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Short Communication

Cytogenetic analysis of benign prostate hyperplasia (BPH) and prostate cancer (PC) patients from Tamil Nadu, South India

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Benign prostate hyperplasia (BPH; n = 63) and prostate cancer (PC; n = 18) patients were ascertained on the basis of prostate specific antigen (PSA) levels from the hospitals located in Tamil Nadu, South India. The patients were analyzed for chromosomal aberrations (CA) using cultured peripheral leucocytes. The patients were grouped into two age group (group I: ≥ 50 yrs; group: II ≤ 51 yrs. Deletions, translocations, inversions and mosaics were the major CA observed in both the groups of chromosome 1, 2, 3 6, 7, 9, 16, 22, and X were the affected chromosome in PC patients and in BPH patients 1, 7 and 16 and Y chromosomes were affected. Chromosomes 1, 7 and 16 were observed in both groups of patients. Group II patients showed higher number of CA than group I. Group comparisons were statistically significant (P<0.001).

Key words: Prostrate cancer patients, benign prostate hyperplasia, chromosomal aberrations, prostate specific antigen, peripheral blood lymphocytes.

INTRODUCTION

Prostate cancer (PC) is the most commonly diagnosed male malignancy and is rare to be diagnosed in men below 50 years age. Above this age, the incidence and mortality rate increase exponentially (Haas and Sakr, 1997). Benign prostatic hyperplasia (BPH) is a common disease of male 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 ≥80 years (Mc Vary, 2006). More than 80% of the cancers concomitantly arise with BPH in prostates (Bostwick et al., 1992).

The frequency of chromosome instability in peripheral blood lymphocytes (PBL) is generally indicative of increased cancer risk for those exposed to DNA damaging agents (Bonassi et al., 1995).

Karyotyping of solid tumours yields information about numerical and/or structural chromosome defects and PC is the most difficult carcinoma to study. Rapid developments in cytogenetics have greatly advanced our knowledge of CA in solid tumours, including PC.

The aim of the present investigation was to find out the major CA present in both BPH and PC patients of Tamilnadu population and to make a comparative study between them. The study also analyses the relationship of the age with the incidence of CA in both PC and BPH patients.

MATERIALS AND METHODS

Subject recruitment

Five ml of blood was collected from each of the 18 PC and 63 BPH patients ascertained from various hospitals of Tamil Nadu, who did not undergo any treatment. The subjects, based on their age were divided into two groups: group I (≥50 yrs) and group II (≤51 yrs). PC patients: 7 in group I and 11 in group II; BPH patients: 34 in group I and 29 in group II. In all the patients, total PSA level was measured and the range of PSA values in BPH patients was 4 to 8 ng/mL and in PC patients, 8 to 12 ng/mL. The work was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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Table 1. Major Chromosomal aberration in benign prostatic hyperplasia and prostate cancer patients.

S/N	Chromosome number	PC	BPH
1	1	46 XY, del ($1p^-$) 46 XY, t ($1p^-$:$6q^+$) 46 XY, del ($7q^-$)	46 XY, del ($1p^-$) 46 XY, t ($1p^+$:$9q^-$)
2	7	46 XY/46 XY, del ($7q^-$) 46 XY, t ($7p^-$:$9q^+$) 46 XY, inv (7p)	46 XY, del (7q-) 46 XY, t ($7p^-$:$1q^+$)
3	16	46 XY, del ($16q^-$) 46 XY, t (16p-:$9q^+$)	46 XY, del ($16p^-$) 46 XY, del ($16q^-$)

PC: Prostate Cancer; BPH: benign prostatic hyperplasia; del: deletion; t: translocation; inv: inversion.

Chromosomal aberration assay

All chemical reagents were purchased from Sigma Chemicals, except colcemid (Gibco Laboratory). Leukocyte cultures were set up following standard procedures in our laboratory (Hoyos et al., 1996). 0.5 ml blood was added to 4.5 ml RPMI 1640 medium supplemented with 10% fetal bovine serum, 2 mM l-glutamine, 1% streptomycin-penicillin, 0.2 ml reagent grade phytohemagglutinin, and was incubated at 37ºC. After 50 h, cultures were treated with 0.1 mg/ml colcemid to block cells in mitosis. Lymphocytes were harvested after 52 h by centrifuging cells to remove culture medium (800–1000 rpm), addition of hypotonic solution (KCl 0.075 M) at 37ºC for 20 min to swell the cells, and treated twice with Carnoy's fixative (3:1 ratio of methanol: acetic acid). Slides were carefully dried on a hot plate (56ºC, 2 min). Three days later, slides were stained using the Trypsin-giemsa technique. For the CA analysis, 100 complete metaphase cells in first cell cycle were evaluated per subject under a Leica microscope (100x)

Statistical application

Statistical analysis was performed using software SPSS version 13. Group difference were assessed by mean ± SD and Mann Whitney – U test

RESULTS AND DISCUSSION

The mean ± SD CA for group I PC patients was: 48.28 ± 1.11 and for BPH patients, 45.52 ± 3.48. For group II the corresponding values were: 60.54 ± 6.0 and 55.68 ± 3.10. The major CA in PC patients were observed on 1, 2, 3 6, 7, 9, 16, 22, and X chromosomes and in BPH patients on 1, 7 and 16 and Y chromosomes (Table 1). Group differences are statistically significant ($P<0.001$).

PC in men is a leading cause of morbidity and mortality. Small prostatic carcinomas in up to 29 percent of men aged 30 to 40 years and 64 percent of men of 60 to 70 years old (Sakr et al., 1994).

Chromosomal instability is considered to be a primary event in neoplastic transformation and also as a marker of cancer progression (Rabinovitch et al., 1999; Hawkins et al., 2000; Burt et al., 2000). For all types of cancers, Bonassi et al. (1995) reported a significant increase in the mortality rate in subjects who had shown increased levels of CA in their lymphocytes. The present study supports this observation. PC patients showed the major CA on chromosome 1, 2, 3 6, 7, 9, 16, 22, and X. Observation of too many numerical aberrations on different chromosomes is not surprising. About 50% of the PC patients were found to have an aneuploid DNA content. In BPH patients, deletion, translocation, inversion and mosaics have been found on chromosomes 1, 7, 16 and Y.

Chromosomes 1, 7, and 16 were affected in both the groups of subjects. Chromosome 1 showed deletion and translocation in both PC and BPH Patients. Chromosome 1 has a breakage-prone site, which has been reported to be sensitive to environmental clastogens (Conforti-Froes et al., 1997) and is thought to be involved in both early and late stages of tumor development (Grosovsky et al., 1996).

In chromosome 7, deletion, translocation, inversion and mosaics were observed in 4 of the 18 PC patients. Deletion and translocations were observed in 11 BPH patients. Aberrations were more frequent in group II than in group I patients. Deletions of 7q were the first CA to be reported in PC patients (Sandberg et al., 1992). Gain of chromosome 7 has been earlier reported (Micale et al., 1992). Similar results were reported in an earlier study on PC patients (Balachandar et al., 2007). Trisomy 7 was found to be a novel marker for human PC progression, but not of survival (Teixera et al., 2000). A previous study also reported trisomy of Chromosome 7 in BPH patients (Aly et al., 1993).

In the present study deletion and translocation were observed on chromosome 16 in both the groups of PC patients whereas in BPH patients only deletions were observed. An increased rate of LOH and structural abnormalities and trisomies were reported in PC patients in some earlier investigations.

Group II subjects showed more CA than group I subjects. An age-related increase in aneuploid cells in human lymphocytes has been reported in a number of studies (Nowinski et al., 1990; Kunimi K. et al., 1991; Miyauchi et al., 1992 and Balachandar et al., 2007).

Age is directly proportional to the CA frequency (Bala-

chandar et al., 2007); the present study suggests a direct relationship between total PSA levels, age and CA. Chromosome 1, 7 and 16 showed CA in both the groups of patients which may be helpful in the early detection and treatment of the disease.

Identification of chromosome aberrations facilitates cloning of the relevant genes that may be involved in tumorigenesis. The present study shows that the CA may be a potential biomarker for BPH and PC. These markers may have relevance in diagnosis and staging of PC and BPH cancers, and thus may reduce the need for invasive testing.

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REFERENCES

Aly MS, Dal CP, Berghe HV, Voorde WVD, Poppel HV, Ameye F, Baert L (1993). Chromosome abnormalities in Benign Prostatic Hyperplasia 9(4): 227–233.

Balachandar V, Lakshman B, Sasikala K (2007). An age based cytogenetic analysis in prostate cancer patients in southern India. (Suppl.1), European. J. Hum. Gen: p.121.

Balachandar V, Lakshman B, Sasikala K, Manikantan P, Sangeetha R, Mohana Devi S (2007).Identification of a high frequency of chromosomal rearrangements in the centromeric regions of prostate cancer patients. J. Zhejiang Univ. ScLB (springer) 8(9):638-646.

Bonassi S, Abbondandolo A, Camurri L, Dal Pra A, De Ferrari M, Degrassi F, Forni A, Lamberti L, Lando L, Padovani M, Sbrana I, Vecchio D, Puntoni R (1995). Are chromosome aberrations in circulating lymphocytes predicitve of future cancer on set in humans Prelimiary results of an Italian cohort study. Genet. Cytogenet. 79:133-335.

Bostwick DG, Cooner WH, Denis L, Jones GW, Scardino PT, Murphy GP (1992). The association of benign prostatic hyperplasia and cancer of the prostate. Cancer. (70): 291-30.

Burt EC, James LA, Greaves MJ, Birch JM, Boyle LM, Varley JM (2000). Genomic alterations associated with loss of heterozygosity for TP53 in Li-Fraumeni syndrome fibroblasts. Br. J. Cancer.(83):467-472.

Conforti-Froes N, El-Zein R, Abdel-Rahman SZ, Zwischenberger JB, Au WW (1997). Predisposing genes and increased chromosome aberrations in lung cancer cigarette smokers. Mutat Res. (379): 53 - 59.

Grosovsky AJ, Parks KK, Giver CR, Nelson SL (1996). Clonal analysis of delayed karyotypic abnormalities and gene mutations in radiation-induced genetic instability. Mol. Cell Biol.(16):6252 - 6262.

Haas GP, Sakr WA (1997). Epidemiology of prostate cancer. CA Cancer J. Clin. (47):273-287.

Hawkins NJ, Gorman P, Tomlinson IP, Bullpitt P, Ward RL (2000).Colorectal carcinomas arising in the hyperplastic polyposis syndrome progress through the chromosomal instability pathway. Am. J. Pathol. 1(57):385 - 392.

Hoyos LS, Carvajal S, Solano L, Rodriguez J, Orozco L, Lopez Y, Au WW (1996). Cytogenetic monitoring of farmers exposed to pesticides in Colombia. Environ. Health Perspect. (104): 535–538.

Kunimi K, Bergerheim US, Larssonl L, Ekman P, Collins VP (1991). Allelotyping of human prostatic adenocarcinoma. Genomics .Il: pp. 530-536.

Mc Vary KT (2006). BPH epidemiology and comorbidities. Am J Manag. Care. 12 (5 Suppl): 122-128.

Micale MA, Mohamed A, Sakr W (1992). Cytogenetics of primary pro-prostatic adenocarcinoma: Clonality and chromosome instability. Cancer Genet Cytogenet. (61):165-173.

Miyauchi T, Nagayama T, Maruyama K (1992).Chromosomal abnormalities in carcinoma and hyperplasia of the prostate. Nippon Hinyokika Gakkai Zasshi. (83): 66-74.

Nowinski GP, Van Dyke DL, Tilley BC, Jacobsen G, Babu VR, Worsham MJ, Wilson GN, Weiss L (1990). The frequency of aneupboidy in cultured lymphocytes is correlated with age and gender but not with reproductive history. Am. J. Hum. Genet. (46):1101-1111.

Rabinovitch PS, Dziadon S, Brentnall TA (1999). Pancolonic chromosomal instability precedes dysplasia and cancer in ulcerative colitis. Cancer Res. (59): 5148 - 5153.

Sakr WA, Grignon DJ, Crissman JD, Heilbrun LK, Cassin BJ, Pontes JJ, Haas GP (1994). High grade prostatic intraepithelial neoplasia (HGPIN) and prostatic adenocarcinoma between the ages of 20-69: an autopsy study of 249 cases. *in vivo*. 8(3):439-443.

Sandberg AA (1992). Chromosomal abnormalities and related events in prostate cancer. Hum. Pathol. (23):368-380.

Teixera MR, Wehre H, Ragnhild AL, Stenwig AE, Pandis N, Giercksky KE (2000). High frequency of clonal chromosome abnormalities in pro~tatic neoplasms sampled by prostatectomy or ultrasound-guided needle biopsy. Genes Chrom.Cancer. (28): 211- 219.