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Cytogenetic Evaluation of an Indian Boy with Ring Chromosome 14 Mosaicism: A Case Study and Literature Review

Neelam Thakur
Assistant Professor, Zoology
Department of Chemistry, Chandigarh University, Punjab
Email: neelamthakur.uis@cumail.in

Abstract

The ring 14 chromosome is a rare chromosomal aberration characterized by a distinct phenotype consisting of dysmorphic features including mental retardation, epileptic seizures, ocular anomalies, microcephaly, pre-mature birth, late birth cry, skin pigmentation, short neck and low set ears. Cytogenetic evaluation was done on 17 years boy who was discovered to have previously undescribed chromosomal abnormality 42, XY, 14(r), -14 +Marker/ 44, XY. The parents had the normal karyotypes that indicate de novo origin of this abnormality. Stanford - Binet test was performed to assess the degree of severity of mental retardation and was found to be mild (IQ: 50-55 to 70). To our knowledge this is the first report evaluated with ring (14) mosaicism. Literature of published cases is reviewed in this article but none of these reports pertain mosaicism of this type.

Key Words: Ring 14, Mosaicism, Epilepsy, Microcephaly, Cytogenetic

Introduction

Ring 14 chromosome is rarely reported in individuals with intellectual disability and its prevalence is also unknown. Approximately 80 cases have been found since the first report in 1971 [1]. The size of the deleted terminal fragment varies and ranges from one to a few megabases. Moreover, combination of deletions to partial duplication of 14q have also been reported in some human beings [2, 3]. The percentage of cells with abnormal chromosomal constitution varies among different patients and mosaicism is also reported in several cases in which in addition to abnormal chromosomal compliment containing cells, normal cells (44, XX or 44, XY) are also present [4,5]. Clinical features associated with r (14) include mental retardation, epileptic seizures, several ocular abnormalities, microcephaly, late birth cry etc. [6, 7]. Some features of 14q32q33 deletion are also shared by r (14) syndrome [8]. In this report, cytogenetics investigation was done of 17 years old boy with above mentioned abnormal clinical anomalies.

The objectives of Present Investigation are:

- To determine the type of chromosomal anomalies in an intellectually disabled male.
- To find out the IQ level of the subject by Stanford- Binet Test.
- To find the origin of this abnormality in the subject.

Material and Methods

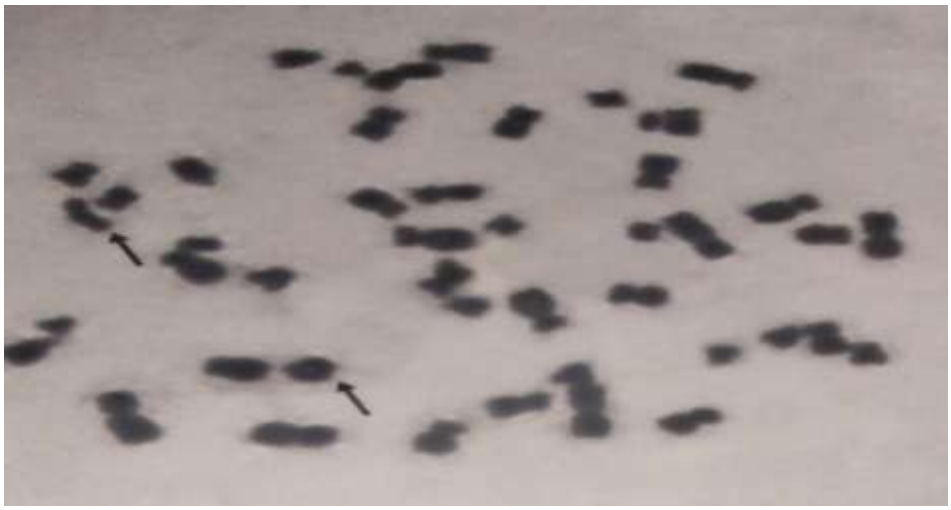
In this investigation, a proforma was filled to get information about clinical features and pedigree of the patient. Degree of intellectual disability was done by Stanford- Binet test of intelligence. Blood samples of the patient and his parents were collected in sodium heparinized vacutainers. Chromosomal preparation was done by standard culture technique

with some amendments [8-9] were followed for chromosomal preparation. Karyotypes were prepared from those chromosomal plates in which all the chromosomes were well spreaded and International system for human cytogenetic nomenclature 2016 (ISCN) classification is followed to find chromosomal irregularities.

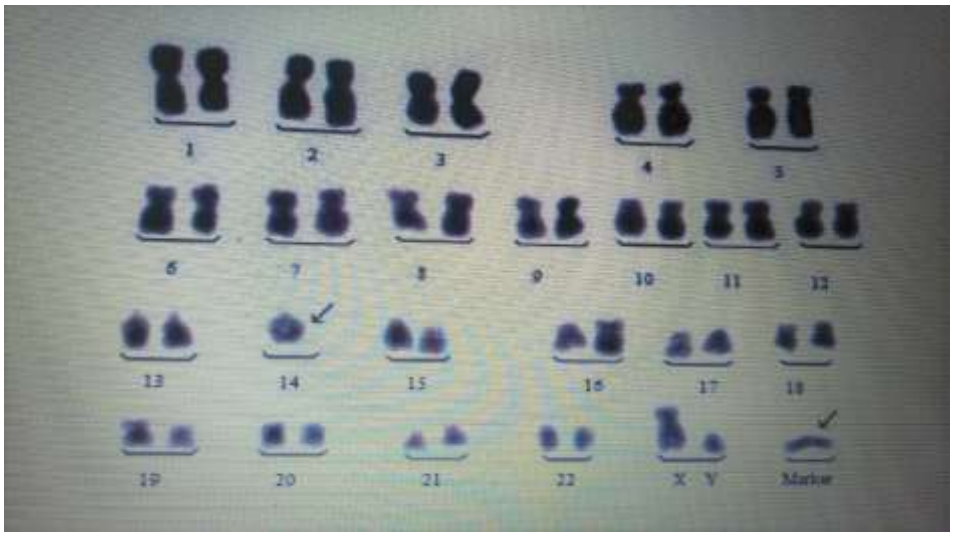
Results and Discussion

Case Report

Karyotype of 17 yrs. old male patient was found to be 42, XY, 14(r),-14 +Marker/ 44, XY (Figure 1.1-1.2) but the chromosomal constitution of parents was found to be normal. He was delivered naturally with late birth cry. Age of mother and father were of younger age. He had hyperactive behaviour with history of epileptic seizures. Family history has hinted the infrequent reason of this abnormality (Figure 2) The degree of intellectual disability was found to be mild with IQ=60.



[A]



[B]

FIGURE 1: [A] Chromosomal Plate Chosen for Karyotype preparation [B] Chromosomal Constitution: 42, XY, 14(r),-14 +Marker/ 44, XY

P – generation

F1-Generation

F2- Generation

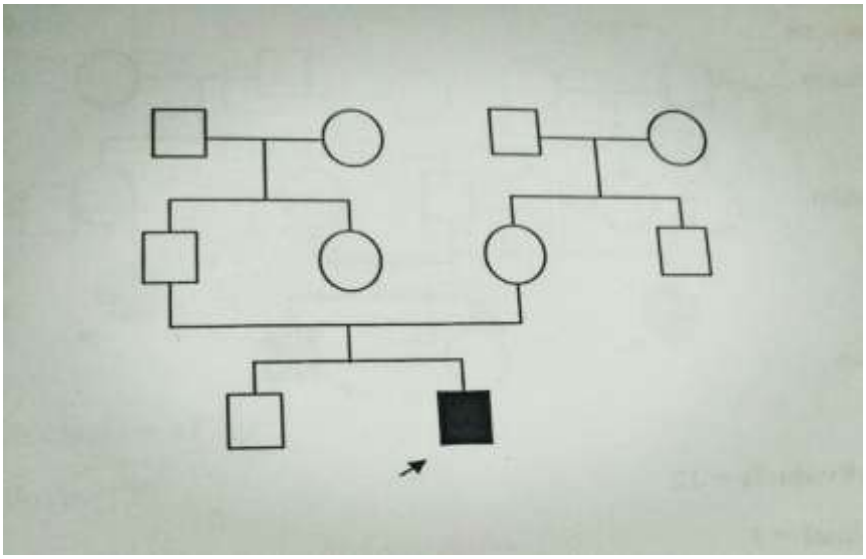


FIGURE 2: Pedigree Chart of the Patient

Discussion

Ring chromosomes are the group of structural abnormalities of the chromosomes, with a ring-shape. Ring chromosomes has been reported for every chromosome of human beings, however most of them affect the acrocentric chromosomes (13, 14, 15, 21, and 22). Ring 14 is a rare chromosomal abnormality characterized by intellectual disability, epileptic seizures and several facial abnormalities. Ring chromosomes are generally formed by deletions of terminal regions in p and q arms which is followed by fusion of the two ends [15]. In some ring chromosomes, a duplication attached to the deletion of terminal regions has been defined, derived from the breaking of a dicentric chromosome [10]. Dicentric chromosome is formed by mitotic instability due to sister chromatid exchange [11]. Most of the ring chromosomes cases, the reason behind origin is *de novo*, but whether it occurs in gametic cells or in post-zygotic cells, it is not clear [12]. In some cases, the ring chromosome is present in only some of a person's cells. This situation is known as mosaicism as reported in present investigation [13-15].

Conventional cytogenetics is the main tool to detect a ring chromosomal abnormality but CGH/SNP array techniques can be used to ascertain a terminal deletion of q arm of chromosome 14. Management of this disease depends on the symptoms in each patient and for addressing each issue requires a team of specialists .But the prediction of symptoms and severity is difficult and depends primarily on the health issues present and difficulties that may ascend.

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