Case report

Subfertile couple with t(4;22)(q23;q11.2)

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Abstract. A couple was referred for cytogenetic examination due to idiopathic miscarriages. The proband proved to be a carrier of chromosomal translocation and her partner’s karyotype was found to be normal. The karyotype of the proband is 46,XX,t(4;22)(q23;q11.2) and can be regarded as a reason of fertility problems in the investigated couple. The risk of further miscarriages is high, but the risk of a progeny with abnormal karyotype is rather low, as the progeny would probably have lethal imbalances.

Key words: t(4;22), infertility, miscarriage, translocation.
male karyotype with a vast translocation between q arms of chromosomes 4 and 22, thus the karyotype was 46,XX,t(4;22)(q23;q11.2). Her partner was found to have a normal male karyotype. Partial karyogram of the proband is shown in Figure 1a, b.

One of the breakpoints was in the region of 22q11, so fluorescent in situ hybridization (FISH) was performed to exclude 22q11.2 deletion in the critical region for DiGeorge syndrome. Q-Biogene (Oncor) probes were used according to producer’s manual: 22qter/FITC (N85A3) 22q11.2/Texas Red (TUPLE1). FISH analysis was performed by use of a fluorescent microscope Olympus BX60 and the CytoVision 3.5 system equipped with the FISH module. All the expected FISH signals were present (Figure 1b, c). DiGeorge critical region (22q11.2) was found on chromosome 22 and der(22), so it was not involved in the translocation. The family pedigree (Figure 1d) was prepared according to Rimoin et al. (2001). The known karyotypes of the family members are: the proband (II-3) 46,XX,t(4;22); proband’s partner (not shown in the pedigree) 46,XY; and proband’s mother (I-2) 46,XX. Proband’s father (I-1) died earlier, so his karyotype is not available, but he could be the carrier of t(4;22) because I-2 had one miscarriage. Other family members have not decided to participate in cytogenetic examinations.

Carriers of balanced aberrations have an increased risk of an unbalanced progeny due to imbalances and delays in meiosis (Gardner and Sultherland, 2004). The presented proband has a vast balanced translocation between q arms of chromosomes 4 and 22. Both 2:2 and 3:1 segregation patterns may lead to large imbalances. The fetus inheriting only der(4) would probably
have a lethal karyotype: deletion in 4q and partial trisomy of 22q. Inheriting der(22) would result in partial trisomy 4q and monosomy of 22q. Alternative 2:2 segregation would lead to either a normal or a balanced karyotype, but adjacent 2:2 segregation would give abnormal unbalanced karyotypes (Figure 1e).

There are only few publications presenting translocations involving 4q and 22q. Mikelsaar et al. (1996) described a girl with a de novo translocation of 4q onto the short arm of acrocentric 22, which was reported as a case of ‘pure’ partial trisomy 4q. However, partial trisomy of 4q comprised region q25→qter. Comparison of reported cases of ‘pure’ partial trisomy of 4q showed the main clinical features to be: growth retardation, psychomotor retardation, microcephaly, large, low-set, malformed ears, prominent nasal bridge, ptosis and epicanthus (Mikelsaar et al. 1996). De Almeida et al. (1991) reported on a girl with de novo t(4;22) (q1200;p13), who had a 4p trisomy phenotype. Both authors describe translocations involving chromosomes 4 and 22, but in presented translocations different breakpoints are involved.

Trisomy 4q syndrome is also described by Lundin et al. (2002). The clinical findings of 4q trisomy are most frequently: mental retardation, seizures, microcephaly, hearing impairment and growth retardation, but epicanthic folds, high/broad/depressed nasal bridge, malformed ears, tooth and thumb anomalies have also been reported. There are some publications presenting partial trisomies of 4q due to duplications or imbalances caused by other parental translocations involving 4q (Elghezal et al. 2004; Lin et al. 2004). Nevertheless, partial trisomy 4q in combination with monosomy of 22q has not been reported in the available literature.

Partial trisomies of 22q were always reported in connection with congenital abnormalities (Rivera et al. 1988; Stoll et al. 1997; Barajas-Barajas et al. 2004). Monosomy 22q was also described resulting in serious dysmorphic features and psychomotor delays (Silengo and Andria 1976; Greenberg et al. 1984; Schroder et al. 1998; Belin et al. 1999). The combination of features concomitant with dup(4q)/del(22q) or del(4q)/dup(22q) would probably be lethal, as there were no abnormalities reported in children in the presented family. The proband’s pregnancy history showed 4 early miscarriages, which supports this hypothesis. We also investigated the possibility of del(22q11.2), as it might cause familial DiGeorge syndrome (Greenberg et al. 1984). One of the breakpoints was 22q11, so we decided to perform a FISH examination, but the deletion in this region was excluded.

To our knowledge, no translocation with such breakpoints t(4;22)(q23;q11.2) has been described previously. The abnormal karyotype of the proband 46,XX,t(4;22)(q23;q11.2) can be regarded as a reason of fertility problems in the investigated couple. The risk of further miscarriages is high due to large segments of duplication/deletion caused by unequal segregation. Basing on the reviewed literature we conclude that the couple has an increased risk of progeny with an unbalanced karyotype, as both partial trisomies of 4q and 22q have been reported. The presented cases showed severe abnormalities. Since there is also a risk of unbalanced recombinants, prenatal diagnosis will be offered if the proband’s future pregnancy is sustained till 15th week.

REFERENCES


