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De Novo Pericentric Inversion of Chromosome 9 Inv (P12;Q13) and Intellectual Disability: Case Report and Literature Review

Neelam Thakur[1]
[1]Assistant Professor, ZoologyUniversity Institute of Biotechnology-BiosciencesChandigarh University, Punjab
Email: [1]neelamthakur.uis@cumail.in

Abstract: The inversionofpericentric type in chromosome 9 is one of the most common (1–3%) chromosomal aberrations in normal and mentally retarded individuals thatoccurs in heterochromatin region of this chromosome. In this investigation, chromosomal analysis after conventional G-banding unveiled a pericentric inversion of chromosome 9 in an intellectually disabled seven years male child.The parents had the normal karyotypes that indicated de novo origin of this anomaly.The patient's partial duplication for chromosome 9 is due to crossing over occurring within the inverted segment during reductional division and retention occurs through Mendelian inheritance without any phenotypic abnormalities. The degree of mental retardation was found to be moderate (IQ: 40-45 to 50-55). In this article, the information related to inversion of chromosome 9 is reviewedand possible significance of this anomaly is also discussed.

Keywords: Pericentric inversion, Intellectual Disability, Chromosome No. 9

INTRODUCTION

Intellectual Disability (MR) is characterized by decreased intellectual, linguistic and communal capabilities that are apparent in infant stages or early childhood (1, 2).The level of Intellectual disability ranges from Mild (IQ:55-69) to profound (less than 25) depending on the IQ levels of these patients. The causes of Intellectual disability (ID) can be genetic (7 to 10 percent) as well as non-genetic (25 to 50 percent). According to an estimate 18.6 to 44.5 percent of cases have non-genetic causes and 25 to 50 percent have genetic causes (3-6). Chromosomal aberrations accounts for 10 percent of total live born among genetic cases (7).Chromosome inversions are a comparatively the most commonbalanced structural aberration. Generally, there are two types of inversions i.e., paracentric and pericentric. If the inverted segment is present on one of the arms of chromosome and involve only one side of the centromere then the inversion is paracentric; if broken parts involve both arms i.e., p and q arms, then it is pericentric inversion. The inversion of pericentric type which occurs in condensed areaof chromosome 9 has been documented without anyabnormal clinical features (8). It is still not clear that whether,inv 9(p12;q13) is a abnormal karyotype or an normal variant has been reported in both normal population and patients with abnormal phenotypes and diseases (9,10). However, association of this heterochromatic variant is occasionally found with congenital abnormalities, increased chromosomal variability and malignancies proneness. These patients have moderate mental retardation, growth retardation, microcephaly, cardiac defects etc.

The Objectives of Present Investigation are:

- To find the cause of this abnormality in the subject

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- To find the type of chromosomal anomaly in an intellectually disabled male.
- To determine the degree of MR in the subject by Stanford- Binet Test.

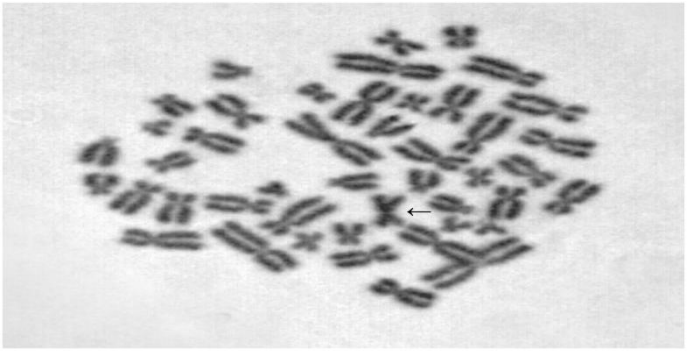
MATERIAL AND METHODS

In present investigation, information about family history and clinical features of patient was taken from him and his parents. Stanford- Binet test of intelligence was performed to get information about degree of mental retardation. For chromosomal preparation, blood samples of the patient and his parents were collected in vacutainers having sodium heparin. Standard culture technique with somemodifications [11,12] were used for chromosomal preparation. Ten well spreaded plates were chosen for preparation of karyotypes.The chromosomal irregularities were reported according to ISCN (International System for Human Cytogenetic Nomenclature) 2016.

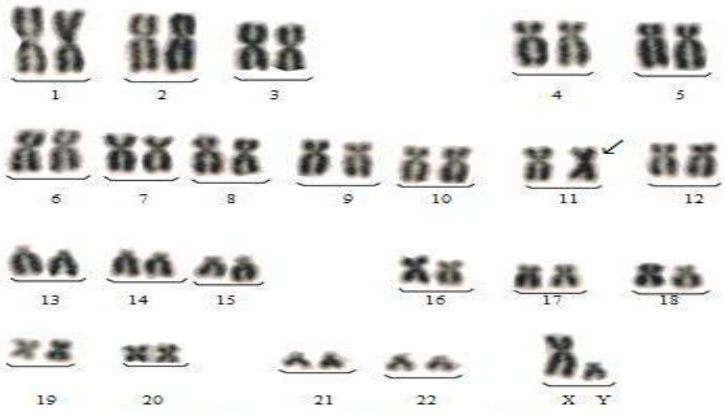
RESULTS

Case Study

A seven years male proband was bornto parents of younger age (less than 35Years) and delivered naturally but with late birth cry. He was first in order of sibship and degree of mental retardation was found to be moderate (IQ=48).



[A]



[B]

FIGURE 1: [A] Plate of Chromosome Chosen for Karyotype Preparation [B]Karyotypic Constitution, 46,XY, inv 9(p12;q13)

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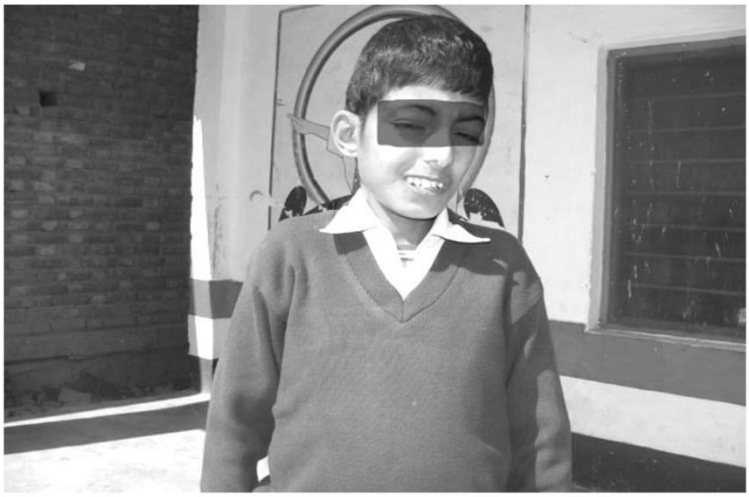
Remarkable clinical features are microcephaly, short stature, high arched palate and cryptorchidism (Figure 2 A). The chromosomal constitution was found to be 46, XY, inv 9(p12;q13)(Figure 1 A, B), but the karyotypes of parents were found to be normal (Figure 2 B).



[A]

P – generation

F1-Generation

F2- Generation

[B]

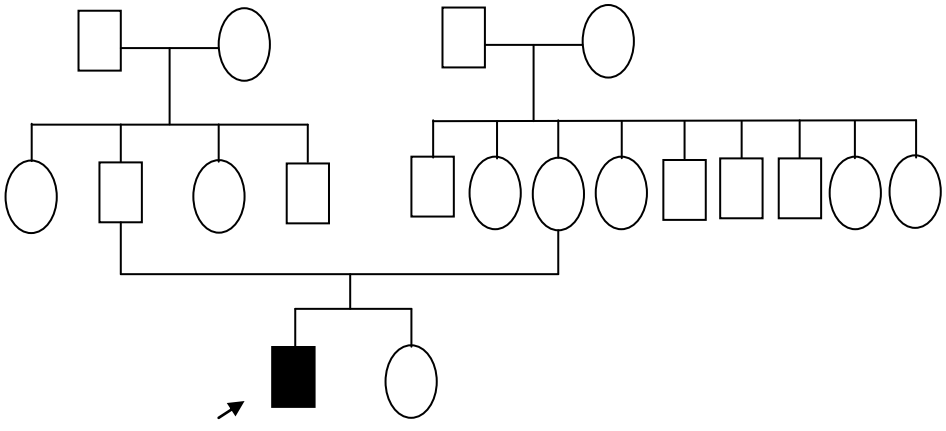


FIGURE 2:[A] Patient [B] Pedigree Chart

DISCUSSION

Chromosome anomalies are significant cause of congenital malformations and reason behind approximately fifty percent of spontaneous abortions (13–15). The occurrence of chromosomal anomalies is 13.8% in the overall population (16), however the rates varied

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between 5.2% and 13.4% (17-19). Among different type of chromosomal abnormalities, inversion in chromosome 9 is most common. This anomaly leads to the highest degree of morphological variations. The mechanism of its origin is still not clear but the mode of inheritance is found to be Mendelian [20].Variations in clinical features ranges from normal to multiple malformations (21). The association of inv(9) with abnormal featuresunveiled that maximum cases had facial abnormalities and delayed signs. The inversions which are not balanced at breakpoints on both the sides of centromere might play a role in development of abnormal phenotype. Parents of this patient had history of spontaneous abortions as reported in previous studies [22]. Variations in phenotypes is due to different locations of breakpoints [23]. The reason behind abnormal development in these patients may be due to suppression of euchromatic regionsduring the process of breakage reunion. Henceforth, there is a necessity to study every breakpoint region of inversion (9) using new techniques like FISH (fluorescent in situ hybridization), array-CGH (comparative genomic hybridization technique).

REFERENCES

[1]. .B. Moeschler and M. Shevell, "Clinical genetic evaluation of the child with mental retardation or developmental delays", Pediatrics, vol. 117, (**2005**), pp. 2304-2316.

[2]. A. Tzchach and H. Ropers, "Genetics of mental retardation", Medicine, vol. 104, (**2007**), no., 20, pp. 1400-1405.

[3]. S. Bundey, T.P. Webb, A. Thake and J. Todd, "A community study of severe mental retardation in the West Midlands and the importance of the fragile X chromosome in its aetiology", J. Med. Genet., vol. 22, (**1989**), pp. 258– 266.

[4]. A.G. Hunter, "Outcome of the routine assessment of patients with mental retardation in a genetics clinic", American Journal of Medical Genetics., vol. 90, (**2000**), pp. 60–68.

[5]. L. Kaufman, M. Ayub and J. B. Vincent, "The genetic basis of non-syndromic intellectual disability: a review", J. Neurodevelop. Disorder, vol. 2, (**2010**), pp.182–209.

[6]. V. Toma, S. Puseljic, I. Skrlec, M. Andelic, M. Kos and J. Wagner, "Etiology and the genetic basis of intellectual disability in the pediatric population", European Medical J., vol. 1, (**2017**), pp. 144-153.

[7].D. Bandopadhyay and S. Kumar, "Chromosomal aberrations in mental retardation: a preliminary study", Ind. J. Clinical Anatomy Physiol., vol. 4, (**2017**), pp.148-151.

[8]. A.S. Ait-Allah, P.M.L. Ming, H.T. Salem, et al, "The clinical importance of pericentric inversion of chromosome 9 in prenatal diagnosis", J.Matern.FetalInvest., vol. 7, (**1997**), pp.126–128.

[9]. G. Ceylan, C.Ceylan andH. Yuce, "A rare seen case with homozygosity for pericentric inversion of chromosome 9 and primary infertility", The American Journal of Case Report, vol. 9, (**2008**), pp. 385–388.

[10]. S. Tural, S.Günes, N. Kara et al, "A case of habitual abortus karyotyped 46, XX, Inv (9) (p11q13) X2 with Inv 9 (p11q13) in both of homolog chromosome pairs",TurkiyeKlinikleri J GynecolObst., vol. 17, (**2007**), pp.331–333.

[11]. P.S. Moorhead, P.C. Nowell, W.J. Mellman, D.M.Battips and D.A. Hungerford, "Chromosome preparations of leucocyte cultured from human peripheral blood", Experimental Cell Research, vol. 20, (**1960**), pp. 613-616.

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Received 16 February 2021; Accepted 08 March 2021.

[12]. N. Thakur,"Chromosomal Abnormalities in Selected Group of Individuals with Intellectual Disability/MR: A Preliminary Study from Himachal Pradesh",Int. J. Advan. Manag. Tech. Eng. Sc.,vol. 8, (**2018**), pp. 1335-1345.
[13]. D.L.Rimoni, J.M. Connor, R.E.Pyeritz et al, "Principles and Medical Genetics." 6th ed. Edinburgh, Scotland: Churchill Livingstone, vol.1.(**2002**).
[14]. E.B .Hook, "Prevalence risks and recurrence". In: D. J. Brock, C.H.Rodeck, Ferguson-Smith, eds. Prenatal Diagnosis and Screening. Edinburgh, Scotland: Churchill Livingstone,(**1992**), pp. 351.
[15]. J.L. Tolmie, "Chromosome disorders". In: Whittle MJ, Conner JM, eds. Prenatal Diagnosis in Obstetric Practice. Oxford, UK: Blackwell Scientific, (**1995**), pp.34.
[16]. F. Düzcan, M.Atmaca, G.O. Cetin et al, "Cytogenetic studies in patients with reproductive failure",ActaObstetGynecol Scand., vol.81,(**2003**), pp.53–56.
[17]. J. R. Lissitsina, R.Mikelsaar and M. Punab, "Cytogenetic analyses in infertile men", Arch Androl. vol. 52, (**2006**), pp. 91–95.
[18]. J.M. Pina-Neto JM, Carrara RC, Bisinella R, et al., "Somatic cytogenetic and azoospermi a factor gene micro deletion studies in infertile men",Braz J Med Biol Res.,vol.39, (**2006**), pp. 555–561.
[19]. P.Nagvenkar, K. Desai, I. Hindujaet al., "Chromosomal studies in infertile men with oligozoospermia and non-obstructive azoospermia", Indian J Med Res., vol. 122, (**2005**), pp.34–42.
[20]. S. Luke, R.S. Verma, R.A. Conte et al.,"Molecular characterization of the secondary constriction region (qh) of human chromosome 9 with pericentric inversion", J Cell Sci., vol.103, (**1992**), pp. 919–923.
[21]. T. Sudha and S.Jayam, "Pericentric inversion in homologues of chromosome 9",Jpn J Hum Genet., vol. 38, (**1993**), pp. 341–343.
[22]. P.Nagvenkar, K. Desai, I. Hinduja et al, "Comparison of the sperm aneuploidy rate in severe oligozoospermic and oligozoospermic men and its relation to intracytoplasmic sperm injection outcome", Indian J Med Res.,vol.122, (**2005**), pp. 34–42.
[23]. M.Sasiadek, O. Haus, M. Lukasik-Majchrowska et al., "Cytogenetic analysis in couples with spontaneous abortions",Ginekol Pol., vol. 68, (**1997**), pp: 248–252.