Characterisation of a satellited non-fluorescent Y chromosome (Y^{nfqs}) by FISH

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Abstract

A fetus was prenatally diagnosed as having a Y^{nfqs} chromosome which was inherited from the father. With the QFQ technique, the Yqh was observed to be non-fluorescent and contained cytological satellites which were attached to the terminal long arm. The satellites were positively stained by the Ag-NOR technique suggesting that the NORs were active. A battery of DNA probes was used to characterise the Y^{nfqs} . Hybridisation experiments using a chromosome 15 specific classical satellite DNA probe (D15Z1) and a Yq telomere DNA probe showed that the additional satellited material on Yq originated from 15p, and that the Yq terminal region had been lost. This is the first reported case in which the origin of cytological satellites on Yq has been determined by FISH, but this does not imply that all satellited Y chromosomes are derived from 15p. However, the clinical significance of this Y^{nfqs} chromosome remains obscure.

(J Med Genet 1997;34:817-818)

Keywords: non-fluorescent Y chromosome; satellited Y chromosome; Y^{nfqs}

A variety of structural aberrations of the Y chromosome has been evaluated by a number of selective banding techniques.¹ Some unusual Y chromosomes which were once thought to be abnormal have now been proven to be inherited variants with no clinical consequences.²⁻³ Such an example is the non-fluorescent Y chromosome (Y^{nf}), which is a rare inherited normal variant⁴ and had presumably originated through an evolutionary process where the brightly fluorescent segment had been deleted.⁵⁻⁷ If a second event occurs where a translocation takes place with one of the short arms of an acrocentric chromosome, then a satellited non-fluorescent Y chromosome (Y^{nfqs}) results. However, the origin of the satellite on the Yq cannot be determined as all acrocentric chromosomes usually possess satellites.⁸⁻¹⁶ The recent availability of chromosome and locus specific probes for the FISH technique has assisted in resolving the origin of many chromosomal abnormalities. We present a case which was prenatally diagnosed as having a Y^{nfqs} chromosome inherited from the father. This is the first reported case involving satellited material that has been evaluated by FISH and was found to originate from chromosome 15.

Materials and methods

GTG, QFQ, and Ag-NOR banding procedures were followed as previously reported¹⁷ and FISH was performed according to the respective manufacturers' suggestions. The following were used: classical satellite DNA probe specific for chromosome 15 (D15Z1, biotin), classical satellite DNA probe specific for the Y chromosome (DYZ1, digoxigenin), alpha satellite DNA probe specific for the Y chromosome (DYZ3, biotin), and Xq/Yq specific telomeric associated sequences (digoxigenin) (Oncor, Gaithersburg, MD). A spectrum orange labelled Y chromosome whole chromosome paint probe was also used (Vysis, Downers Grove, IL). All chromosomes were counterstained with DAPI.

Results and discussion

A 41 year old female was referred for genetic amniocentesis because of advanced maternal age. Cytogenetic findings with Q banding showed a 46,XY nfqs karyotype in her amniocytes. A Y^{nfqs} chromosome was also found in the father. The fetus was prenatally diagnosed by G banding as having cytological satellites on the long arm of the Y chromosome (fig 1a). The NORs were stained positively using silver staining (fig 1b). By QFQ banding the long arm was non-fluorescent (fig 1c). The father's Y^{nfqs} (fig 1B) was similar to that of the fetus (fig 1A) suggesting its inheritance from the father. The use of the FISH technique using a chromosome 15 specific classical satellite DNA biotin probe (D15Z1) showed that the extra material on Yq originated from the short arm

Figure 1 GTG (a), Ag-NOR (b), and QFQ (c) banding of (A) the proband's and (B) the father's Y^{nfqs} . The positive silver stain suggests active NOR. QFQ banding shows the non-fluorescent property of the Y chromosome chromatin.

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Received 23 July 1996
Revised version accepted for
publication 26 March 1997

Figure 2 FISH using D15Z1, green (a,b), DY21, red and DY23, green (c), Y WCP, spectrum orange (d), and Xq/Yq telomeric associated sequence, red (e) probes on (A) the proband and (B) the father. The chromosome 15 specific classical satellite DNA probe (D15Z1) indicates chromosome 15 as the origin of the satellites. In (a) and (b) chromosomes 15 and Y of the proband and father come from the same metaphase. The negative signal for the Yq telomeric probe (e) suggests loss of Yqter on the Y^{nf}.

of chromosome 15. Chromosomes 15 and Y of the proband and father come from the same metaphase (fig 2a, b). When the Y chromosome was hybridised with a Y specific alpha satellite DNA probe (biotin) combined with a Y specific classical satellite DNA probe (digoxigenin), positive hybridisation signals on the Y chromosome were observed. Furthermore, a Y specific whole chromosome painting probe (spectrum orange) completed the identity of the Y chromatin (fig 2d). Use of Xq/Yq telomeric associated sequence probes showed that the Yq terminal region has been lost (fig 2e). Furthermore, the short arm of chromosome 15 had been translocated to the Yq during an earlier generation because both chromosomes 15 of the father were normal.

In the past, the origin of a satellite on Yq has been the subject of scrutiny and debate, being postulated that they result from a reciprocal translocation between Yq and 15p or 22p.⁸ The Xp and Yp are apparently normal in such cases and there should not be any problems during meiotic pairing. Nevertheless, recent observations suggest that there is another pseudoautosomal region on the long arm of the X and Y chromosomes¹⁸⁻¹⁹ which, if altered, may cause an aberrant outcome and produce sex chromosome anomalies such as XXX, XXY, and iso-X.²⁰⁻²³ Nevertheless, the father in our case is cytogenetically normal and we conclude that the Y^{nf} region originated from 15p. The present report does not imply that similar cases of satellited material are derived from 15p since all acrocentric chromosomes have the propensity to be involved in translocations. Obviously, this case is a rare variant whose nature is familial and may have clinical consequences when it

originates de novo, depending on the amount of genetic material deleted from the critical region of Yq.²⁴ Therefore, the utmost caution should be exercised during pre- and postnatal counselling.

We thank Robert Robinson for photography and Mark A R Sealy for typing the manuscript.

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