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Original Article

Cytogenetic analysis of benign prostate hyperplasia [BPH] patients

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ABSTRACT

Background & objectives: Benign prostate hyperplasia [BPH] is the classical age related disease of prostate, present in 20% of men at the age of 40 years with progression to 70 % by the age of 60 years. BPH is associated with various lower urinary tract symptoms, which affect their day to day life. The aim of the present investigation was to find out the major chromosomal aberrations present in BPH patients and to make a comparison with other study. Methods: In present study 20 cases of benign prostate hyperplasia were taken on the basis of clinical diagnosis from the various hospitals located in Ahmedabad, Gujarat, India, during the period of March 2011 to October 2011. The patients were analyzed for chromosomal aberrations using cultured peripheral blood lymphocytes with their pre-informed written consent. Results: In the present study, 15 (75 %) cases were in the age group of > 60 years. In this study, Karyotype analysis reveals 01 (5%) BPH patient had 46, XY, del (16q-). AUASI score is >20 in 16 (80%) patients. Conclusion: BPH is found in > 60 years of age in 75 % of cases. Common chromosomal aberration 46, XY, del (16q-) found in 01 (5%) BPH patient. Severe AUASI score (>20) is found in 80% of cases.

1. Introduction

Of the many species with prostate glands, only Human, Chimpanzees and Dogs are known to develop benign prostatic hyperplasia [BPH] [1].

BPH is characterized by the non-malignant overgrowth of prostatic tissue surrounding the urethra, ultimately constricting the urethral opening and giving rise to associated lower urinary tract symptoms [LUTS] such as urgency, frequency, nocturia, incomplete bladder emptying, and weak urine stream [2].

BPH is a common disease of prostate gland and occurs in about one quarter of men in their fifties, one third of men in their sixties, and in about half of men in ≥ 80 years. As age advances chances of chromosomal aberrations are also increases [3].

Prostate specific antigen (PSA) level increases with age. Patients with BPH produce larger amounts of PSA.

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American urological association symptom index (AUASI) score is self-administered questionnaires, used to assess the severity of three storage symptoms (frequency, nocturia, urgency) and four voiding symptoms (feeling of incomplete emptying, intermittency, straining, and a weak stream) and to help diagnose BPH. How frequently the patient experiences each symptom is rated on a scale of 1 to 5 [2].

Various treatment modalities for BPH include watchful observation, open or minimal invasive surgery e.g., Trans urethral resection of prostate (TURP), Trans urethral needle ablation (TUNA) etc., medication like alpha-blocker, hormonal therapy. Among these modalities of treatment surgical management may affect sexual functions of individual.

The frequency of chromosome instability in peripheral blood lymphocytes is generally indicative of increased cancer risk for those exposed to DNA damaging agents. Deletions, translocations, inversions and mosaics were the major chromosomal aberrations observed in BPH. Chromosome 1, 7, 16, Y and many more chromosomes were affected in BPH patients [3].

This study of clinical & Karyotypic profile of patients with BPH has been helpful to find out chromosomal abnormalities & genetic cause of BPH so that proper management and genetic counselling can be done.

2. Material and method

For the present study, 20 clinically diagnosed BPH patients were selected from the Surgery department of Civil Hospital & Sharadaben hospital, Ahmedabad, Gujarat, India, during the period of March 2011 to October 2011. Their detailed clinical history & clinical examination finding were noted. About 2 ml of venous blood was collected in sodium heparinized vaccutte from each patient after their pre-informed written consent.

Culture setting was done on the same day of sample collection in Genetic laboratory, Anatomy department, B. J. Medical college, Ahmedabad, using freshly tapped blood with MEM media, Foetal Bovine Serum and PHA (phytohemagglutinin) and put it in incubator at 37°C. After an Incubation period of 69½ hours, metaphase was arrested by adding colchicine. After total 72 hours of incubation the lymphocytes were harvested by centrifuging cells to remove culture medium (3000 rpm for 10 minute) & addition of hypotonic solution (KCl 0.075 M) at 37°C for 20 min to swell the cells, and treated thrice with chilled Carnoy's fixative (3:1 ratio of methanol : acetic acid) and finally the metaphases on the slides were obtained. Then those slides showing metaphases with good morphology were selected and kept under dry wooden boxes for aging process.

After 7 days, GTG banding procedure was done using freshly prepared Trypsin-EDTA solution and Giemsa stain [4]. About 25 metaphase plates were observed in each case and finally, a photograph was obtained from a good quality metaphase slide with the help of a Leica's automatic karyotyping machine (100x). The chromosomal findings were described according to the International system of Human Cytogenetic Nomenclatures and finally, karyotypes were prepared using Leica's Automatic Karyotyping software.

3. Results

In the present study 20 clinically diagnosed BPH patients were studied for cytogenetic assessment by conventional Karyotyping. Out of total 20 patients 5 were below 60 years while 15 were above 61 years [Table-1].

Out of all the cases 4 cases also had a positive family history of BPH. As per AUASI score assessment 4 patients had moderate (8-19) score while 16 patients had severe (20-35) score [Table-2].

Following observation were found on PSA level findings. Out of all 20 patients, 13 patients had normal PSA level while 7 patients had elevated PSA level [Table-3].

In our karyotype analysis we found that only one 71 years old patient had 46 XY, del (16q-) [Image-1], While 17 cases had normal Karyotype and in rest 2 cases metaphase was not found [Table-4].

Table-1: Age distribution in BPH patients studied

Age groups (in Years)	≤60 years	≥61 years	Total
No. of patients	5	15	20

Table-2: AUASI score in BPH patients studied.

AUASI score	Mild (1-7)	Moderate (8-19)	Severe (20-35)	Total No. of cases
No. of patients	0	4	16	20

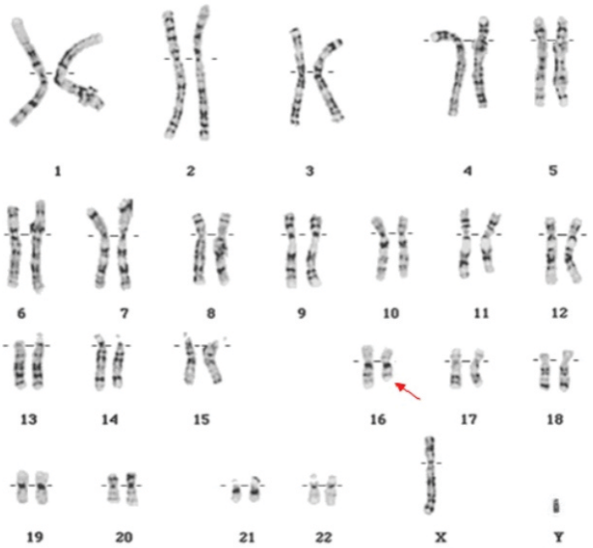
Table-3 : PSA level in BPH patients studied.

PSA Level	Normal (≤4ng/ml)	Increased	Total
No. of patients	13	7	20

Table-4 : Cytogenetic findings by Conventional Karyotyping in BPH patients studied.

Metaphase Finding	Numerical Abnormality	Structural abnormality (deletion)	Normal	Meta-phase not found	Total No. of Cases
No. of patients	0	1	17	2	20

Figures: Image- 1. Karyotype showing 46 XY, del (16) (q-)



4. Discussion

BPH is the classical age related disease of prostate. As age advances chances of chromosomal aberrations are also increases. V. Balachandar et al [3], found that out of 63 BPH patients 34 (53.97%) were in group I (≤50 yrs) and 29 (46.03%) were in group II (≥ 51 yrs). Group II patients showed higher number of

chromosomal aberrations than group I. Muneer M. S. Sharaf et al [5], found that out of 78 patients, 12 (15.4 %) were between 40-59 years, 21 (26.9 %) were between 60-70 years and 45 (57.7 %) were more than 70 years of age. Sushma T.A. [6], noted that among 179 benign lesions, majority of the benign cases belonged to the age group of 61-70 years. Mohamed Labib M [7], found in autopsy data that anatomic (microscopic) evidence of BPH is seen in about 25 % at the age between 40-50 year, 50 % at the age between 50-60 year, 65 % at the age between 60-70 year, 80 % at the age between 70-80 year, and 90 % at the age between 80-90 year. In the present study out of 20 patients; 05 (25%) were in the age group ≤ 60 years, 15 (75%) were≥61 years of age.

O'Leary MP et al [8], studied 4325 men with lower urinary tract symptoms caused by BPH had moderate to severe symptoms (AUASI score ≥12). Roehrborn C.G. et al [9], found that man with lower urinary tract symptoms (LUTS) & clinical BPH and no history of urinary retention, the AUASI score are useful parameters for clinicians in identifying patients at risk for future prostate surgery. In the present study out of 20 patients; 04 (20%) patients have moderate (8-19) AUASI score and 16 (80%) patients have severe (20-35) AUASI score.

Sushma T.A. [6], found that Serum PSA values over 10ng/ml were seen in 10 benign (16.6%) cases & between 4-10 ng/ml were seen in 21 benign (35%) cases. While Serum PSA values between 0-4 ng/ml were seen in 29 benign (48.33%) cases. V. Balachandar et al [3]. in 2008, noted in his study that range of PSA values in BPH patients it was 4 to 8 ng/ml. V. Balachandar et al. [10], in 2010 found that out of 27 BPH patients, PSA level of collected blood samples was the < 10.0 ng/ml (86.6 %) in 23 subjects and ≥ 10.0 ng/ml (13.3%) in 4 subjects. In present study out of 20 patients, PSA level of collected blood samples was the < 4.0 ng/ml in 13 (65%) patients and elevated (≥4.0 ng/ml) in 7 (35%) patients.

Miyauchi T et al [11], studied 10 cases of BPH were karyotyped by the G-banding method. Structural analysis disclosed 2 cases of BPH were diploid. Normal male karyotypes were seen in 6 BPH. Trisomy of chromosomes 7 and 16 were observed in 2 BPH. Magdy S. Aly et al [12], found that out of 28 samples of BPH, loss of the Y chromosome was the most common chromosome change, followed by trisomy 7. Tapio Visakorpi et al [13], out of 10 BPH patients, BPH specimens were diploid by DNA flow cytometry and showed no numerical chromosome aberrations by FISH. V. Balachandar et al [3], in 2008, studied 63 BPH and 18 prostate cancer patients. The patients were grouped into two age group, group I: ≤50 yrs; group II: ≥ 51 yrs. Deletions, translocations, inversions and mosaics were the major chromosomal aberrations observed in both the groups. Chromosome 1, 7, 16 and Y were affected in BPH patients. V. Balachandar et al [10], in 2010, out of 27 blood samples of BPH patients, major chromosomal aberrations like deletion, translocation, inversion were frequently observed in chromosomes 1, 6, 8, 13, 16, 18. In present study out of 20 BPH patients one (5%) 71 year old BPH patient had structural abnormality 46, XY, del (16q-), while 17 (85%) patients showed normal chromosomal constitution. In 02 (10%) cases metaphase was not found.

5.Conclusion

Identification of chromosome aberrations facilitates cloning of the relevant genes that may be involved in BPH. The present study shows that the chromosome aberrations may be a potential biomarker for BPH. These markers may have relevance in diagnosis and staging of BPH, and thus may reduce the need for invasive testing. This may help to establish the basis to augment our ability to counsel person on the recurrence risk with greater accuracy. However the cases that are found normal karyotypes by conventional cytogenetics, require to be confirmed by more specific molecular genetic studies like Fluorescence in Situ Hybridization (FISH) technique, to exclude any molecular level anomaly

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