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Short Communication

Mosaicism for trisomy 21 and ring (21) in a male born to normal parents: A case report

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ABSTRACT

We present a case of a ring (21) in a mentally challenged patient with mosaicism for trisomy 21 showing karyotype 47, XY, +21/47,XY, +21(r)/46,XY, born to normal parents. The parents and female sibling were phenotypically normal. This is a unique case report from Central India, on occurrence of trisomy 21 and r (21) in the same individual born to normal parents. Also being documented for the first time is the immuno-FISH analysis revealing differential expression of hTERT and a linked over expression of TRF2 in proband, probably corresponding to a high percentage of acrocentric associations.

1. Introduction

A ring chromosome is type of structural chromosomal aberration formed when a break occurs in each arm of the chromosome, leaving two 'sticky' ends and subsequent end-to-end fusion. Mostly, ring chromosomes are *de novo* in origin. Ring chromosome 21 "r (21)" is a rare chromosomal abnormality characterized by deletion of part of chromosome 21, and is often associated with mental retardation and wide variety of dysmorphic features (Stetten et al., 1984). The frequency reported for the ring chromosomes is one in 25,000 recognized conceptions; almost all human chromosomes are involved in the formation of the ring and 50% are supposed to be derived from acrocentric chromosomes of the D and G group (Wong et al., 1989).

On the other hand, Trisomy 21, the Down syndrome (DS), is fairly common, occurring in approximately one out of every 700 births (Hassold and Jacobs, 1984). In 95% of DS, the extra 21 is in a free state, originating from maternal meiotic non-disjunction phenomenon during gametogenesis. Translocation seen in 4% of DS has the extra 21 translocated to other chromosomes or to the acrocentric chromosomes of D and G group. The chromosomal arrangement in 1% of DS is mosaicism for chromosome 21 (Hook, 1981). Thus, Down syndrome is generally caused by trisomy 21 in somatic cells in 95% of cases and more rarely by partial trisomy of portions of chromosome 21 (Gilbert and Opitz, 1982). In mosaicism, the typical DS features may be less prominent, depending on the percentage of the normal to the trisomy 21 cell lines. The origin of the extra 21 may be from the zygote with 46 or 47 cell lines. In the former, non-disjunction phenomenon leads to the mosaic cell lines of 45/46/47 chromosomes where the cell lines with 45 chromosomes (– 21), become nonviable. On the other hand, cell lines with 47 anaphase lag of the extra 21 result in 46 and 47 cell lines and is associated with the maternal age as in free trisomy 21 (Tolmie and MacFayden, 2007).

Till date, there has been no report detailing the co-occurrence of r (21) and trisomy 21 in the progeny of normal parents. The first case of two children with two different abnormalities of chromosome 21, r(21)/idic(21) mosaicism and trisomy 21 respectively, born to normal parents was reported (Cho et al., 2005), suspecting that some cryptic abnormalities on the maternal 21p were the source of the children's abnormalities, but warranting further evaluation. Here we report a rare case of co-occurrence of a ring (21) in patient with mosaic trisomy of chromosome 21 born out of wedlock to normal parents, suggesting a *de novo* origin.

2. Case report

The proband was a 6 years 9 months old male born at term after an uneventful pregnancy as a second child of consanguineous parents with no linked family history. He was referred by outpatient of Psychiatry Department, Gandhi Medical College, Bhopal, for cytogenetic analysis to determine the extent and origin of his mental retardation. Patient had a history of mental retardation since 3 years of age and was under medical supervision since then. The patient had body weight of 12 kg, height 96.5 cm and head circumference 44 cm, all below the normal range of his age, thus presenting a condition of delayed somatic

Abbreviations: r (21), ring (21); hTERT, human Telomerase Reverse Transcriptase; TRF2, Telomeric Repeat-binding Factor 2; IgG, Immunoglobulin G; FITC, Fluorescein isothiocyanate; DS, Down syndrome; AD, Alzheimer disease; GTG, G-banding with Trypsin and Giemsa; ACA, Acrocentic chromosome associations; BMI, Body Mass Index; C.T. scan, Computed Tomography scan.

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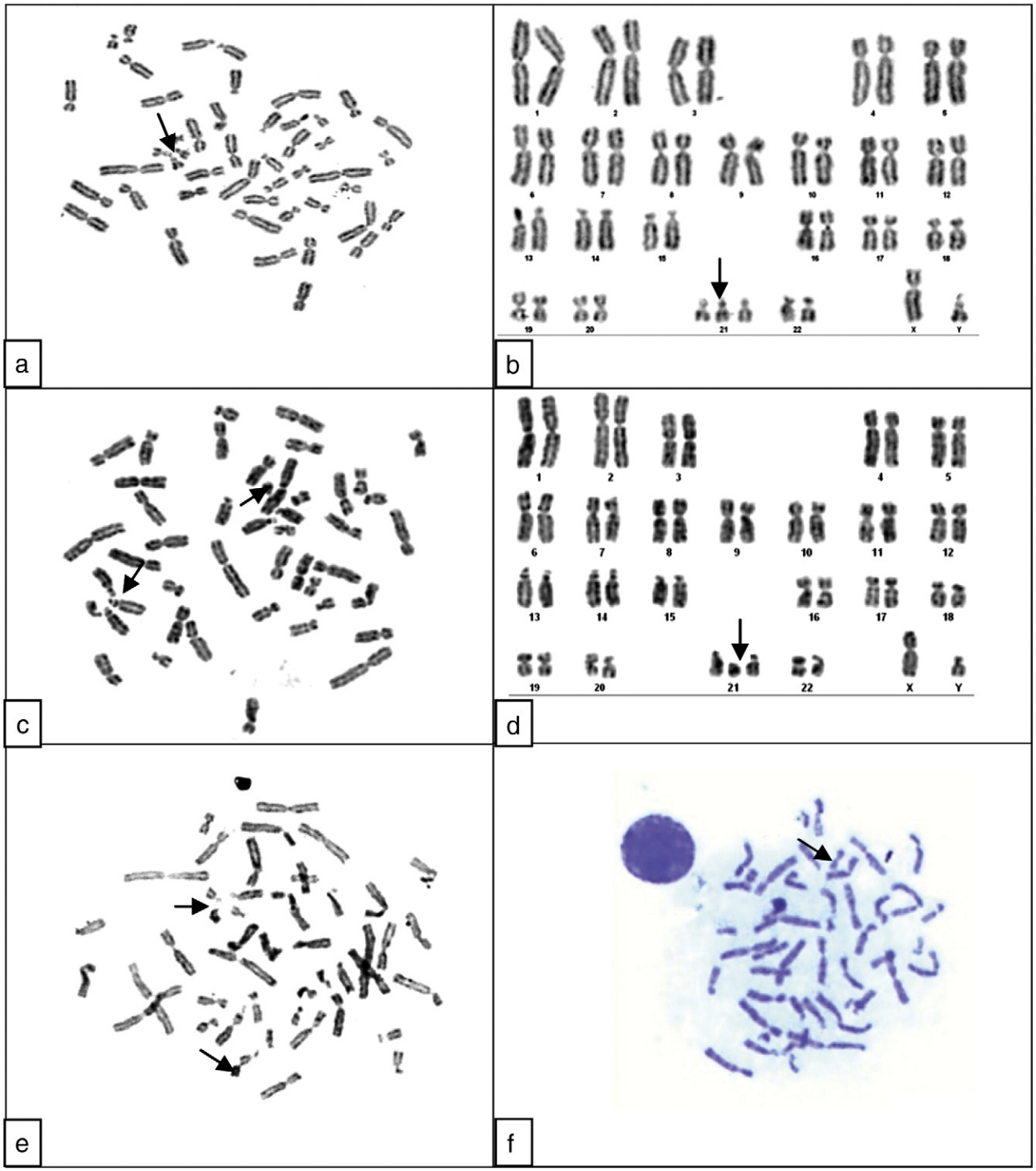

Fig. 1. Karyotype and chromosomal associations in patient with mosaicism for trisomy 21. Metaphase plates (a) showing 47 chromosomes and acrocentric association, (b) karyotype of 47, XY, +21, (c) metaphase plate showing ring chromosome (r21), acrocentric associations (D–D) and (D–G), (d) D–D–G. (d) Karyotype of 47, XY, +r21, (e) metaphase plate showing fragment and ring, (f) colored microphotograph showing GTG banded chromosomes with trisomy and associations.

growth (BMI<13). The facial features were marked by a broad forehead and slanting eyes. Ophthalmic examination showed ocular movement as normal but with orthophoria. The ear lobes were small with curved pinnae. Otoscopic examination showed dry and clean ears, intact tympanic membrane with retracted grade III in (L) and grade II in (R). The findings of C.T. scan head (P) were within normal limits. Disability and psychological evaluation stated 60% disability with cognitive delay and speech impairment since birth. The patient's father, mother and younger sister aged 28, 25 and 03 years respectively, were phenotypically normal.

Both the hands of the patient showed mild bilateral clinicodactyly. For atd angle measurement, entire palm was inked including wrist creases and hypothermal border. Palm print of patient revealed atd angles t′ (45°) and t″ (81°) in both left and right palms. Finger nails were normal in the proband but toe nails showed bilateral periungual fibroma.