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Original Article

Relationship between prostate cancer and atypical small acinar proliferation

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Abstract

Aim: To investigate the prostatic adenocarcinoma (PA) detection rate in follow up biopsies with an initial diagnosis of atypical small acinar proliferation (ASAP).

Materials and Methods: In this study, the cases of ASAP diagnosis in prostate needle biopsy materials between January 2010 and December 2016 were retrospectively analyzed and the correlation between the results and the follow-up diagnoses of ASAP-diagnosed cases was investigated.

Results: 62 cases with ASAP were included in the study and 21 (34%) of them were detected as PA after the follow-up diagnoses. Also ASAP and PA were detected at different localizations in 38% of the cases.

Conclusion: We are on the opinion that it is important to increase the number of samples taken from other localizations as well as ASAP diagnosed quadrants when taking follow-up biopsies.

Keywords: Atypical Small Acinar Proliferation; Prostate Cancer; Prostate Needle Biopsy.

INTRODUCTION

Prostate cancer is the most common type of cancer in men after lung cancer. For males, cancer takes the fifth place among the causes of deaths. Globally 1.1 million men were diagnosed with prostate cancer in 2012 and this reportedly increased in frequency. For this reason, information about this disease is increasingly significant (1).

Some of the prostate biopsies can not be clearly distinguished from benign and malign, and in these cases atypical small acinar proliferation, which is suspicious for adenocarcinoma but lacks sufficient diagnostic value, is called ASAP (2). ASAP as a term was first used by Bostwick et al. in 1993 in the cases of unclear malign-benign distinction from the cytologic and architectural side (3,4). On condition that atypical glandular structure has insufficient infiltrative growth, it exists in a small focus, it is seen in a very little gland, it has less than 10% of the number of cells with nucleoli specificity, and it has insufficient nuclear expansion and hyperchromatism, ASAP is preferred instead of prostatic adenocarcinoma (3,4,5). Approximately 2-5% of biopsies are reported as ASAP, and the rate of detection of prostatic adenocarcinoma (PA) in recurrent biopsies of ASAP-diagnosed cases ranges from 21% to 51% (6,7,8). Because of this high risk, these patients are re-biopsied within 3 to 6 months (6).

Fine-needle biopsy performed with the presence of trans-rectal ultrasound (TRUS) under the follow-up of ASAP and in PA is the most preferred and reliable method. In this study, we also investigated the rate of PA recurrence and the relationship between ASAP and PA localizations in recurrent biopsies of ASAP-diagnosed patients.

MATERIAL and METHODS

The cases with ASAP diagnosed in 12 dial prostate needle biopsy materials between January 2010 and December 2016 in our institution were retrospectively reviewed. In 6 years, 75 patients were diagnosed with ASAP (figure

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1 a-b) and 62 of these (82%) were re-biopsied. The follow-up data of 13 patients couldn't be reached. Sixty-two cases with follow-up biopsies were included in this study. Follow-up diagnoses (benign, PA) were noted. PA diagnosed quadrants (figure 2 a-b) of the cases with PA diagnosis after the follow-up were compared with the ASAP diagnosed quadrants. In addition, the prostate-specific antigen (PSA) levels of the patients, prostate volumes (taken by ultrasonography as the upper limit of 20 ml) and patient ages were recorded and classified with the follow-up diagnosis.

The study was approved by our local ethics committee (2017/08/070).

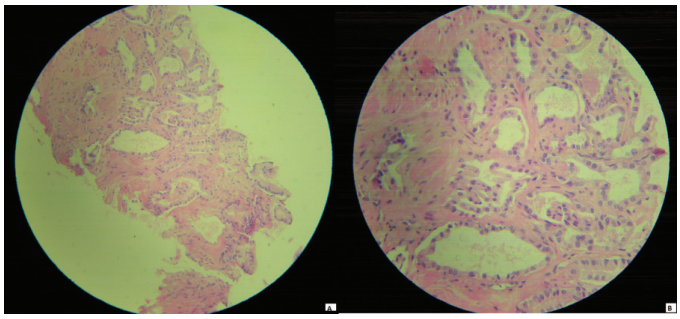

Figure 1a-1b. Atypical small acinar proliferation, suspicious for cancer. A cluster of acini with atrophy and architectural distortion. Despite architectural distortion, nuclear features are not enough for diagnosis of cancer (figure 1a: hematoxylin-eosin, original magnification x 200)- (figure 1b: hematoxylin-eosin, original magnification x 400)

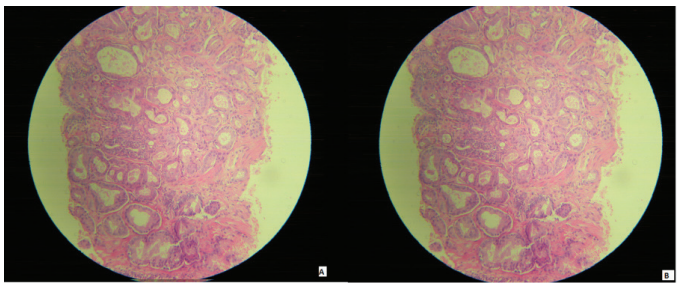

Figure 2a-b. Adenocarcinoma focus in the follow-up biopsy that diagnosed as ASAP in the first biopsy (figure 2a: hematoxylin-eosin, original magnification x 200)- (figure 2b hematoxylin-eosin, original magnification x 400)

Statistical Analysis

The D'Agostino-Pearson test was used to determine whether the data is consistent with the normal distribution. The variables with normal distribution between the two groups were analyzed by independent t test, and those without normal distribution were analyzed using Mann-Whitney test. The correlation between continuous variables was analyzed using Pearson correlation. P value was calculated as double-edged, and p values less than 0.05 were considered significant. Statistical analysis was performed with the Medcalc program (Medcalc, ver 12, Ostend, Belgium).

RESULTS

The mean age of patients diagnosed with ASAP was 66, the mean age of patients diagnosed with cancer was 67, and the mean age of the patients reported as benign was 65. There was no significant age relationship between patients with PA and those without PA (p: 0.642). PSA values of the patients ranged from 2.1 to 19.8 ng / mL and median PSA value was 6.2 ng / ml. The PSA level of 13 patients was below 4 ng / ml, and 4 (19%) of them were found to have PA. In other words, 4 of the 21 patients whose PA was detected had a PSA level below 4 ng / ml. When the PSA values were compared, it was observed that there was no significant relationship between PA seen and not seen after follow-up (p: 0.296). Patients were divided into two groups with prostate volumes less than or more than 20 ml. There was no significant relationship between prostate volumes and follow-up diagnoses (p: 0.648).

It was seen that 21 (34%) patients were diagnosed with PA and 41 (66%) were diagnosed as benign after the follow up of the patients. In 5 (24%) of the cases, the cancer was in right and left lobes while ASAP was localized in the left lobe, in 4 (19%) of the cases, the cancer was right and left lobes while ASAP was localized in right lobe, in 4 (19%) of the cases, the cancer was again in the right lobe while ASAP was localized in the right lobe, in 4 (19%) of the cases, the cancer was in the left lobe while ASAP was localized in the right lobe, in 2 (9.5%) of the patients, the cancer was in the left lobe while ASAP was localized in the right and left lobes, in 2(9.5%) of the patients, both cancer and ASAP were in the same lobe (right + left lobe) (Table 1).

Table 1. Location of atypical small acinar proliferation in the first biopsy and cancer in follow-up biopsy

Patients No	ASAP site	Cancer site	Patients No	ASAP site	Cancer site
1	1	6, 7, 8, 9, 10	12	2	5, 9, 11
2	5	9, 11	13	4	10, 13
3	5	5, 7, 8	14	4	4, 9, 11
4	7,9	1, 3, 6, 7, 8, 9, 10	15	3	11
5	1	5, 6	16	6	1,2
6	8	4, 5, 8	17	11	2, 3, 11
7	3, 9, 11, 12	1, 3, 11	18	7, 10	1, 7, 8, 10
8	5, 10, 11	10, 11	19	4, 6, 7, 9	7, 9
9	2	9	20	2	1, 2
10	3	1, 3	21	12	1, 3, 12
11	9	1, 6, 9			

1: Right Base, 2: Right Lateral Base, 3: Right Medial, 4: Right Median-Lateral, 5: Right Apex, 6: Right Lateral Apex, 7: Left Base, 8: Left Lateral Base, 9: Left Medial, 10: Left Median-Lateral, 11: Left Apex, 12: Left Lateral Apex

DISCUSSION

As prostate cancer is one of the common cancers and deaths due to prostate cancer are located in the upper ranks among cancer-caused deaths, the significance of early diagnosis studies is increasing. Prostate needle biopsies are the most commonly used method for diagnosing prostate cancer and the most useful method for diagnosis. Approximately 2-5% of the prostate biopsies cannot clearly distinguish between benign and malign, and in these cases, they are termed as ASAP, atypical small acinar proliferation which has inadequate diagnostic features.

ASAP was originally used by Bostwick et al. in 1993, but Iczkowski and colleagues conducted the first study using statistical data in 1997. In the first study by Iczkowski and colleagues with 33 cases, 15 (45%) cases were found PA after the followed up. Then, in a broader study, they conducted with 295 cases, 125 (42%) cases after the follow-up were found to have PA. In the study of Ericson and colleagues in 2017, 15 (31%) of 49 cases were found PA (2,9,10). In the present study, 75 patients were diagnosed with ASAP within 6 years, 62 of them underwent follow-up biopsy and 21 (34%) of 62 patients were found to have PA. The result of this study was found to be consistent with the literature. This once again reminds us of the importance of the follow-up of ASAP patients.

Studies have reported that 14% of patients with prostate cancer have PSA below 3 ng / ml, 23-24% at 3-4 ng/ml, and 62% over 4 ng/ml. According to this, PSA levels in 38% of patients with prostate cancer are lower than 4 ng/ml (11,12-13). In our study, when PSA values of patients were examined, it was seen that PSA levels in 4 (19%) of 21 patients were lower than 4 ng/ml in PA patients. Cancer could have been missed in 19% of patients if ASAP-diagnosed cases had been followed up with PSA values instead of being followed by prostate needle biopsy. Furthermore, when the prostate volumes of patients were examined, it was seen that there was no significant relationship between prostate volume and the diagnoses after follow-up. This suggests that follow-up of prostate volume in patients with ASAP diagnosis is not a definitive method for distinguishing benign and malign.

It is unclear what the most useful follow-up biopsy approach is in ASAP diagnosed cases. In the literature, the rate of cancer seen on the same side of the ASAP site and the follow-up biopsy was reported as 65%, and this rate was found to increase to 88% with the near region biopsy (14). It was reported that the rate of getting cancer increased by taking a biopsy from the parts except for ASAP localization (14,15,16). In a study consisting of large patient groups, 56% of the cancer cases with ASAP were reported to be ipsilateral and 27% of them were contralateral. In 39% of the cases, cancer was detected in the areas outside the place where ASAP was detected in the first biopsy. Therefore, if the needle biopsy had been performed only in the ASAP place, cancer could have been missed in the 39% of the patients (2). In our study, ASAP were located in the right lobe while cancer was found in the left lobe in 4 (19%) cases. If the follow-up biopsy had been performed on only ASAP-detected lobotomy, 19% of the patients could not have had cancer. In addition, 4 patients with cancer and ASAP had the same lobe but in different localization. If the follow-up biopsy had been performed only in the same localization, cancer could not have been detected in 38% of the patients (8 patients). This demonstrates once again the necessity of prostate needle biopsy in numerous and different localizations in follow-up biopsies of cases detected in ASAP in first biopsies.

CONCLUSION

In our center, prostatic adenocarcinoma was detected in 34% of the follow-up biopsies of ASAP-diagnosed cases in the first biopsies. In 38% of cases, cancer localization and ASAP are in different parts. Consistently with the literature, this situation shows that recurrent biopsies in ASAP cases and biopsies performed from different localizations are significant in catching malign cases.

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REFERENCES

1. Prostate Cancer Estimated Incidence, Mortality and Prevalence Worldwide in 2012 (Internet web page). http://gco.iarc.fr/today/data/factsheets/cancers/27-Prostate-fact- sheet.pdf.
2. Iczkowski KA, Bassler TJ, Schwob VS, et al. Diagnosis of "suspicious for malignancy" in prostate biopsies: predictive value for cancer. Urology 1998;51:749-8.
3. Bostwick DG, Srigley J, Grignon D, et. al. Atypical adenomatous hyperplasia of the prostate: morphologic criteria for its distinction from well-differentiated carcinoma. Hum Pathol 1993;24:819-32.
4. Mancuso PA, Chabert C, Chin P, et al. Prostatecancer detection in men with an initial diagnosis of atypical small acinarproliferation. BJU Int 2007;99:49-52.
5. Iczkowski KA, Bostwick DG. Criteria for biopsy diagnosis of minimal volumprostatic adenocarcinoma: analytic comparison with nondiagnostic but suspicious atypical small acinar proliferation. Arch Pathol Lab Med 2000;124:98-107.
6. Koca O, Calışkan S, Oztürk Mİ, et al. Significance of atypical small acinar proliferation and high-grade prostatic intraepithelial neoplasia in prostate biopsy. Korean J Urol 2011;52:736-40.
7. Saul Suster, Demos. Surgical Pathology Guides. Debra L. Zynger and Anil V. Parwani. In: Prostate Pathology: Premalignant Conditions and Prostate Carcinoma. New York: Bang Printing; 2015. pp. 67-162.

8. Borboroglu PG, Comer SW, Riffenburgh RH, et al. Extensive repeat transrectal ultrasound guided prostate biopsy in patients with previous benign sextant biopsies. J Urol 2000;163:158-62.
9. Iczkowski KA, MacLennan GT, Bostwick DG. Atypical small acinar proliferation suspicious for malignancy in prostate needle biopsies: clinical significance in 33 cases. Am J Surg Pathol 1997;21:1489-95.
10. Ericson KJ, Wenger HC, Rosen AM, et al. Prostate cancer detection following diagnosis of atypical small acinar proliferation. Can J Urol 2017;24:8714-20.
11. Mistry K, Cable G. Meta-analysis of prostate-specific antigen and digital rectal examination as screening tests for prostate carcinoma. J Am Board Fam Pract 2003;16:95-101.
12. Törnblom M, Norming U, Adolfsson J, et al. Diagnostic value of percent free prostate-specific antigen: retrospective analysis of a population-based screening study with emphasis on men with PSA levels less than 3.0 ng/mL. Urology 1999;53:945-50.
13. Lodding P, Aus G, Bergdahl S, et al. Characteristics of screening detected prostate cancer in men 50 to 66 years old with 3 to 4 ng. /ml. Prostate specific antigen. J Urol 1998;159:899-903.
14. Park S, Shinohara K, Grossfeld GD, et al. Prostate cancer detection in men with prior high grade prostatic intraepithelial neoplasia or atypical prostate biopsy. J Urol 2001;165:1409-14.
15. Scattoni V, Roscigno M, Freschi M, et al. Predictors of prostate cancer after initial diagnosis of atypical small acinar proliferation at 10 to 12 core biopsies. Urology 2005;66:1043-7.
16. Chan TY, Epstein JI. Follow-up of atypical prostate needle biopsies suspicious for cancer. Urology 1999;53:351-5.