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Research Article

ATYPICAL SMALL ACINAR PROLIFERATION OF PROSTATE IN PROSTATE NEEDLE BIOPSIES

Ambika Ramani Baru¹, Kanya kumari^{2*}, Durga Kharidehal³

¹Intern, Kakatiya Medical College, Warangal, India

²Assistant prof. Department of Pathology, Mediciti Institute of Medical Sciences, Ghanpur, Medchal, India

³Professor and HOD Department of Pathology, Kakatiya Medical College, Warangal, Andhra Pradesh, India

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*Corresponding Author: **Dr Kanya kumari**

Assistant Prof. Department of Pathology, Mediciti Institute of Medical Sciences, Ghanpur, Medchal, India

Email: dr.kanya23@rediffmail.com

ABSTRACT

Atypical small acinar proliferation of prostate refers to small acinar structures that are suspicious of malignancy but lack sufficient cytological and architectural atypia to establish a definitive diagnosis. The section usually shows a small size of focus with lack of definite cytologic criteria for malignancy morphologically falling in the gray area between recognizable benign glands and frankly malignant acini. present study was conducted to know the prevalence of Atypical small acinar proliferation in prostate needle biopsies.

Materials and Methods: Both Prospective study and retrospective study done. Prospective study for 6months i.e from July 2012 to December 2012 and retrospective study for 2yrs from January 2010 and January 2012 at Kakatiya Medical College/MGM Hospital Warangal, 14 cases were reported as atypical small acinar proliferation suspicious of malignancy out of 104 Transrectal ultrasound (TRUS)- guided prostate needle biopsy specimens.

Results: In our study 104 cases have been studied.14(13.4%) cases reported as Atypical Suspicious of malignancy with serum PSA(Prostate Specific Antigen) levels of 4-32 ng/dl.and remaining cases diagnosed as 28(26.9%) Benign hyperplasia, 6(5.7%) as chronic inflammation,4(3.8%) as Prostatic intra epithelial neoplasia (PIN),52(50%) as high grade carcinoma.

Conclusion: Atypical foci suspicious of malignancy are seen in 3-5% of needle biopsy specimens and these patients have a 50% risk of cancer on repeat biopsy. This is a distinct diagnostic entity based on the absolute uncertainty regarding its diagnosis. Repeat biopsy is a must if deeper sections and immunohistochemistry are inconclusive. When an atypical small acinar proliferation (ASAP) diagnosis represents under sampled cancer, the cancer is clinicopathologically similar to cancer diagnosed on first biopsy. Cancer detected on the second or third round of biopsies after an atypical small acinar proliferation (ASAP) diagnosis is also similar in grade, stage, and size to cancer detected in control patients in the first biopsy set .

Keywords: Acinar Proliferation, Prostate Needle Biopsies, TRUS.

INTRODUCTION

Atypical small acinar proliferation of prostate refers to small acinar structures that are suspicious of malignancy but lack sufficient cytological and architectural atypia to establish a definitive diagnosis. The section usually shows a small size of focus with lack of definite cytologic criteria for malignancy morphologically falling in the gray area between recognizable benign glands and frankly malignant acini. This is a distinct entity based on the absolute uncertainty regarding the diagnosis.

Reasons – Small size of focus <4mm.(11acini), Limited number of minimally atypical glands, Disappearance on step levels, Cannot rule out adenosis / high grade prostatic intra

epithelial neoplasia (HGPN). Cannot differentiate atrophy from atrophic cancer, Associated inflammation giving to reactive atypia, Crush artifact distorting the tissue. SPSA (serum prostate specific antigen), DRE (digital rectal examination) and IHC (immunohistochemistry) not very useful¹.

Aims and objectives:

To study the prevalence of Atypical small acinar proliferation in prostate needle biopsies.

MATERIALS AND METHODS

Both Prospective study and retrospective study done. Prospective study for 6months i.e from July 2012 to December 2012.and retrospective study for 2 yrs from January 2010 to

January 2012 at Kakatiya Medical College/MGM Hospital Warangal.14 cases were reported as atypical small acinar proliferation (fig 1) suspicious of malignancy out of 104 TRUS guided prostate needle biopsy specimens.

DRE and SPSA findings were recorded in each case.

8-10 cores were taken for each case, formalin fixed, paraffin processed, and stained with Hematoxyllin & Eosin (H&E).

3 step sections were taken for each sample received.IHC for 34BE12 and AMACR (Alpha Methyl Acyl coA Racemase) was done wherever necessary.

FOLLOW UP

The 14 cases of ASAP were followed up with SPSA, DRE, and Repeat Prostate Biopsy after 3 months. Case 1 and 2 were

lost to follow up. Case 3 on deeper sections showed fragments of basement membrane which stained positive for 34BE12(fig. 2)Case 4 on deeper sections showed adenocarcinoma changes.Case 5,6,7,8,9 and 13 on repeat biopsy revealed Prostatic adenocarcinoma.(fig.3) Case 10,11,14 on repeat biopsy showed benign lesions. Case 12 was treated as prostatic adenocarcinoma in view of raised SPSA (62ng/ml).

RESULTS

AGE: Out of 104 cases, commonest age group with ASAP were among 71-80yrs (62.5%) (table 1).

Table 1 : Age wise distribution of ASAP cases

Age in yrs	No. of cases	%
50-60	3	2.8%
61-70	36	34.6%
71-80	65	62.5%
TOTAL	104	99.9

ASAP – Atypical small acinar proliferation of prostate
HISTOPATHOLOGICAL FINDINGS: Out of 104 cases, 14(13.4%) Atypical Suspicious of malignancy .28(26.9 %)Benign hyperplasia, 6(5.7%), Chronic inflammation,

4(3.8%) Prostatic Intraepithelial Neoplasia, 52(50%)High grade carcinoma,
 SERUM PSA- 14 (13.4%) of Atypical suspicious of malignancy with serum PSA levels of 4-62ng.dl.

Table 2: Serum prostate specific antigen levels

LESION	Se. PSA levels	No. of cases	%
Benign hyperplasia	4 – 32	28	26.9
Chronic inflammation	4-20	6	5.7
Prostate intraepithelial hyperplasia	8-30	4	3.8
High grade carcinoma	28-238	52	50
Atypical suspicious of malignancy	4-62	14	13.4
TOTAL		104	99.8

Out of 14 cases of ASAP deeper sections were taken in 2 cases. 1 case was diagnosed as infiltrating adenocarcinoma and in the 2nd case fragments of basement membrane were seen indicating benign hyperplasia.

9 cases of ASAP were rebiopsied – of which 6 cases had frank carcinoma with Gleasons score of 6-10 .remaining 3 cases were diagnosed as benign adenomatous hyperplasia with inflammation

2 cases – lost to follow up.

1 case – treated as Prostatic carcinoma in view raised serum PSA (62ng/ml).

DISCUSSION

Atypical foci suspicious of malignancy are seen in 3-5% of needle biopsy specimens & these patients have a 50% risk of cancer on repeat biopsy.

Though they make up 5% of needle biopsies they may vary between pathologists & institutions as there are no set combinations of histological and clinical criteria for distinguishing atypical glands that are suspicious of malignancy from minimal adenocarcinoma.

Iczkowski and colleagues found that the histological features that most often preclude a definitive diagnosis of malignancy

are the small size of focus(70% of cases),disappearance on step levels (61%) lack of cytological atypia such as nucleomegaly (55%)and associated inflammation (9%) raising the possibility of one of many mimics of adenocarcinoma².

In the present study small size of focus, associated inflammation, crush artifact and minimal cytologic atypia precluded a definitive diagnosis of prostatic cancer.

Strand et al study of ASAP workup, by preparing new recut sections from the paraffin block and staining with H&E and immunostains. ³ Preliminary diagnosis of ASAP in 33 cases was changed to a definitive diagnosis of carcinoma (10) and specific benign diagnosis (13) solely on ASAP work up.

In the present study deeper sections and use of immune histochemical stains such as HMK (High Molecular weight Keratin) and AMACR were useful in establishing diagnosis of prostatic cancer .

Ploussard et al also found in their study that repeated biopsy is warranted when ASAP is diagnosed, because of a high risk of prostate cancer⁴. In our present study 6(66.6%) were diagnosed as carcinoma on repeat biopsy.

Iczkowski KA, Chen HM et al Rates of cancer diagnosed on subsequent prostate biopsy vary according to different reports⁵. However, contemporary studies indicate a mean

predictive value for cancer of 39% on repeat biopsy. The high predictive value of atypical small acinar proliferation (ASAP) for subsequent adenocarcinoma indicates a need for repeat biopsy. Cancer is found in a different sextant site from the initial atypical small acinar proliferation (ASAP) site in 39% of patients, suggesting that repeat sampling should include multiple sites of the gland.

However, also concentrating repeat biopsy sampling at the site of atypical small acinar proliferation (ASAP), knowing that such foci often represent marginally sampled cancer, may also be prudent. Most studies have shown that DRE & SPSA levels are not useful in the differential diagnosis of atypia vs minimal adenocarcinoma.

If one looks at some of the criteria diagnostic of malignancy such as irregular glands, regular luminal borders, amphophilic cytoplasm, prominent nucleolus there is considerable overlap of these features with atypical small acinar proliferation such that different thresholds exist among histopathologists in the diagnosis of minimal adenocarcinoma.

At times ascertaining the criteria may be compromised because of crush artifact, small size of focus, obscuring inflammation, or suboptimal preservation of cellular details.

It is not a wastebasket diagnosis, needs intradepartmental consultation, Deeper sections taken for Immunohistochemistry 34BE12, AMACR, p63. Repeat biopsy is mandatory- all men with an atypical diagnosis should be rebiopsied irrespective of serum PSA levels.

How should they be rebiopsied for maximum detection of cancer-Urologist should submit all sextant biopsies in separate containers. 3 cores should be taken from the site of initial atypical sextant site. 2 cores should be sampled from the area adjacent to the atypical sextant site. 1 core from other sextant sites can be taken which may also be positive.

CONCLUSION

Atypical foci suspicious of malignancy are seen in 3-5% of needle biopsy specimens and these patients have a 50% risk of cancer on repeat biopsy.

This is a distinct diagnostic entity based on the absolute uncertainty regarding its diagnosis.

Repeat biopsy is a must if deeper sections and immunohistochemistry are inconclusive.

When an atypical small acinar proliferation (ASAP) diagnosis represents under sampled cancer, the cancer is clinicopathologically similar to cancer diagnosed on first biopsy. Cancer detected on the second or third round of biopsies after an atypical small acinar proliferation (ASAP) diagnosis is also similar in grade, stage, and size to cancer detected in control patients in the first biopsy set.

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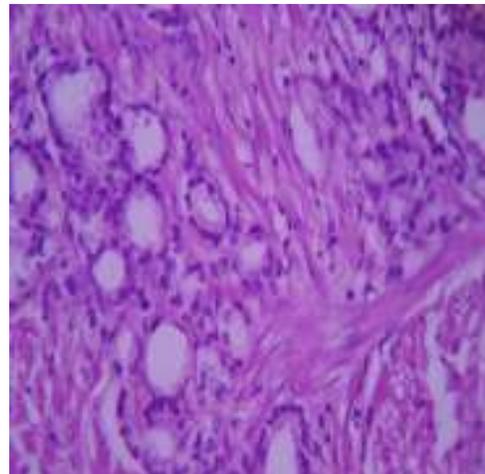


Figure 1: HPE 40X: Atypical Small Acinar Proliferation

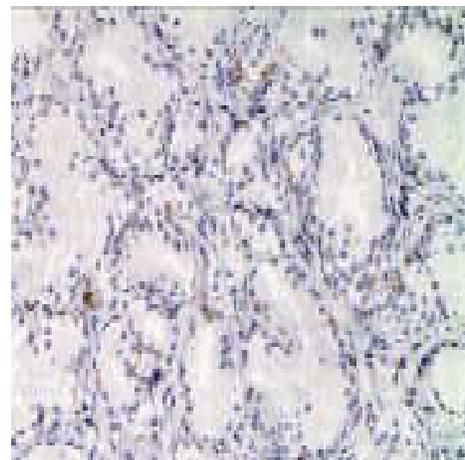


Figure 2: HPE 40X: Fragments of basal cell layer positive for HMW Keratin

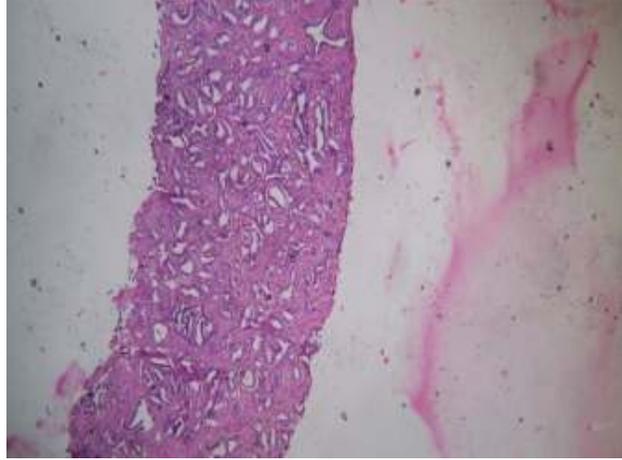


Figure 3: HPE 10X: Prostatic Adenocarcinoma

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