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Short communication

PREVALENCE OF PRADER-WILLI SYNDROME IN WESTERN INDIA

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ABSTRACT

The prevalence of Prader-Willi Syndrome (PWS) was studied using both classic cytogenetic and FISH techniques in referred cases of microdeletion 15q11-13 to our laboratory from Western India. A total of 53 cases were registered, of which 08(15%) were found positive for Prader-Willi Syndrome i.e. 15q11-13 microdeletion syndrome. FISH technique found to be suitable and sensitive to confirm clinically diagnosed PWS.

Keywords: Prader-Willi syndrome, Western India, FISH, 15q11-13

INTRODUCTION

Prader-Willi syndrome (PWS) is a complex multisystem disorder due to the absent expression of the paternally active genes in PWS region on chromosome 15.[1] In 75 to 80% of affected individuals there is a microdeletion of paternal chromosome 15q11-13.[2] PWS is a complex genetic disorder attributed to genomic imprinting. It is relatively common prevalence of 1/15,000 – 30,000. Despite genetic cause it appears to be sporadic, sex-ratio equals and occurs in all races.[3,4] The differential diagnosis includes obesity, cryptorchidism, short stature, mental retardation, sleep apnoea and squint myopia.

The microdeletion syndrome is characterised by hemizygous microdeletion less than 5 mb of chromosome in which one or group of genes are lost.[5] G-banded karyotyping is approach to detect genomic resolution more than 5 mb. This resolution has been overcome by FISH. It is possible to detect cryptic chromosomal rearrangement such as microdeletion by conventional FISH technique.

MATERIALS AND METHODS

The study was conducted at S. N. Gene Laboratory and Research Centre, Surat, India between August 2010 and February 2014. A total of 53 suspected cases were refereed to us from different parts of Western India and inform consent form was taken from all the subjects. From all patients EDTA and heparinised blood sample (1 – 2 ml.) were collected and were cultured for 72-hours by standard method developed by Moorehead et al.[6] The karyotypes were examined using GTG banding and the automatic scanning system (Axioimager Z_2–Carl-Zeiss) and karyotyping software (IKAROS, Germany) was used to make karyotype. Fluorescence in situ hybridization (FISH) was carried out in both interphase cells and metaphases by using Vysis probes of LSI SNRPN and D15S10 Prader-Willi/Angelman. The LSI D15S10 probes identify deletion of the locus D15S10 and UBE3A gene located within 15q11-13 region of chromosome 15. The procedure was performed as per instruction given by manufacturer. From each patient minimum of 25

interphase cells and 25 metaphases or 50 metaphases were scored and analysed for presence or absence of 15q11-13 microdeletion.

RESULTS AND DISCUSSION

A total of 53 patients clinically diagnosed as Prader-Willi syndrome (PWS) were referred to us for chromosome study and FISH analysis. Out of 53 patients, 30 were males and 23 females ranging in age from 8 days to 41 years. G-banded karyotypes of all patients did not show any deletion on chromosome # 15. Only 08 (15%) patients (Table-1) confirmed positive with microdeletion (Figs. 2,3) of 15q11-13 by FISH analysis. Prader-Willisyndrome is single most commonly known genetic cause of obesity. It has been estimated to have a population prevalence about 1:10,000 to 1:52,000 as reported by Whittington et al.,[7] In large database population study was carried out by Grugni et al.,[4]on the Italian National survey for Prader-Willi syndrome.

Table: 1 shows age and sex distribution among confirmed Prader-Willi syndrome

Patients no.	Age	Sex	FISH result	Deletion
1	4 Years	M	20 metaphases and 20 interphase cells with microdeletion	15q11-13
2	1 year	M	25 metaphases and 25 interphase cells with microdeletion	15q11-13
3	8 years	M	50 metaphases with microdeletion	15q11-13
4	7 years	M	25 metaphases and 25 interphase cells with microdeletion	15q11-13
5	6 years	M	25 metaphases and 25 interphase cells with microdeletion	15q11-13
6	2 years	M	50 metaphases with microdeletion	15q11-13
7	3 years	M	50 metaphases with microdeletion	15q11-13
8	2 years	F	25 metaphases and 25 interphase cells with microdeletion	15q11-13

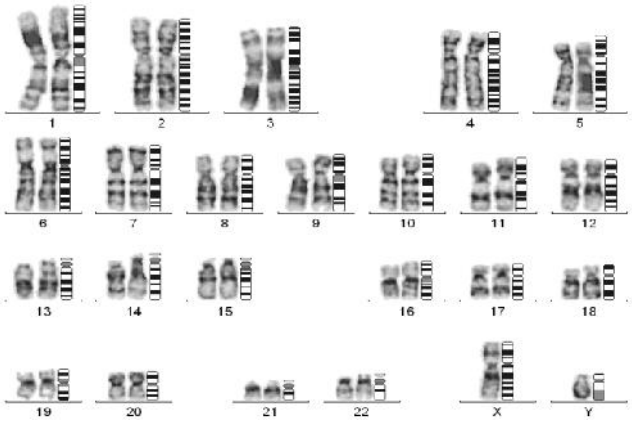

Fig 1: G-banded karyotype of male patient shows no deletion in chromosome # 15

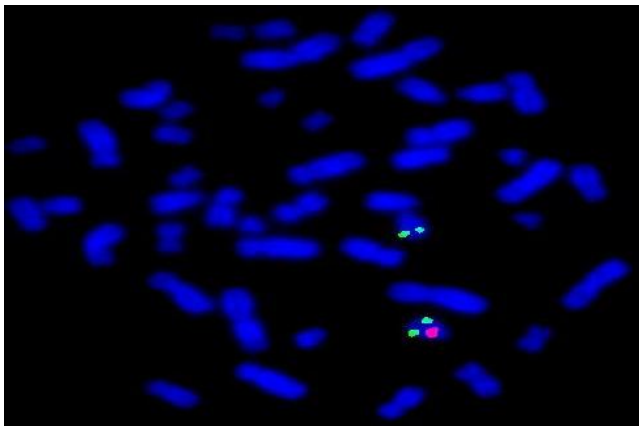

Fig 2: Metaphase showing 2 green and one orange signals confirming micro deletion of 15q11-13

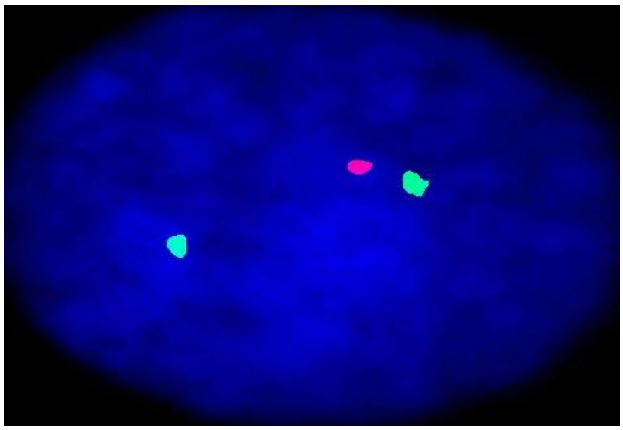

Fig 3: Interphase cell showing 2 green and 1 orange confirming micro deletion of 15q11-13

The study revealed; out of 425 subjects del 15 was found in 238 cases. It is generally known that PWS patients developed morbid obesity.[8]

The complications associated with obesity are the main risk factor for the death in PWS[9].

In the present study, we found only one older person with age of 41 years. Rest of all patients were under age of 12 years. In addition, it is interesting to note that out of 08 affected patients, 07 were males and only one female (Table-1). On the contrary, few published studies have reported that PWS affects males and females equally[10,11]. In another study from India, Halder et al.,[5] has reported 4 positive cases (2 pure and 2 mosaic) out of 38 patients studied for

suspected Prader-Willi/Angelman syndrome. They have further suggested that whole genome screening may be used as a first line of test and FISH may be used for confirmation of screening results.

CONCLUSION

In conclusion, we propose that routine use of FISH for diagnosis of microdeletion of 15q11-13 is considered to be a gold standard technique which confirm accurately done diagnosis of microdeletion in general and Prader-Willi syndrome in particular.

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