A new case of Yq microdeletion transmitted from a normal father to two infertile sons

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During the last few years, microdeletions of the long arm of the Y chromosome, involving loci AZFa, AZFb, and AZFc, have been identified as a major cause of infertility, leading to the disruption of genes involved in spermatogenesis. These microdeletions are usually de novo mutations, but in six cases transmission from fertile fathers to infertile sons has been reported. In four cases, the transmission occurred to a single son, and in one of these a widening of the deletion was shown. In the remaining two cases, the microdeletion was transmitted to multiple sons, resulting in different defects of spermatogenesis. Here, we describe a third family with a Yq microdeletion transmitted by a father to his two infertile sons.

CASE REPORTS

Two brothers, aged 36 and 35 years respectively, were examined in 1998 and 2000. The first had azoospermia, shown by repeated semen analyses, while the second had oligozoospermia (sperm count 200 000/ml, with reduced motility and abnormal morphology in 96% of sperm). In both patients, hormone values, ultrasound analysis, and karyotype were normal. Screening for microdeletions was performed in the two patients and in their father using PCR and FISH analyses with specific primers and probes for the Y chromosome.

Both the father and the two sons showed a similar deletion involving the AZFc locus, with loss of the DAZ, VCY2 (BPY2), and CDY1 genes.

This case confirms that Yq microdeletions can be associated with different phenotypes within the same family, suggesting the presence of genetic or environmental factors affecting the phenotypic effect of AZFc deletions.

DISCUSSION

Like the other two reported cases, in our family the father and sons had an identical deletion involving AZFc with loss of the genes DAZ, VCY2, and CDY1, but showed different phenotypes. This confirms that AZFc microdeletions can be associated with features ranging from normal fertility, to mild...
oligozoospermia, to infertility, characterised by severe oligo-
zoospermia or azoospermia. These differences are not age
related, since the father was fertile until the age of 34 years,
while the sons were already infertile at that age. Other genetic
or environmental factors affecting the phenotype of patients
with AZFc deletions must be present. Since one in six couples
requires assisted reproduction for a pregnancy, knowledge of
the phenotype resulting from the transmission of a Yq micro-
deletion is crucial. While these factors remain unknown, care
should be taken in the counselling of patients with AZFc dele-
tions undergoing ICSI, since data from these families suggest
that the son will not invariably inherit the same pattern of
spermatogenesis. Further studies on families with multiple
carriers of the same deletion, but showing different pheno-
types will be of help for the identification of these factors.

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