CASE REPORT

DOWN SYNDROME CAUSED BY 21; 21 ROBERTSONIAN TRANSLOCATION

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Abstract

Down syndrome, also known as Trisomy-21, is the most common viable aneuploidy in humans. It was first described as a syndrome by John Langdon Down in 1866 and later Jerome Lejeune and Patricia Jacobs explained the association between the third copy of the 21st chromosome and syndromic manifestations. The usual incidence of Down syndrome is 1 in 700 live births. Of all cases of Down syndrome, 95% are caused by non-disjunction. Robertsonian translocation of 21; 21 is extremely rare. To the best of our knowledge, we are reporting the first case of 21;21 translocation causing Down syndrome from Sri Lanka.

Key words: Trisomy 21, Robertsonian translocation, de novo mutation, mosaicism

Background

The genetic basis of Down syndrome includes chromosomal non-disjunction, genetic mosaicism and translocation/ ring chromosomes or isochromosomes. Down syndrome due to 21; 21 translocation is extremely rare.

Case history

A one and half year old baby girl was admitted with bronchopneumonia. This was her first major respiratory tract infection. She was started on intravenous antibiotics and supportive therapy, resulting in full recovery in 7 days.

She was the first-bornbaby to non-consanguineous healthy parents. The mother was 34 years and the father 36 years in age. The pregnancy was uneventful and the baby was delivered by normal vaginal delivery at 37 weeks of gestation, with a birth weight of 2.56 kg. She was found to have the typical physical characteristics of trisomy 21. The postnatal period was complicated by idiopathic pulmonary hypertension and feeding difficulty. She was discharged home after establishment of breast feeding and resolution of pulmonary hypertension, at 3 weeks of age.

The initial assessment of vision and hearing, as well as thyroid function test donewithin the first three months were

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found to be normal. There was no evidence of gastrointestinal abnormalities. Repeated cardiovascular evaluation was normal.

Karyotyping was performed from blood lymphocytes using GTL banding according to standard protocol. The chromosome spread showed the presence of Robertsonian translocation between two long arms of chromosome 21, and her karyotype was 46, XX, rob (21; 21) (q10; q10) (Figure 1). Her parents were found to have the normal karyotype; therefore this was a result of a rare occurrence of de novo mutation of 46, XX, rob (21; 21).

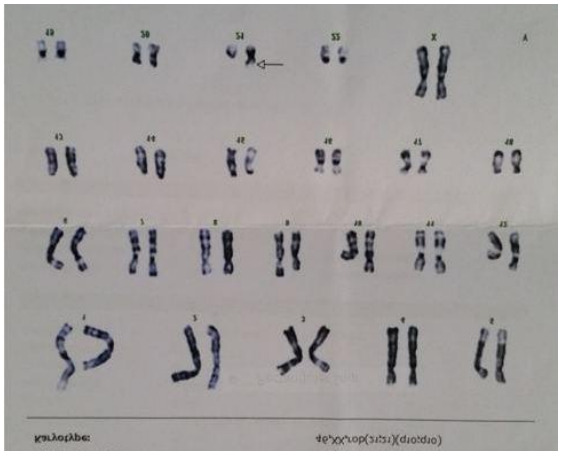

Figure 01: Karyotype of the index case

Discussion

Down syndrome is the most common chromosomal anomaly in humans, with characteristic dysmorphism, congenital malformations and systemic manifestations involving gastrointestinal, thyroid, hematological, respiratory, systems, as well as hearing and vision. The manifestation of the syndrome has variable expressivity and penetrance, although features such as some degree of learning difficulty, developmental delay and hypotonia have 100% penetrance [1].

Even though the phenotype would support the clinical diagnosis, genetic diagnosis is mandatory for the confirmation of diagnosis and management. Genetic counselingwith regards to recurrence and prevention is a mandatory and important aspect of management [1]. If Robertsonian translocation is identified in an offspring, it is mandatory to explore the karyotypeof both parents, since a carrier with balance translocation in a parent has 100% recurrence in next pregnancy [3-5].

Balanced Robertsonian translocation carriers are phenotypically normal[4]. Rob(21;21) (q10,q10) is the rarest of all translocations causing Down syndrome [2-4]. These patients cannot be clinically differentiated from Down syndrome caused by other genetic causes. Fifty percent of rob (21q, 21q) occur as spontaneous de novo mutations and 95% occur during Oogenesis [3, 4]. For the de novo mutation of rob (21q; 21q) with genetically normal parents, the risk of recurrence is 2-3% [3-5].

Conclusions

This is a rare occurrence of Trisomy 21 with 46, XX, rob (21; 21) (q10; q10), withnormal parental karyotype, suggesting ade novo mutation. Since this is the first born, risk of recurrence according to current data is 2-3%.

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