p11)[2%]/	+
rX-p11.21/1-1	33	r(X)(p11.21q13.2)	+
rX-p11.2/1-1	16	r(X)(p11.2q13)	+
rX-p11/1-2	22	r(X)(?p11q13)[76%]/r(X)(?p11q13)x2[2%]/	+
rX-p11/2-4	10	r(X)(p11q11)	–
iX-p11.1/1-1	30	idic(X)(p11.1q12::q12q11.1)[54%]/XX[16%]	+
Y-chromosomal origin			
f-rY-p11.2/1-1	42	r(Y)(p11.2q11.2)	+
f-rY-p11.2/1-2	40	r(Y)(p11.2q11.23)	+
f-iY-p11.32/1-2	73	idic(Y)(p11.32)	+
f-iY-p11.32/2-1	+ (% n.a.)	idic(Y)(p11.32)/mos complex	–
f-iY-p11.3∼11.2/1-1	23	idic(Y)(p11.3∼11.2)	+
f-iY-p11.2/2-1	88	idic(Y)(p11.2)[10%]/idic(Y)(p11.2)x2[1%]/XY[1%]	+
f-iY-q11.1/1-1	82	idic(Y)(q11.1)	+
f-iY-q11.1/1-2	23	idic(Y)(q11.1)	+
f-iY-q11.2/1-1	86	idic(Y)(q11.2)	+
f-iY-q11.2/1-3	19	idic(Y)(q11.2)	–
f-iY-q11.2/1-6	60	idic(Y)(q11.2)	+
f-iY-q11.2/1-7	66	idic(Y)(q11.2)	+
f-iY-q11.2/1-9	61	idic(Y)(q11.2)	+
f-iY-q11.2/1-10	>5	idic(Y)(q11.2)	+
f-iY-q11.2/1-11	10	idic(Y)(q11.2)	+
f-iY-q11.2/1-12	63	idic(Y)(q11.2)	+
f-iY-q11.2/1-13	–	idic(Y)(q11.2)	+
f-iY-q11.2/1-19	77	idic(Y)(q11.2)	+
f-iY-q11.23/1-3	80	idic(Y)(q11.23)	+
f-iY-q11.23/1-4	24	idic(Y)(q11.23)	+
f-iY-q11.23/2-3	23	idic(Y)(q11.23)[46%]/del(Y)(q11.23)[31%]	+
f-iY-q11.23/2-4	34	idic(Y)(q11.23)[32%]/del(Y)(q11.23)[34%]	+
f-iY-q12/1-2	52	idic(Y)(q12)	+
f-iY-q12/1-4	9	idic(Y)(q12)	+
f-iY-q12/1-6	16	idic(Y)(q12)	+
Y-chromosomal origin – male			
m-rY-p11.3/2-1	27	r(Y)(p11.3q11.2)	–
m-rY-p11.32/1-1	38	r(Y)(p11.32q11.1)	–
m-rY-p11.32/1-2	5	r(Y)(p11.32q11.1)	–
m-rY-p11.32/2-1	45	r(Y)(p11.32q11.21)	–
m-rY-p11.32/2-2	5	r(Y)(p11.32q11.21)	–
m-rY-p11.32/2-3	–	r(Y)(p11.32q11.21)	–
m-rY-p11.32/3-1	–	r(Y)(p11.32q11.222)	–
m-iY-p11.32/1-1	75	idic(Y)(p11.32)	+
m-iY-p11.32/1-2	+ (% n.a.)	idic(Y)(p11.32)	–
m-iY-p11.2/1-1	77	idic(Y)(p11.2)[21%]/idic(Y)(p11.2)x2[1%]/XY[1%]	+
f-minY-p11.1/1-1	–	min(Y)(p11.1∼11.2q11.22)	–
m-iY-q11.1/1-2	11	idic(Y)(q11.1)	–
m-iY-q11.2/1-3	18	idic(Y)(q11.2)	–
m-iY-q11.22/1-1	+ (% n.a.)	idic(Y)(q11.22)	–
m-iY-q11.22/1-3	14	idic(Y)(q11.22)	+
m-iY-q12/1-3	+ (% n.a.)	idic(Y)(q12)	+

n.a.: Not available.

cases are detected either prenatally or shortly after birth. Since there are practically no follow-up reports, data on puberty or fertility are not available. Also, in a major part of the literature, authors report only on 'patients with Ullrich-Turner syndrome' without detailing clinical data for individual patients [e.g. Tharapel et al., 1992].

In table 5 we summarize those rare cases with both, cytogenetic characterization of the $sSMC^T$ and information on lack or presence of puberty and/or amenorrhea. In 5/6 cases with $sSMC^T$(X) lack of puberty and/or amenorrhea was reported. The same holds true for 23/25 cases with $sSMC^T$(Y) and a more female phenotype. The three cases without problems in sexual development had a karyotype 45,X[10%]/46,X,r(X)(p11q11)[90%], mos 45,X/46,X,idic(Y)(p11.32)/other complex aberrations involving gonosomes, and 45,X[19%]/46,X,idic(Y)(q11.2)[81%].

In 16 male cases with $sSMC^T$(Y) only 4 are reported with delayed or no pubertal development – the karyotypes of these were 45,X[75%]/46,X,idic(Y)(p11.32)[25%], 45,X[77%]/46,X,idic(Y)(p11.2)[21%]/47,X,idic(Y)(p11.2)×2[1%]/46,XY[1%], 45,X[14%]/46,X,idic(Y)(q11.22)[86%], and mos 45,X/46,X,idic(Y)(q12).

In figure 5 we summarize the imbalances caused by the cytogenetically well characterized $sSMC^T$ from table 5. However, practically no correlation was possible concerning size of imbalance induced by $sSMC^T$ and sexual development. The only obvious fact is, that in presence of an $sSMC^T$(X) no male development was observed. Presence of an $sSMC^T$(Y) – irrespective of presence or absence of *SRY* – could lead to both – male or female development. According to table 5 a correlation of mosaicism, i.e. size of the clone with an $sSMC^T$(Y), and (fe)male development might be suggested, as also reported for monozygotic twins, born as male and female [Fujimoto et al., 1991].

Conclusion

$sSMC^T$ are a long known cytogenetic entity. Hundreds of cases have been reported [Liehr, 2007]. Nonetheless, a detailed (molecular) cytogenetic characterization of $sSMC^T$ was performed only in exceptional cases. This might be due to the fact that a mos 45,X/46,X,+mar karyotype was regarded as something well known, and thus further studies would not be indicated or straightforward. This review shows that further detailed cytogenetic reports with thorough clinical data are worth to be performed, especially to learn more about formation and effects of an $sSMC^T$.

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