International Journal of Otorhinolaryngology and Head and Neck Surgery
Antil A et al. Int J Otorhinolaryngol Head Neck Surg. 2023 Sep;9(9):745-749
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20232526

Case Report

A rare craniofacial anomaly associated with balanced reciprocal translocation between chromosome 1 and 7: a case report

Amit Antil[1]*, Umesh Kumar[1], Saugat Ray[1], Barun K. Chakrabarty[2], Paresh Singhal[3]

[1]Department of Orthodontics and Dentofacial Orthopaedics, [2]Department of Pathology, Armed Forces Medical College, Pune, Maharashtra, India
[3]Department of Pathology, Army Hospital (R & R), New Delhi, India

Received: 01 June 2023
Revised: 04 August 2023
Accepted: 10 August 2023

***Correspondence:**
Dr. Amit Antil,
E-mail: akkiantil@gmail.com

ABSTRACT

The occurrence of balanced reciprocal translocation of chromosome 1 and 7 is one of the rare anomalies. The present case report focuses on a case of 07-year-old male patient with craniofacial anomaly due to balanced reciprocal translocation of chromosome 1 and 7 manifesting as microcephaly, microstomia, oligodontia and scrotal hypospadias with bilateral retractile testis. The patient had severe retrognathic and hyperdivergent mandible along with multiple carious and unerupted permanent teeth. After complete oral prophylaxis of the patient, the restorations of all carious teeth were carried out. Extraction of root stumps under conscious sedation has been planned in later phase. The patient will further be followed up for orthodontic correction of maxillary and mandibular arches in all three planes keeping in view of the growth status of the patient. The present case report intends to provide an overview of the clinical and radiographical features of this rare anomaly who need a prolonged interdisciplinary management and long term follow up. Further, this will add value to the existing prevalence in the available literature.

Keywords: Balanced translocation, Microcephaly, Microstomia, Oligodontia, Retractile testis, Scrotal hypospadias

INTRODUCTION

A balanced reciprocal translocation defined as reciprocal exchange of chromosomal material between two nonhomologous chromosomes. The estimated global occurrence of balanced translocations is 1 on 1,000 persons. Approximately 0.5% of new born infants found to have structural chromosomal abnormalities using conventional cytogenetic karyotype analysis. In most of cases, apparently balanced structural chromosome anomalies are not linked with anomalous phenotypes and therefore may be transmitted through successive generations unrecognised. Six % cases of de novo balanced structural abnormalities are associated with abnormal phenotypes. Abnormal phenotype in these cases is thought to be due to involvement of genes at the breakpoint region/ cryptic duplications/ deletions/ insertion/ inversions beyond the resolution of conventional karyotyping. The other viewpoint explains the occurrence of phenotype and karyotype abnormalities relation as mere coincidence.[1]

The occurrence of balanced translocation between chromosome 1 and 7 is not common and scarcely documented in literature. Associated clinical manifestations with rare balanced translocation between chromosome 1 and 7 is less known making this anomaly one of the rare occurrences of its kind. In the present article, a rare case of balanced reciprocal translocation of chromosome 1 and 7 associated with craniofacial anomaly affecting dental eruption and development of jaws is presented with an effort towards reporting on such rare anomaly in literature.

CASE REPORT

A 07-year-old male child reported with the chief complaint of multiple unerupted permanent teeth since exfoliation of deciduous teeth. On eliciting the past medical and dental history, the parents revealed natural exfoliation of deciduous teeth more than 6 months back, along with non-eruption of permanent teeth. Patient was a known operated case of scrotal hypospadias with bilateral retractile testis for which urethroplasty along with chordae correction was carried out 4 months ago.

Patient's parent reported to the pediatrician 4 years back where on complete evaluation and clinical presentation a provisional diagnosis of Pierre Robin sequence was given following which Karyotyping was advised by pediatrician. Conventional karyotyping was performed on the peripheral blood samples using standard cytogenetic protocols. An automated karyotyping system (Metasystems, GmbH, Altlussheim, Germany) was used for analysis. The karyogram (Figure 1) revealed balanced reciprocal translocation between long arms of chromosome no 1 and 7 resulting modal karyotype :46, XY, t (1;7) (q23; q32).

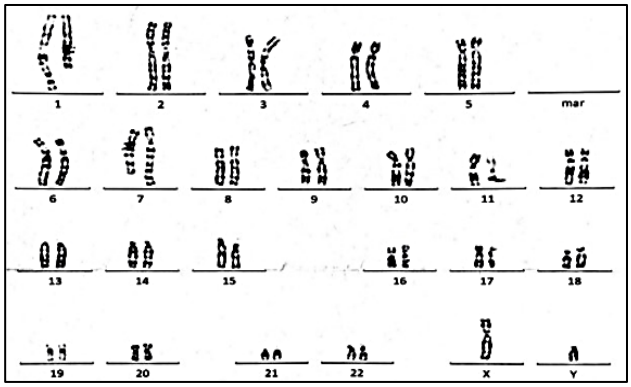

Figure 1: Karyotyping pictogram of the patient.

Further detailed medical, familial and personal history of the patient as given by his parents revealed that the patient was the first child from a non-consanguineous marriage and have no relevant familial history of hereditary or metabolic disorders in the family. Patient had positive behavior as per Frank L behavior rating scale.[2] Patient was thin built and had normal posture and gait, with BMI of 12.4 kg/m^2 which is classified as severely thin according to WHO 2007 guidelines.[3] His head circumference as per standard anthropometric measurements suggested by Pindrik et al was 48 cm which classifies the patient to have microcephaly.[4] Face of the patient is not proportionate in horizontal fifths, due to chin deviation towards left side and vertical thirds due to increase lower anterior facial height (Figure 2 A-C).

Patient had convex soft tissue profile with incompetent lips. Interpupillary distance of 51.5 mm and inter commissural width is 37.8 mm indicating towards microstomia with reduced mouth opening of 17 mm. Since incisors were missing, therefore inter labial gap was taken as guide for measuring mouth opening.

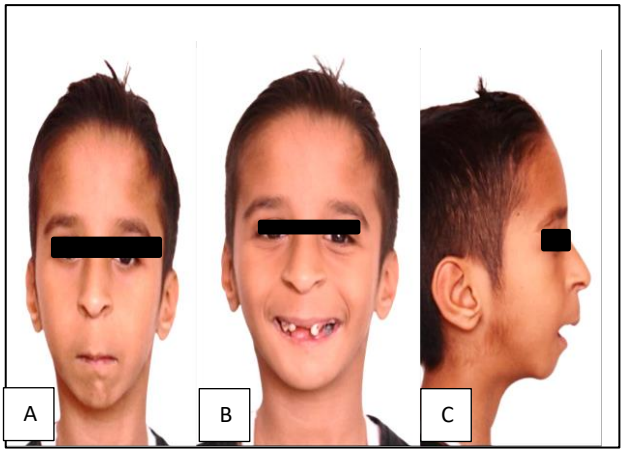

Figure 2 (A-C): Frontal profile at rest, frontal profile at smile and lateral profile.

On examination of temporomandibular joint (TMJ), no abnormal joint sounds could be elicited during opening and closure of lower jaw. There was no tenderness to palpation in TMJ, however mandibular opening and closure path was found to be deviated towards left.

Intraorally, patient was in early mixed dentition with total number of 11 teeth seen clinically with carious 11, 52, 53, 55, 62, 63, 65, 26, 75 and root stumps in respect to 54 and 63 and had narrow intermolar width 22 mm in mandibular arch high with arch palate with palatal depth of 16 mm (Figure 3 A-C).

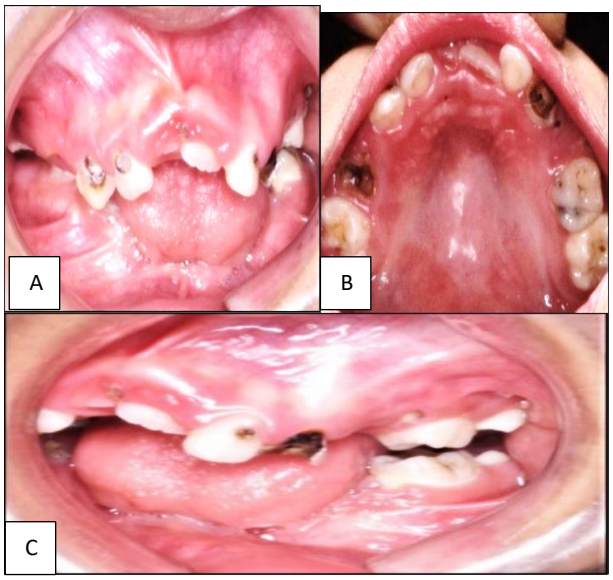

Figure 3 (A-C): Right buccal, maxillary arch and left buccal.

The facial deformity in all three planes along with multiple unerupted permanent teeth indicated towards

further radiographic, biochemical and hematological investigations. Orthopantomogram (OPG) of the patient revealed mixed dentition stage with twenty-one teeth at different levels of development and radiographic absence of multiple teeth. OPG revealed abnormal gonial angle morphology on left side (Figure 4).

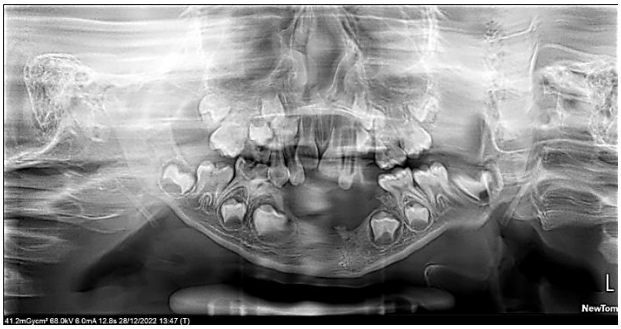

Figure 4: OPG.

Lateral cephalometric analysis revealed Sagittal skeletal discrepancy was due to combination of hypoplastic maxilla and mandible which got further worsened by Type I downward backward rotation of mandible with gonial angle of $162^{0.5}$ Soft tissue profile was convex with incompetent lips having prominent upper and retrusive lower lip (Figure 5).[6]

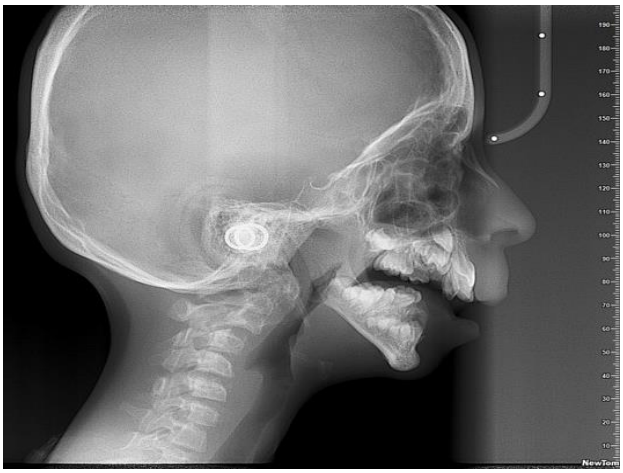

Figure 5: Lateral ceph.

A complete multidisciplinary systemic evaluation of the patient was carried out including opinion from departments of ophthalmology, neurology and cardiology. Hematological investigations, complete biochemistry profile, electroencephalogram (EEG) were carried out.

Patients hemogram, serum enzymes, and serum electrolytic findings were within normal limits. EEG report was also normal with negative indication for any epileptic discharge, sleep markers and activation procedure did not produce any abnormality in the activity (Figure 6).

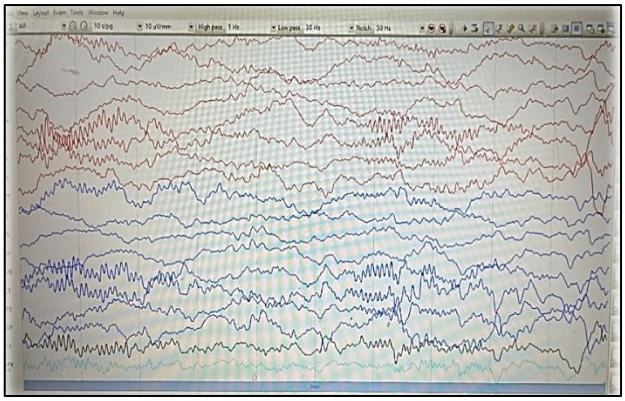

Figure 6: EEG.

Karyotyping of parents was also carried out to rule out any possibility of familial inheritance. However, the karyotyping findings of parents were normal (Figure 7).

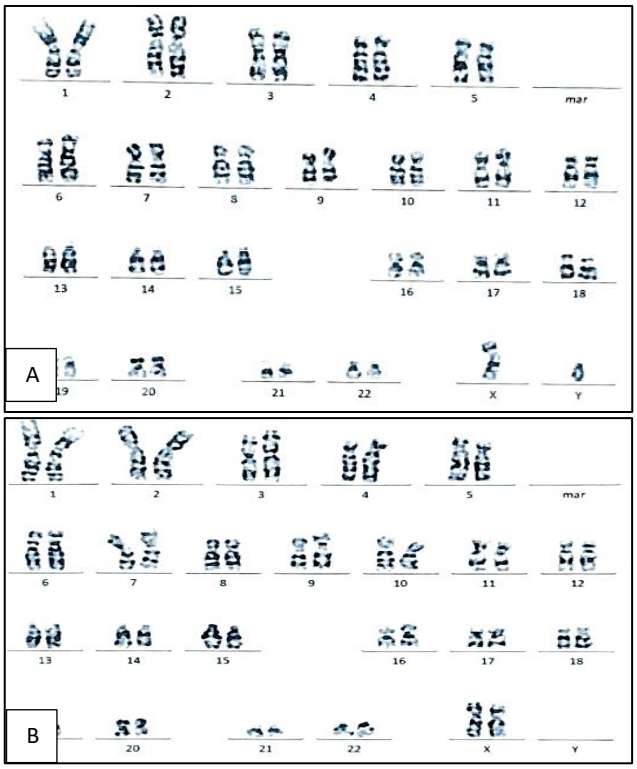

Figure 7 (A and B): Karyogram father and Mother

Finally, the patient was diagnosed with chromosomal anomaly with balanced reciprocal translocation between long arms of chromosome 1 and 7 with presentation of microcephaly, microstomia and oligodontia.

Treatment progress

The complete oral prophylaxis of the patient was carried out followed by the restoration of all carious teeth. He has been planned for extraction of root stumps under conscious sedation in later phase as the patient was not cooperative with the instruction being given while

inducting nitrous oxide conscious sedation. The patient will further be followed up for orthodontic correction of maxillary and mandibular arches in all three planes keeping in view of the growth status of the patient.

DISCUSSION

A translocation is an interchange of chromosomal material between specific chromosomes, and it may be the result of fork stalling and template switching, microhomology-mediated break-induced repair, breakage-fusion-bridge cycles, or chromothripsis. These are balanced when the exchange does not result in loss of genetic material and unbalanced when genetic material is gained and/or lost.[7]

Further to complex the scenario, the probability for abnormal phenotypic presentations varies between familial and de novo balanced translocation anomalies. In familial cases, the risk for same balanced translocation associated phenotypic abnormality in the descendants is supposed to be very low due to repeated miscarriages. The clinical abnormal phenotype in both de novo and familial balanced translocations may be apparent due to one of these mechanisms[8]: Change of a dosage-sensitive effect of gene, variable expression of genes involved in breakpoint area due to position alteration effect, uniparental disomy, cryptic unbalanced rearrangement occurred during meiosis and cryptic complex chromosomal rearrangements (CCRs) resultant to chromosomal rearrangements.

Conventional cytogenetic techniques, can easily explain an abnormal phenotype occurrence due to unbalanced chromosome rearrangements. However, in balanced chromosomal rearrangements it become a challenge due to nonappearance of chromosomal gains or losses seen in the karyotype.

Two cases of BCP ALL in adolescence boys, has been reported in literature with t (1;7) (q25; q32).[9] Therefore, our patient also needs to be kept under close long term follow up.

A balanced translocation carrier individual has the following probability outcome associated with each conception. They either have an appearance of unbalanced karyotype abnormalities in 50% of progenies or identical balanced karyotype in 25% of progenies, and remaining 25% of cases have chances of normal karyotype. As a general rule, if there are no persons in the family affected by an imbalanced translocation, abnormal phenotype occurred in 7% cases if the carrier is the mother and 3% if the carrier is the father. This risk for abnormal phenotype depends on the mode of ascertainment i.e., balanced or unbalanced, the spatial localization of breakpoints and chromosomes involved. Therefore, with advent of medical knowledge as a greater number of cases of balanced translocation cases are reaching to reproductive age they should be provided with genetic counselling and preimplantation genetic diagnosis (PGD) for achieving a normal pregnancy avoiding repeated miscarriage or termination of pregnancy.[10]

The unbalanced chromosomal translocations are often associated with myelodysplastic syndromes with poor clinical outcome. Commonly associated clinical features of unbalanced chromosomal translocation between chromosome 1 and 7 include presence of eosinophilia, trilineage dysplasia, high rates of progression to AML and poor prognosis with less than 1 year of median survival. Unbalanced translocations are commonly found in 1.5-6% in myelodysplastic syndrome, 0.2-2.1% in acute myeloid leukaemia and rarely in myeloproliferative disorders. Clinical features associated with unbalanced translocation is less clearly defined compared with its genomic structure.[11-12]

Common clinical features associated with unbalanced translocations includes a previous history of chemotherapy/or radiotherapies in more than half cases, presence of eosinophilia, trilineage dysplasia, high rates of progression to AML in MDS cases and poor prognosis with less than 1 year of median survival.[6] Few cases of chromosomal t (1;7) translocations have been reported to be associated with neuropsychiatric manifestations or congenital brain malformation, early psychiatric disorders, developmental delay, hypotonia, seizures, early onset schizophrenia, and autistic behaviour.[13]

The incidence of balanced chromosome translocations is approximately one in 500. Balanced reciprocal translocations are associated with a 50% risk of spontaneous abortions and a 20% risk of genetic abnormalities.[14] The present case of balanced translocation has not manifested in any haematological or neurological disorders instead it was associated with clinical features of craniofacial anomaly microcephaly, microstomia and oligodontia.

Common clinical features associated with balanced translocations apart from recurrent pregnancy loss are neurological disorders. In the present case the patient presented initially with hypospadias and bilateral retractile testis. Further investigations by paediatricians based on this craniofacial morphology resembling like Pierre Robin sequence resulted in revelation of the chromosomal translocation. The patient's parents further concern about non eruption of permanent teeth resulted in further referral to orthodontist and observation of few more craniofacial findings including microcephaly, microstomia and oligodontia. Till date no evidence could be found in literature review indicating association of microcephaly, microstomia and oligodontia with no neurological, haematological and cardiovascular anomalies with balanced reciprocal translocation between long arms of chromosome 1 and 7. Hence the incidental finding of this chromosomal abnormality should be considered as one of the rare occurrences.

CONCLUSION

This case report represents a rare chromosomal anomaly of balanced translocation between long arms of chromosome 1 and 7. This case manifested as microcephaly, microstomia, oligodontia associated with hypospadias and bilateral retractile testis. The management of this case was started with simple procedures like oral prophylaxis and restoration of carious lesions. However, these patients do require a long term follow up for holistic management of craniofacial and other defects. Further, detailed studies on genetic mutations in such cases may be required. The patient will reach to reproductive age as he has normal life expectancy. Genetic counselling is recommended for the patient's marriage. This case in particular will add value to the existing prevalence in available literature.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Antil A, Kumar U, Ray S, Chakrabarty BK, Singhal P. A rare craniofacial anomaly associated with balanced reciprocal translocation between chromosome 1 and 7: a case report. Int J Otorhinolaryngol Head Neck Surg 2023;9:745-9.