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AUTOSOME-AUTOSOME RECIPROCAL TRANSLOCATION: IMPLICATIONS IN THE FERTILITY

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Chromosomal abnormalities have been described as important causes of male infertility. Structural rearrangements have been reported as 10 times more frequent among infertile men than in the general population.

The most common chromosomal abnormality is Klinefelter's syndrome, but translocations may also cause reduction in testicular volume and testosterone level, which may impact spermatogenesis, resulting in oligozoospermia or azoospermia and thus male infertility. The involvement of acrocentric chromosomes and the presence of translocation breakpoints in close proximity to the centromere are associated with the most destructive effects on spermatogenesis.

It has been suggested in some publications that the most likely reason for the development of azoospermia in patients with reciprocal translocations is a very high proportion of an association between XY bivalents and quadrivalent formations in prophase I; the instability in chromosome segregation during consecutive cell divisions might be a contributing factor inducing spermatogenic disruption.

The authors present a male patient, aged 41, with azoospermia and reduced testicular volume, without family history of infertility.

The karyotype revealed an autosome-autosome reciprocal translocation: 46,XY,t(20;22)(q11.21;q11.21). Chromosomal analysis has become increasingly important for characterizing possible causes of human infertility, and has shown that male infertility might be associated with autosomal chromosome abnormalities. Infertile men who have chromosomal abnormalities such as translocations but normal phenotypes have shown that these translocations may have a devastating impact on spermatogenesis during meiotic division. In addition, detailed meiotic analysis may be recommended for each translocation, to obtain better diagnosis, prognosis and genetic counselling to the patient.

The authors will establish the relationship between male infertility and chromosomal translocations and compare the findings of this patient with similar cases described in the literature.

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MOLECULAR PROFILE OF MYOTONIC DYSTROPHY TYPE 1 (DM1) IN PORTUGUESE FAMILIES

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Myotonic Dystrophy type 1 (DM1), also known as Steinert disease, is the most common adult form of muscular dystrophy. It is an autosomal dominant disorder caused by the expansion of unstable [CTG] repeats in the 3' untranslated region (3'UTR) of the gene of myotonic dystrophy protein kinase (*DMPK*), located at 19q13.3. The expanded mRNA products are toxic to cells, affecting normal splicing of other proteins in different tissues.

Myotonia is the principal manifestation of DM1, but other organ systems are also affected (e.g. ocular, cardiac and respiratory). Clinically, DM1 may be phenotipically classified into four main subtypes: i) mild, ii) classical or adult-onset, iii) juvenile and iv) congenital. The age of onset and severity are variable and directly associated with the number of expanded [CTG] repeats: larger expansions usually result in earlier onset and a more severe phenotype. Due to the instability of the expanded [CTG] repeats during transmission, it is common to observe in affected families a decreasing in age at onset and an increasing degree of severity in successive generations (anticipation).

In this work we present the molecular profile of DM1 in affected families studied at our diagnostic service, on a national basis, since the implementation of the molecular genetic testing for this disorder in 1997.

All the cases were tested for the presence of expanded pathogenic alleles. Depending on the size of the expanded alleles, a combination of three different methods was used to determine the number of [CTG] repeats in 3'UTR of the *DMPK* gene: 1) conventional PCR amplification of the [CTG]-repeat region; 2) Triplet repeat-Primed (TP)-PCR and 3) Southern blotting (SB) technique. Larger expansions (about $[CTG]_{>100}$ repeats) are only detected by the last two methods; moreover, the exact size of these larger expanded repeats can only be assessed by SB. In order to establish the most accurate molecular diagnosis, the SB technique is therefore essential, particularly in the prenatal diagnostic setting.

We also present both clinical and genotype heterogeneity in the DM1 families, thus demonstrating some of the characteristics associated with this triplet repeat disorder: somatic mosaicism, anticipation, influence of gender of the