Original Research Article

Association of high-grade prostatic intraepithelial neoplasia (HGPIN) in patients of prostate adenocarcinoma

Pragya Gautam Ghimire[1], Ashok Kumar Kapoor[2], Yamini Jindal[3], Sandeep Gupta[4]

[1]Pragya Gautam Ghimire (MD Pathology), Department of Pathology, Nepalganj Medical College, Kohalpur Teaching Hospital, Kohalpur, Banke, Nepal

[2]Ashok Kumar Kapoor (MD Pathology), RML Mehrotra Pathology, Niralanagar, Lucknow, UP, India

[3]Yamini Jindal (MD Pathology), RML Mehrotra Pathology, Niralanagar, Lucknow, UP, India

[4]Sandeep Gupta (Mch Urology, MS Surgery) Department of Surgery, Nepalganj Medical College, Kohalpur Teaching Hospital, Kohalpur, Banke, Nepal

*Corresponding author

Dr. Ashok Kumar Kapoor

Email: drashokkapoor2016@gmail.com

Abstract: Present study aims at assessment and histopathological examination of prostate tissues from 50 subjects having lower urinary tract obstruction. Forty of 50 subjects had benign prostatic hyperplasia (BPH) and other 10 subjects had adenocarcinoma prostate. Subjects with prostatic carcinoma were labeled as patients. Age of the patients ranged from 56 to 82 (median 70) years. All the patients were farmers. Nine of 10 patients consumed both red and white meat. Prostate carcinoma was graded according to Gleason's criteria. Accordingly, 5 patients had Gleason score 9 or 10. Four patients had Gleason score 6 to 8. Another patient had Gleason score 4. Two of 10 patients also had prostatic intraepithelial neoplasia (PIN). Perineural invasion (PNI) was seen in 2 patients. One patient also had vascular invasion. PIN appeared to be associated with prostatic adenocarcinoma in 2 patients and may have the role in prognosis of prostatic adenocarcinoma.

Keywords: PIN, BPH, adenocarcinoma prostate, Gleason's criteria

INTRODUCTION:

Incidence of adenocarcinoma prostate varies in different geographical regions. For example, highest age-related death-rates are found in United States and Scandinavian countries and lowest in Mexico, Greece and Japan [1]. Higher values of body mass index (BMI) and higher incidence of peripheral subcutaneous obesity and visceral obesity were noted in the men with prostate cancer [2].

Farming is associated with an increased risk of prostate cancer in Caucasians but not in African-Americans, suggesting a relationship between the use of pesticides and prostate cancer [3]. Use of chlorinated pesticides among applicators over 50 years of age and methyl bromide use were significantly associated with prostate cancer risk [4].

Morphological evidence linking PIN to invasive prostate cancer includes (1) both lesions are peripheral (2) cytological similarity of high-grade PIN to invasive cancer (3) close topographic proximity of high-grade PIN to invasive cancer (4) Finally, PIN lesions are more frequent in prostates with cancer than those without tumours [1].

MATERIAL AND METHODS:

Fifty men with lower urinary tract infection (LUTI) or subjects with late complications of bladder obstruction were examined. Per rectal digital examination was done and ultrasonographically, weight of the prostate was calculated [5]. Later, prostate biopsies and radical prostatectomy (RP) tissues were examined. Specimens were fixed in formal saline. Sections were prepared from paraffin embedded tissue blocks. Sections were stained by hematoxylin and eosin and examined.

RESULTS:

On the basis of microscopic examination, 10 of 50 subjects were found to have adenocarcinoma. These subjects were labeled as Patients. Other 40 subjects

had benign prostatic hyperplasia. Present study relates with the results of these 10 patients.

Age of the patients ranged from 56 to 82 (median 70) years. All the patients were farmers, suggesting possible exposure to chemicals. Two of 10 patients were underweight and others had normal body weight. All the patients were non-vegetarian. Socioeconomic status of each patient was determined by modified Kuppuswamy socioeconomic status scale [6]. Accordingly, socioeconomic status of all the patients fell in the lower class with per capita income of Nepali Rs.3124.

Hemoglobin of patients ranged from 9 to 13 (median 12) g/dl. Two of 10 patients had raised serum creatinine levels. Seven of 10 patients had mild prostatomegaly (weight between 25-50 gm). Two other patients had severe prostatomegaly (weight >75 gm). Another patient had normal weight of prostate.

Digital rectal examination was done and prostate biopsy pieces were collected from 5 patients using trucut biopsy needles. Transurethral resection of prostate was done in 3 patients and specimens were collected. RP specimens were collected from 2 other patients. All the specimens were fixed in formal saline and histopathological examination was done using conventional hematoxylin eosin method. Adenocarcinoma was graded according to Gleason's criteria as described earlier [7].

This system assesses the architectural details of malignant glands under low to median magnification. Cytological features under high magnification are not considered. This system defines 5 patterns or grades with decreasing differentiation. The primary and secondary patterns i.e. the most prevalent and the second most prevalent pattern, are added to obtain a Gleason score. Its prognostic value was tested in a large population that included the use of survival [8]. Lower scores correlated with better prognosis.

Criteria for defining high-grade PIN included (1) epithelial cell proliferation within the ducts and acini, forming pseudo stratified layers, (2) enlargement, elongation, irregularity and hyperchromasia of the nuclei and (3) multiple prominent nucleoli. High grade PIN was classified as 'focal' if there were 3 or fewer separate foci/acini of high-grade PIN and as extensive, if there were >3 foci or acini of high-grade PIN in different sections [9]. According to TNM classification, all the patients with malignancy had early lesion localized to prostate belonging to T1 stage. Six of 10 patients had voiding dysfunction (VD), storage dysfunction (SD) and bladder outlet obstruction (BOO). Three other patients had BOO alone. Another patient had VD and BOO.

Gleason score of 9 was the commonest pattern in 3 of 10 patients. Gleason scores of 8 and 10 were the next common pattern seen in 2 patients each. Scores of 4, 6 and 7 were seen in 1 patient each. Two of 10 patients had high-grade prostatic intraepithelial neoplasia (figure 1) in association with adenocarcinoma. All cases were graded according to Gleason score. Gleason grade 4 with stromal invasion (Figure 2a), grade 3a (Figure 2b), grade 4 with fused glands (Figure 2c) were also reported. One of the patients had budding of malignant glands (figure 2c). Another patient had evidence of BPH, high-grade PIN and adenocarcinoma in the same patient. However, PIN lesion was not seen in the control subjects having BPH alone. Perineural invasion (PNI) was seen in 2 patients (figure 3a, b). Another patient had vascular invasion (figure 3c). Lymphocytic infiltration of tumour cells was seen in 5 of 10 patients.

Fig-1: High-grade PIN showing crowding, stratification and variation in nuclear size and prominent nucleoli (HE x 450).
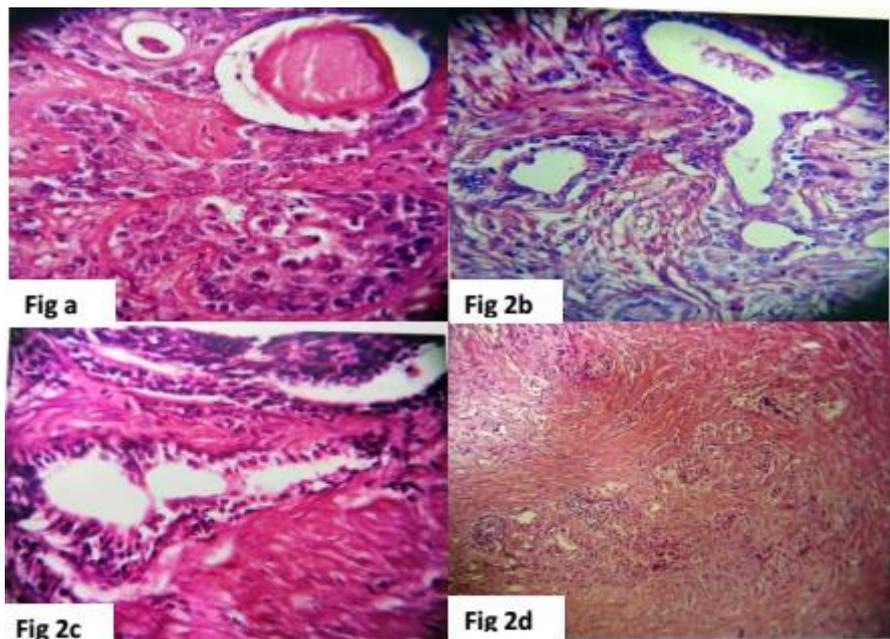
Fig-2: (a) Gleason grade 4 showing stromal invasion by malignant glands (b) Gleason grade 3a showing angulated glands and (c) Gleason grade 4 showing fused glands (HE x 450). (d) Gleason grade 5 showing stromal invasion (HE x 100).
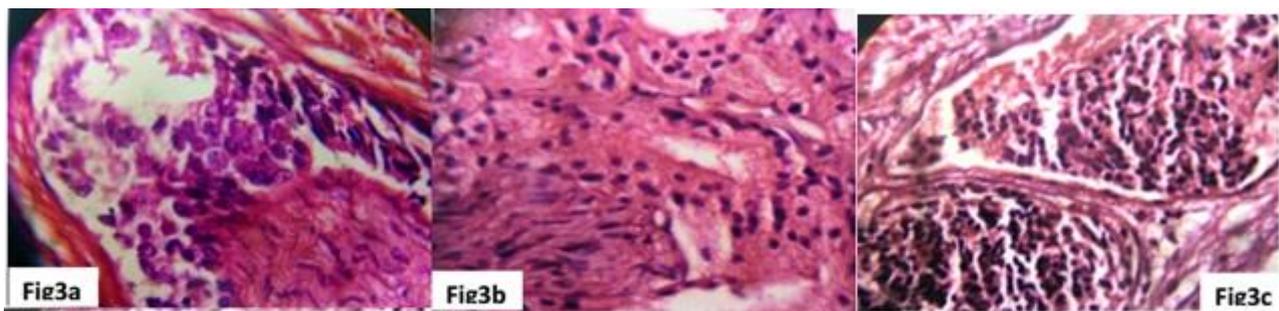

Fig-3: Photomicrographs showing nerve invasion by (a & b) tumour cells and (c) Vascular invasion by tumour cells (HE x 450).
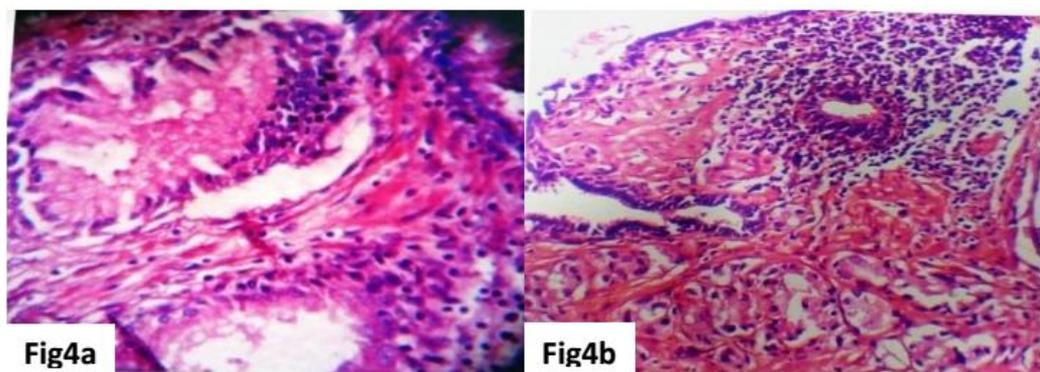

Fig 4: Lymphocytic infiltration of (a) malignant glands (HE x 450) and (b) non-malignant gland at the periphery of the tumour (HE x 250).

DISCUSSION:

The most significant findings of the present study were the detection of high-grade PIN in 2 patients with prostate cancer. One of the patients showed high-grade PIN with budding of malignant glands. High-grade PIN have been detected in several earlier studies [10-12].

Another interesting finding of the present study was the detection of adenocarcinoma in 10 of 50 (20%) prostatic specimens. This finding was different from another Asian study where prostate cancer was found in 7% of Indian patients [13]. Our findings were similar to earlier Asian studies from Nepal [14] and KSA [15].

In the present study, 2 patients showed perineural invasion. This lesion was also detected in an earlier study [16]. PNA may predict extra prostatic extension [17]. It may be a marker of poor survival [18]. All of our patients were farmers which suggested exposure to chemical fertilizers and antimycotic drugs. Similar observation was made in an earlier study [3].

Another interesting observation was meat-intake by all the patients of this study. In an earlier study, it was suggested that high intake of cooked processed meat might contribute to prostate cancer risk among black men of United States [19]. In the present study, tumor cell recognition was seen in 5 of 10 patients. In another study, immune cell infiltrate in prostate carcinoma consisted of T-cells, B-cells and histiocytes. Predominant cell population was $CD3^+$T-cells and $CD68^+$ cells. In addition, a significant decrease in immune cells was observed in high-grade prostatic carcinoma when compared with BPH. Decreased density of immune cells in high-grade adenocarcinoma reflected immunosuppression [20].

CONCLUSION:
PIN appeared to be associated with prostatic adenocarcinoma and may has the role in prognosis of prostatic adenocarcinoma. Prostate cancer is associated with multiple risk factors that include chemicals, non-vegetarian diets, reduction of immune cells etc.

Conflicts of interest: The authors declare that there are no conflicts of interest.

Ethics Approval: the study was approved by the ethics committee of the Nepalgunj Medical College, Nepal

REFERENCES:
1. Damjanov I, McCue PA. In situ and invasive adenocarcinoma of the prostate. In Rubin's Pathology, 7th ed. Strayer D, Rubin E, Saffitz JE and Schiller AL (editors) 2015; Philadelphia : Wolters Kluwer p 990-994.
2. Goluch-Koniuszy Z, Rygielska M, Nowacka I. Nutritional status and nutritional habits of men with benign prostatic hyperplasia or prostate cancer-preliminary investigation. Acta Scientiarum Polonorum Technologia Alimentaria. 2013 Sep 30; 12(3):319-30.
3. Meyer TE, Coker AL, Sanderson M, Symanski E. A case–control study of farming and prostate cancer in African-American and Caucasian men. Occupational and environmental medicine. 2007 Mar 1; 64(3):155-60.
4. Alavanja MC, Samanic C, Dosemeci M, Lubin J, Tarone R, Lynch CF, Knott C, Thomas K, Hoppin JA, Barker J, Coble J. Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort. American Journal of Epidemiology. 2003 May 1; 157(9):800-14.
5. Brant WE, Helmes CA. Genital tract: radiographic imaging and MR. Fundamentals of Diagnostic Radiology. 3rd ed. Philadelphia, PA: Lippincott, Williams and Wilkins. 2007:920-3.
6. Kumar N, Shekhar C, Kumar P, Kundu AS. Kuppuswamy's socioeconomic status scale-updating for 2007. Indian journal of pediatrics. 2007 Dec; 74(12):1131-1132.
7. Humphrey PA. Gleason grading and prognostic factors in carcinoma of the prostate. Modern pathology. 2004 Mar 1; 17(3):292-306.
8. Montironi R, Mazzuccheli R, Scarpelli M, Lopez-Beltran A, Fellegara G, Algaba F. Gleason grading of prostate cancer in needle biopsies or radical prostatectomy specimens: contemporary approach, current clinical significance and sources of pathology discrepancies. BJU international. 2005 Jun 1; 95(8):1146-52.
9. Kim HL, Yang XJ. Prevalence of high-grade prostatic intraepithelial neoplasia and its relationship to serum prostate specific antigen. Int Braz J Urol. 2002 Sep; 28(5):413-6.
10. Jagannath J, Krishnpal Singh T, Vidyanand P, Sudha I, Jain B. Characterization of prostatic lesions in surgically resected specimens. Ind J of Aplied Res 2015; 5: 444-446.
11. George E, Thomas S. A histopathologic survey of prostate disease in the sultanate of Oman. Journal of Pathology: The Internet. 2004;3(2):500-506.
12. Angwafo III FF. Zaher A, Befidi Mengue R, Wonkam A, Takougang I, Powell I, Murphy G and the National health survey team of National epidemiology board of Cameroon. High grade intra-epithelial neoplasia and prostate cancfer in Dibombari, Cameroon. Prostate Cancer and Prostate diseases. 2003; 6 : 34-38.
13. Mittal BV, Amin MB, Kinare SG. Spectrum of histological lesions in 185 consecutive prostatic specimens. Journal of post graduate medicine. 1989 Jul 1; 35(3):157-161.
14. Belbase NP, Agrawal CS, Pokharel PK, Agrawal S, Lamsal M, Shakya VC. Prostate cancer

screening in a healthy population cohort in eastern Nepal: an explanatory trial study. Asian Pacific journal of cancer prevention: APJCP. 2012 Dec; 14(5):2835-8.

15. Albasri A, El-Siddig A, Hussainy A, Mahrous M, Alhosaini AA, Alhujaily A. Histopathologic characterization of prostate diseases in Madinah, Saudi Arabia. Asian Pacific journal of cancer prevention: APJCP. 2013 Dec; 15(10):4175-9.

16. Montie JE, Wood DP, Pontes JE, Boyett JM, Levin HS. Adenocarcinoma of the prostate in cystoprostatectomy specimens removed for bladder cancer. Cancer. 1989 Jan 15; 63(2):381-5.

17. Bismar TA, Lewis JS jr, Vollmer RT, Humphrey PA. Multiple measures of carcinoma extent versus perineural invasion in prostatic needle biopsy tissue in prediction of pathologic stage in a screening population. Amer J Surg Pathol 2003; 27: 432-440.

18. Liebig C, Ayala G, Wilks JA, Berger DH, Albo D. Perineural invasion in cancer. Cancer. 2009 Aug 1; 115(15):3379-91.

19. Rodriguez C , Marjorie L , McCullough ML, Mondul AM, Jacobs EJ, Chao A, Patel AV, Thun MJ, Calle EE. Meat consumption among Black and White men and risk of prostate cancer in the Cancer Prevention Study II Nutrition Cohort. Cancer Epidemiology Biomarkers & Prevention. 2006 Feb 1; 15(2):211-6.

20. Hussein MR, Mana AA, Musalam AO. Phenotypic characterization of the infiltrating immune cells in normal prostate, benign nodular prostatic hyperplasia and prostatic adenocarcinoma. Experimental and molecular pathology. 2009 Apr 30; 86(2):108-13.