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LETTERS TO THE EDITOR

Two new cases of *de novo* small supernumerary marker chromosomes (sSMC) detected at prenatal diagnosis

Small supernumerary marker chromosomes (sSMC) can be defined as structurally abnormal chromosomes that cannot be identified or characterized unambiguously by conventional banding cytogenetics alone, and are (in general) equal in size or smaller than chromosome 20 of the same metaphase spread (Liehr *et al*., 2004). sSMC are relatively uncommon in the general population. They have been detected with a frequency of 0.076% at prenatal diagnosis and at a much higher frequency of 0.426% in mentally retarded patients (Liehr *et al*., 2004). The phenotypes associated with the presence of a *de novo* sSMC vary from normal to severely abnormal. In general, the risk associated with an abnormal phenotype in prenatally detected *de novo* cases with sSMC is 13% (Warburton, 1991), while for sSMC *de novo* derived from non-acrocentric chromosomes the risk is estimated to be approximately 28% (Crolla, 1998). The phenotypic consequences of particular sSMC are difficult to predict because of differences in euchromatic DNA content, different degrees of mosaicism and/or uniparental disomy (UDP) of the parental chromosomes homologous to the sSMC (Starke *et al*., 2003).

The origin of sSMC is impossible to determine by routine cytogenetics alone but fluorescence *in situ* hybridization (FISH) enables the identification of its chromosomal origin. However, because of the several possibilities of different phenotypes attributable to the chromosomal origin of the sSMC, their characterization and also an adequate long-term follow-up are necessary (Starke *et al*., 2003; Liehr *et al*., 2006). In cases with apparently normal phenotypes, the characterization of sSMC can provide important information about regions that are phenotypically silent in the presence of gene dosage imbalances (Sumption and Barber, 2001; Starke *et al*., 2003; Barber, 2005; Liehr *et al*., 2006).

In this report, we describe two new cases of *de novo* sSMC detected at prenatal diagnosis derived from chromosome 2, with apparently normal phenotypes ascertained during the neonatal period and until the age of 2 years.

The first case is the prenatal diagnosis of a 39-year-old pregnant woman who underwent an amniocentesis at 17 weeks' gestation due to advanced maternal age and also positive serum screening. Routine cytogenetics with GTG-banding (G-bands obtained by Trypsin and Giemsa) (Figure 1(A)) revealed the presence of sSMC in 15 of the 70 metaphases analysed. The sSMC were CBG positive (silver staining of the nucleolus organizer regions) (Figure 1(B)) and NOR negative (C-bands induced by barium hydroxide and Giemsa) Chromosomal analysis of both parents' lymphocytes revealed normal karyotypes. FISH with the I-Multiprobe System (Cytocell) (complete set of alpha-satellite/satellite III probes for the 24 chromosomes) (Figure 1(C)) enabled the identification of the chromosome 2 origin of the sSMC. The sSMC showed hybridization with the centromeric probe D2Z2 and the karyotype of the fetus was mos47,XX,+mar.ishder(2)(D2Z2+)[15]/46,XX[55]. Ultrasound analysis did not reveal any abnormalities in the fetus. After counselling, the parents decided to carry on with the pregnancy, and the presence of the sSMC was confirmed in lymphocytes after birth although with different frequencies of the two cell lines (50% of metaphases analysed had the sSMC).

In the second case, amniocentesis of a 38-year-old pregnant woman was performed at 16 weeks' gestation because of advanced maternal age. The GTG-banding (Figure 1(D)) study revealed the presence of sSMC in 14 of 30 metaphase spreads analysed. The sSMC were CBG positive (Figure 1(E)) and NOR negative. The parents' karyotypes were normal. The origin of this sSMC was identified to be derived from chromosome 2 using the OctoChrome System (Cytocell) (includes whole chromosome painting probes for the 24 chromosomes) (Figure 1(F)). The sSMC hybridized with the wcp (whole chromosome paint) for chromosome 2 and the karyotype of the fetus was mos47,XY,+mar.ishder(2)(wcp2+)[14]/46,XY[16]. Ecographic evaluation of the fetus was normal. After genetic counselling, the parents decided to continue the pregnancy, and postnatal chromosomal analysis confirmed the presence of the sSMC in 73% of the blood lymphocytes.

Chromosome 2 is rarely involved in the formation of marker chromosomes (Crolla, 1998; Ostroverkhova *et al*., 1999). Only 11 other cases have been reported in the literature (Plattner *et al*., 1993; Daniel *et al*., 1994; Ostroverkhova *et al*., 1999; Villa *et al*., 2001; Giardino *et al*., 2002; Lasan Trcic *et al*., 2003; Starke *et al*., 2003; Guanciali-Franchi *et al*., 2004; Mrasek *et al*., 2005; Liehr *et al*., 2006) and of these only 2 at prenatal diagnosis (Villa *et al*., 2001; Mrasek *et al*., 2005; Liehr *et al*., 2006). Only 8 of the 11 cases were characterized in detail for their chromosomal content, and analysis of the data seems to indicate a correlation between the centromere-near sequences of 2p11.2 and the presence of clinical abnormalities, and the absence of clinical symptoms with presence of proximal sequences of 2q11.2. (Starke *et al*., 2003; Mrasek *et al*., 2005; Liehr *et al*., 2006). Small partial trisomies of material derived distally from 2q11.2 are associated with clinical abnormalities (Giardino *et al*., 2002; Mrasek *et al*., 2005; Liehr *et al*., 2006).

The normal phenotype and development of both children up to the age of 2 years leads us to suspect that both cases are probably proximal trisomies of 2q. Nevertheless, a thorough characterization of both sSMC reported is still necessary and will be pursued.

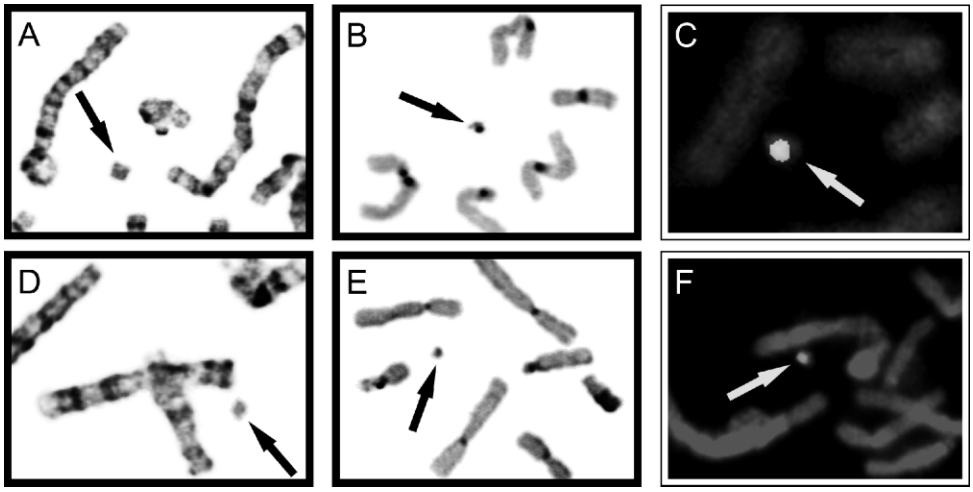

Figure 1—(A) GTG, (B) CBG and (C) FISH with centromeric probe D2Z2 for the sSMC (indicated by arrow) in case 1; (D) GTG, (E) CBG and (F) FISH with wcp for chromosome 2 for the sSMC (indicated by arrow) in case 2

As soon as the parents give their consent, we intend to determine the euchromatic content of the sSMC by using microdissection and also bacterial artificial chromosomes (BACs) of the pericentromeric region of chromosome 2. The complete characterization of both sSMC as well as the continued follow-up of the children will take us one step further towards a more comprehensive genotype–phenotype correlation and thus ensure a more informed genetic counselling in the future.

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Prenatal diagnosis of double duodenal atresia by ultrasound and magnetic resonance image

Duodenal atresia is the most common type of foetal atresia. It is suspected to be linked to the presence of a ‘double bubble’ due to a dilated fluid-filled stomach and proximal duodenum. This appearance corresponds to the gas-filled ‘double bubble’ seen on postpartum radiographs. However, if more than one obstruction level is