Original Article

Touch imprint cytology of prostate core needle biopsy specimens: A useful method for immediate reporting of prostate cancer

ABSTRACT

Background: Cytology plays an important role in the preoperative assessment of many cancers. It is used as a first-line pathological investigation in both screening and diagnostic purposes.

Aims: To determine the diagnostic value and accuracy of touch imprint cytology (TIC) smear of prostate core needle biopsy (CNB) specimens in the diagnosis of prostate carcinoma.

Materials and Methods: One hundred and twenty-one patients had ultrasound-guided transrectal prostate CNB. A total of 1210 TIC smears were prepared from all CNB specimens.

Results: Diagnoses of 1210 TIC smears were compared with the histopathological findings of the CNB specimens. One hundred and seventy (14%) TIC smears were found positive for malignancy, 35 (2.9%) were diagnosed as suspicious for malignancy and 1005 (83.1%) were found negative for malignancy. Twenty-five of 35 suspicious imprints and 150 of 170 malignant smears were confirmed to be malignant on histopathological evaluation. Although 20 malignant TIC smears were defined as benign in standard histological preparations, 10 of them had definitive diagnosis of malignancy following extensive serial sectioning. Last of all, there were 10 false-positive cytology results. Moreover, 10 of the 35 suspected TIC smears were false negative when compared with the histopathological diagnosis. The sensitivity, specificity, positive predictive value and negative predictive value of touch imprint smear results were 100%, 98%, 90.2% and 100%, respectively.

Conclusions: TIC smears can provide an immediate and reliable cytological diagnosis of prostate carcinoma. It may clearly help the rapid detection of carcinoma, particularly in highly suspected cases that had negative routine biopsy results for malignancy with abnormal serum prostate specific antigen (PSA) levels and atypical digital rectal examination.

Key words: Carcinoma; core needle biopsy; prostate; touch imprint cytology.

Introduction

Prostate cancer is one of the leading causes of mortality and morbidity in developed countries.[1] Most cases of prostate cancer are detected by abnormal serum total prostate specific antigen (PSA) levels and atypical digital rectal examination leading to transrectal biopsy.[2] Although the diagnosis of prostate cancer from biopsy specimens is considered definitive, there are reports pointing out that the standard biopsy regimens miss 15–35% of prostate cancers.[3] Several modifications in biopsy technique, number, and localization of biopsy cores have been described to increase cancer detection.[4,5] However, investigations on these issues are still ongoing. Touch imprint preparation from core needle biopsy (CNB) is a useful adjunct technique for histopathological evaluation of the prostate cancer. Touch imprint cytology (TIC) smears of CNB specimens would allow immediate reporting with no additional intervention or risk to the patient other than the needle biopsy itself.

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This technique may achieve high levels of sensitivity and accuracy.[6] In this study, we evaluated the diagnostic accuracy of the TIC smear technique in the diagnosis of prostate cancer.

Materials and Methods

In 2009, between January and December, 1210 transrectal tru-cut biopsies from 121 patients were collected in the Department of Urology. The biopsies were taken by the urologist, using a 17-gauge coaxial introducer and 18-gauge tru-cut core biopsy needle under transrectal ultrasound guidance. The median number of the core needle biopsies per patient was 10, with a range between 8 and 12. Each core biopsy was imprinted on glass slides by the pathologist. The biopsy cylinder was rolled over the surface of the glass slides. Imprint smears were air dried and stained with May-Grünwald–Giemsa. After the preparation of the touch imprints, biopsies were fixed in buffered 10% formaldehyde and embedded in paraffin. Each biopsy was cut in three step sections and stained with hematoxylin and eosin (H and E). All cases were retrospectively and independently reviewed, with a surgical pathologist reviewing the core needle biopsies and a separate cytopathologist reviewing the touch imprints. The pathologists were blinded to the final diagnoses and clinical impressions. The only information provided was serum PSA levels. The touch imprint diagnoses were categorized as negative, positive and suspicious for carcinoma [Figures 1-3]. The nuclear pleomorphism, molding of nuclei, presence of prominent nucleoli, granular chromatin pattern and increased nuclear–cytoplasmic ratio were accepted as malignancy criteria. In addition, loss of polarity of the nuclei at the edge of cohesive clusters with acinar arrangement was also considered. Finally, cytological and histological diagnoses were compared. For analysis, a designation of malignancy and suspected malignancy on imprint smear were considered as a positive result. Cytologically positive but histopathologically negative biopsies underwent serial sections.

Results

The age of the patients ranged from 52 to 68 years, with a median age of 59 years. The median of the serum PSA levels was 6.5 ng/ml (range 2.9–24.5 ng/ml). Of the 1210 touch imprint smears, 170 were diagnosed as positive for malignancy (14%), 35 were diagnosed as suspected positive (2.9%) and 1005 were negative (83.1%). Twenty-five suspected positive smears and 150 of all malignant TIC smears were also reported as malignant in standard histopathological evaluation [Table 1]. Gleason score was 6 in 83% of all histologically malignant biopsies, and the score was 7 in 17% of them. Furthermore, 20 touch imprint smears which were diagnosed malignant by cytology were reported as benign in the standard histological preparations. In 10 of the 20 samples, prostate carcinoma with Gleason score 6 was diagnosed after more sectioning of these tissues [Table 2]. The remaining 10 samples, which were benign in the histological sections, contributed to false-positive results. Besides, there were 10 more false-positive

Table 1: Correlation of standard histological sectioning and touch imprint cytological findings in 1210 prostate core needle biopsies before serial sections

	Histological findings		Total *n* (%)
	Malignant *n* (%)	Benign *n* (%)	
Touch imprint cytology findings			
Malignant	150 (12.4)	20 (1.6)	170 (14)
Suspicious for malignancy	25 (2.1)	10 (0.8)	35 (2.9)
Benign	-	1005 (83.1)	1005 (83.1)
Total	175 (14.5)	1035 (85.5)	1210 (100)

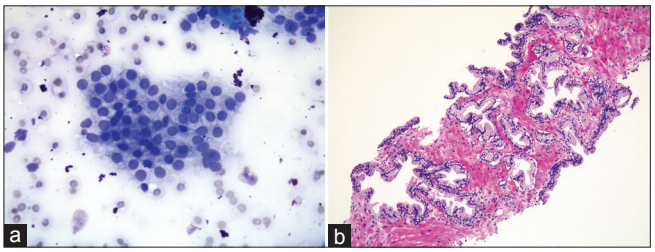

Figure 1: (a) Sheet of uniform epithelial cells without atypical features (Giemsa, ×400); (b) benign prostate tissue (H and E, ×100)

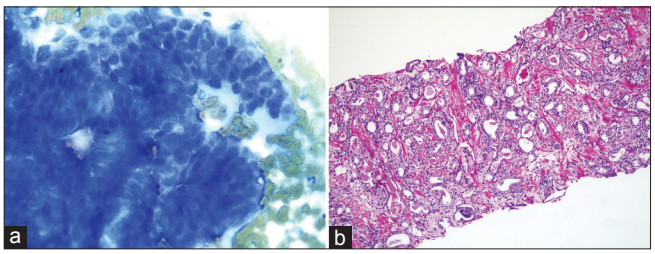

Figure 2: (a) Epithelial cell groups with nuclear crowding, overlapping, marked macronucleoli and increased nuclear–cytoplasmic ratio (Giemsa, ×400); (b) prostate adenocarcinoma, Gleason score 6 (H and E, ×100)

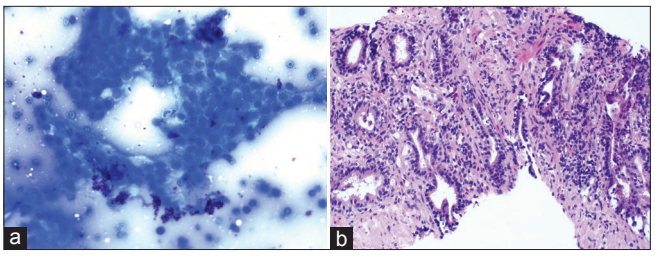

Figure 3: (a) Suspected malignant TIC smears with marked nucleoli in crowded epithelial cells (Giemsa, ×400). Reactive atypia due to polymorphonuclear leucocytes and artificial material obscuring some epithelial cells caused the false-positive result; (b) benign prostate tissue with neutrophilic inflammatory infiltration (H and E, ×200)

Table 2: Correlation of final histopathological and touch imprint cytological findings in 1210 prostate core needle biopsies after serial sections

	Final histological findings		Total *n* (%)
	Malignant *n* (%)	Benign *n* (%)	
Touch imprint cytology findings			
Malignant	160 (13.2)	10 (0.8)	170 (14)
Suspicious for malignancy	25 (2.1)	10 (0.8)	35 (2.9)
Benign	-	1005 (83.1)	1005 (83.1)
Total	185 (15.3)	1025 (84.7)	1210 (100)

TIC smears reported as suspicious for malignancy. There were no false-negative TIC smear results in this study. The sensitivity, specificity, positive predictive value and negative predictive value of touch imprint smear results were 100%, 98%, 90.2% and 100%, respectively.

Discussion

The touch imprint smear is an acceptable and reliable method within the field of cytopathology, and is described in standard textbooks of surgical pathology.[7] This technique involves touching a specimen on to a glass slide without compressing the tissue.[8] The technique is simple, cost effective, preserves the original sample for permanent fixation and appears to be reliable.[7,8] Aspiration effect during core biopsy sampling is one of the important factors that increase the effectiveness of this technique. Tumor cell groups are generally characterized by reduced cohesiveness which makes them easier to aspirate even by minimal forces. Therefore, the tissue fluid covering the sample surface may be selectively enriched in detached tumor cell groups, giving a unique source for cytological analysis [Figure 2].[9] The pathologist can instantly interpret the smears that are prepared, whereas histological analysis of the core biopsy takes a minimum of 24 h.

The efficiency of the touch imprint preparation technique has been proven so far in the diagnosis of diverse tumors including breast,[6] gastrointestinal tract,[10] lymph nodes[11] and bone marrow.[12] Jacobs *et al.*[13] demonstrated that TIC smears of core needle biopsies of non-palpable breast cancers was highly informative and it decreased the number of biopsies required for diagnosis. Gentry *et al.*[14] showed that TIC smears of pelvic lymph nodes in patients with prostate cancer was a simple and highly sensitive method for the detection of lymph node metastases. Similarly, Chieco *et al.*[15] and Lo *et al.*[16] revealed that touch imprint cell preparation from CNB of the prostate was a useful technique contributing to histopathological evaluation. Likewise, our study established that the TIC smear was a quick, easy and reliable method to evaluate the prostate carcinomas. Sensitivity and specificity of cytology were determined to be very high. When we re-examined the 20 false-positive touch imprint smears, we realized that the reactive atypia, due to dense neutrophil infiltration, caused the overdiagnosis [Figure 3]. Despite these false-positive cytology results, there were 10 cases with prostate carcinoma which were not detected in standard histological evaluation but diagnosed with TIC smears. Several reasons may lead to this misrepresentation in histology. As it is known, cutting biopsy cylinders imperfectly along their axis or embedding more than one cylinder in a block can lead to problems of detecting small foci of prostate cancer. Optimal sectioning of the core, which was the maximal surface area, was obtained when a biopsy core was sectioned at a 0° angle that is horizontal to its long axis. It was much more likely when each biopsy core was embedded individually.[17] In addition to these faults, Kao *et al.*[17] have exposed that detection of small carcinoma foci was related to the amount of tissue represented in the prostate core biopsy. Another issue that we experienced was to miss very scanty tumour cells, although adequate sectioning was performed. As we know, single histological section of a prostate needle biopsy often fails to sample a significant portion of available tissue. This could occasionally result in failure to sample a small focus of prostate carcinoma. Lane *et al.*[18] demonstrated the necessity of cutting at least three levels of the prostate biopsy cylinder, showing that sampling the cylinder at only one level misses an average of 23.4% of the total biopsy length and sampling the tissue at three levels improves this to 7%. In our study, although we examined the sections in three levels, it was inadequate to determine malignancy in 10 biopsies. By the assistance of TIC smears in these cases, the biopsies underwent more sectioning and we had the opportunity to expose the malignancy.

Besides false-positive cytology results, 13.5% of malignant biopsies ($n = 25$) were classified as suspected malignant in TIC smears. Possible reasons for not diagnosing malignancy precisely in these smears included extensive necrosis, very scanty tumor cells and excessive fibrosis or fatty tissue.

In the literature, there is little published information about the use of imprint cytology in diagnosing prostate cancer. Mannweiler *et al.*[9] found imprint cytology helpful in diagnosing prostate malignancy, particularly in clinically suspicious cases with an elevated PSA level and atypical digital rectal examination, which had previous routine biopsies with an inconclusive result for malignancy. Willems *et al.*[19] concluded that this method had a central role in diagnosis and management of prostate carcinoma, including post-therapy follow-up.

Conclusions

Malignancy determined with TIC smears of prostate CNB highly suggests a definitive malignancy in histopathological evaluation. Nevertheless, when cytology is suspicious, final diagnosis would be cancer with high probability. In these cases, even if biopsies show no tumor in standard examination of histopathological sections, serial sectioning should be done. Hereby, it will help to prevent the necessity of biopsy repetition, particularly in patients with high PSA levels with bleeding disorders and in patients intolerable to transrectal approach. In prostate carcinoma, even if TIC smears is considered as it does not provide any additional information to histological sections of prostate core biopsies, its role in rapid and accurate diagnosis should not be ignored.

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