

## 전이된 가성증식성 전립선 샘암종의 세침흡인 세포소견

-1예 보고-

국립암센터 병리과

권영미 · 박원서 · 이건국 · 홍은경

### Fine Needle Aspiration Cytology of Metastatic Prostatic Adenocarcinoma, Pseudohyperplastic Variant

Youngmee Kwon, M.D., Won Seo Park, M.D.,  
Geon Kook Lee, M.D., and Eun Kyung Hong, M.D.

Department of Pathology, National Cancer Center  
Hospital, Goyang, Gyeonggi, Korea

논문접수: 2008년 7월 21일  
논문수정: 2008년 9월 3일  
게재승인: 2008년 9월 8일

책임저자 : 홍 은 경  
주 소 : (410-769) 경기도 고양시 일산동구 정발산로  
111 국립암센터 병리과  
전 화 : 031-920-1739  
팩 스 : 031-920-1369  
E-mail address : hongek@ncc.re.kr

Pseudohyperplastic prostatic adenocarcinoma is a rare histologic variant of prostatic adenocarcinoma that resembles benign nodular hyperplasia. Immunohistochemistry can verify the absence of basal cells, but it is frequently admixed with conventional adenocarcinoma. Because fine needle aspiration cytology is rarely performed in primary prostatic adenocarcinoma, the cytology of the pseudohyperplastic variant has not been described. We experienced a case of metastatic pseudohyperplastic adenocarcinoma in a pulmonary nodule of 75-year-old man. The cytologic smear was mostly composed of large, flat sheets with elongated branching papillae in a clean background. The sheets showed a well-defined honeycomb appearance of tall columnar, regularly arranged monotonous cells with little cytologic atypia. In subsequent prostatic biopsy, pseudohyperplastic variants were identified together with conventional adenocarcinoma of Gleason's grade 3 and 4. The cytologic features of pulmonary nodules were identical to those of pseudohyperplastic components of prostatic adenocarcinoma.

(*Korean J Cytopathol* 2008;19(2):183-187)

**Key Words :** Fine needle aspiration cytology, Pseudohyperplastic variant, Prostate, Adenocarcinoma, Metastasis

## INTERDUCTION

Fine needle aspiration cytology of the prostate gland has been a major diagnostic tool for prostate cancer for more than 20 years after being developed in 1930. It is still an important diagnostic tool in Europe,<sup>1</sup> but was replaced by transrectal or transperineal needle biopsies in the 1950s. With the introduction of transrectal ultrasound-guided (TRUS) core biopsies in the late 1980s,

systematic sextant or two sets of sextant core biopsies have been the standard methods in diagnosing prostate cancer.<sup>2</sup> Cytology samples of prostate cancer can be encountered in the metastatic work-up, but a diagnosis of prostate adenocarcinoma does not usually require histologic or cytologic confirmation of the metastatic nodule because prostate specific antigen (PSA) is increased and can be easily detected serologically.

The pseudohyperplastic variant of prostatic adeno-

carcinoma is an uncommon neoplasm that resembles benign nodular hyperplasia of the prostate.<sup>3-5</sup> Diagnosis is based on architectural patterns and cytologic atypia, even though immunohistochemical stains are almost always needed to verify the absence of basal cells.<sup>6</sup> The cytologic features of this variant has not been described in prostate or in metastatic sites. We experienced a case of metastatic prostatic pseudohyperplastic adenocarcinoma in the pulmonary aspirate of a 75-year-old male subsequently diagnosed with pseudohyperplastic prostatic adenocarcinoma by prostatic needle biopsy.

## CASE REPORT

The patient was a 75-year-old Korean male who presented with multiple lung nodules in his routine chest X-ray. He was previously healthy except having benign prostatic hypertrophy. The largest nodule was in his right lower lobe and multiple smaller nodules were scattered throughout other lung fields. The possibility of primary lung cancer with lung to lung metastasis or metastatic lung cancer was considered. His serum total PSA and free PSA were 28 ng/ml and 4.99 ng/ml, respectively. Fine needle aspiration cytology was performed in the right lower lobe nodule. The prostate was stony and multinodular on digital rectal examination. After fine needle aspiration cytology of the pulmonary nodule, transrectal ultrasound-guided needle biopsy of the prostate was performed.

### Cytologic Findings

The pulmonary aspirate showed a moderately cellular smear composed of cohesive clusters of epithelial cells. The smear background was clean without necrosis or secretory materials such as mucin. Singly scattered cells were not observed. Most cellular aggregates were flat monolayer sheets of variable size with sharp borders. Bigger sheets had more irregular branching like pseudopapillae. The periphery of the sheets partly

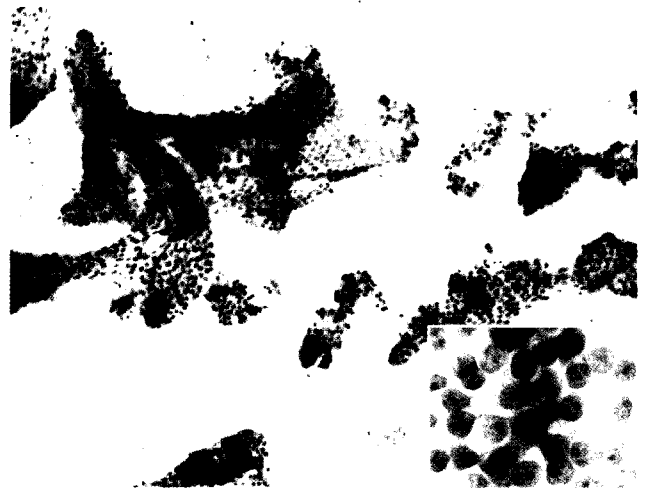


Fig. 1. Cytologic findings of pulmonary nodule. Variable sized monolayered sheets in clean background. No isolated cells are noted. The periphery of sheets shows en profile view of tall columnar cells, having basally located nuclei and abundant pale eosinophilic cytoplasm. (Inset) Close-up view of these sheets shows monotonous small round and centrally located nuclei and distinct but not prominent nucleoli. Cytoplasmic borders are well defined, hexagonal, showing honeycomb appearance. (Papanicolaou stain).

showed an en profile view of tall columnar epithelia having a smooth luminal border, abundant cytoplasm, and basal nuclei (Fig. 1). The flat sheets of tumor cells showed a uniformly honeycomb arrangement with evenly scattered, monotonous round nuclei, clear cytoplasm, and a distinct cytoplasmic membrane. At higher magnification, the epithelial cells were round to oval and had centrally located nuclei with smooth, thin nuclear membrane, fine chromatin and small but distinct nucleoli. The cytoplasm was clear to pale eosinophilic, filmy, and abundant (Fig. 1, inset). These cytologic features were similar to benign prostatic hypertrophy. Some clusters showed several small luminal structures within the sheets, resembling a cribriform arrangement (Fig. 2). Cytologic atypia was not conspicuous, and areas resembling more conventional acinar adenocarcinoma of Gleason's grade 3 or 4 were not present in these smears.

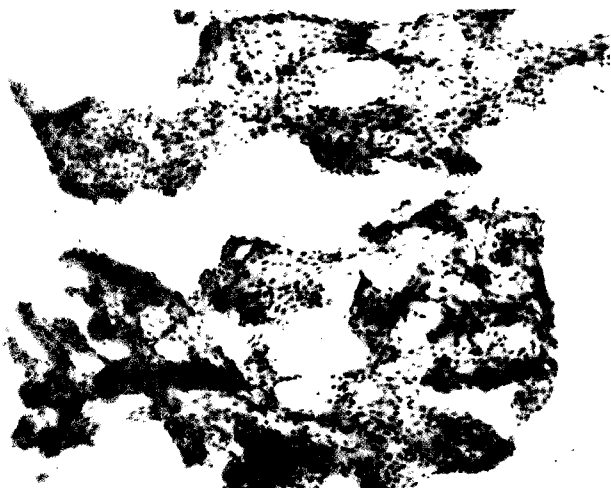


Fig. 2. Cytologic findings of pulmonary nodule. These broad irregular shaped sheets show some luminal structures, indicating complicated glandular structures (Papanicolaou stain).



Fig. 3. Histopathologic findings of prostate needle biopsy. In pseudohyperplastic adenocarcinomatous component, filiform or complicated branching papillae of tall columnar cells are noted. These papillary structures are complicated by frequent fusion and bridging. (Inset) High power view of the tumor cells shows monotonous small round nuclei, identical to those of pulmonary nodule.(H&E).

Histologic Findings in the Prostate

Eight out of 12 cores had foci of adenocarcinoma. There was mixture of Gleason's grade 3, grade 4, and pseudohyperplastic components, which represented about two thirds of the tumor volume. The pseudohyperplastic component showed tall filiform papillae and infoldings of tall columnar cells, small round basal nuclei, and abundant pale eosinophilic cytoplasm, identical to those in the pulmonary aspirate(Fig. 3). Cytologic atypia was very limited. Close inspection revealed distinct but not prominent nucleoli, and some

cells did not show distinct nucleoli(Fig. 3, inset). The morphology was very similar to that of benign hyperplastic glands in the vicinity. However, the tumor seemed to be more hyperplastic, with a more elongated papillae and infoldings, close packing without intervening stroma, and larger glands than in benign nodular hyperplasia(Fig. 4A). Immunohistochemistry for basal cells were uniformly negative(Fig. 4B).

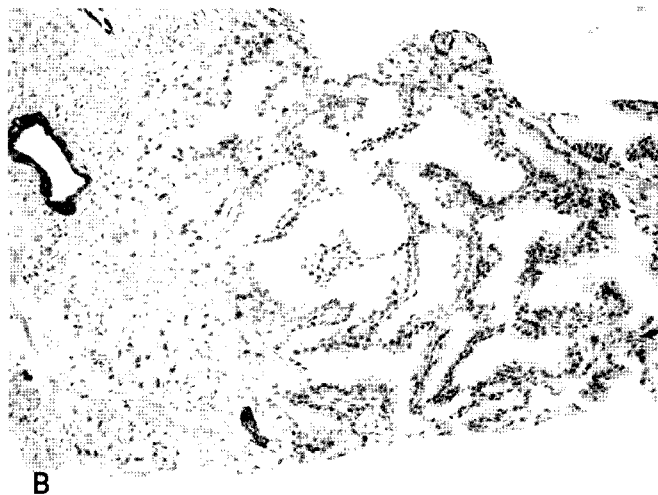
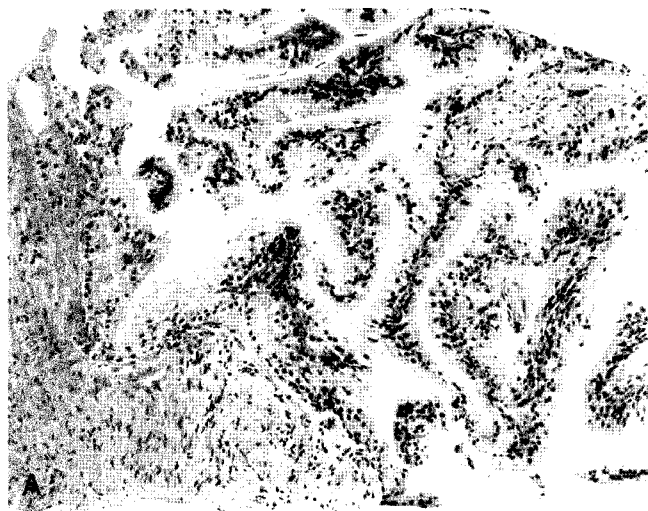


Fig. 4. (A) Histopathologic findings of prostate needle biopsy. The neoplastic glands of pseudohyperplastic adenocarcinoma are large and closely packed or compact with elongated papillae. (B) Immunohistochemical staining for 34E12. Pseudohyperplastic component shows complete loss of basal cells. (Immunohistochemical stain).

## DISCUSSION

Pseudohyperplastic prostatic adenocarcinoma is a rare histologic variant of prostatic adenocarcinoma.<sup>3-4</sup> Its close resemblance to benign hyperplastic glands makes diagnosis difficult. In a retrospective review of 150 cases of benign nodular hyperplasia, Arista-Nasr et al. found two cases (1.3%) of pseudohyperplastic adenocarcinoma.<sup>5</sup> The recognition of this pattern is based on the architectural pattern of numerous closely packed glands as well as nuclear features more typical of carcinoma, and a lack of basal cells in immunohistochemistry. However, in most cases, the diagnosis of adenocarcinoma is not problematic because it is usually admixed with or in transit to ordinary acinar adenocarcinoma in the vicinity, and high power examination of these hyperplastic glands allows identification of cytologic atypia to classify them as malignant.<sup>3-6</sup> Pseudohyperplastic adenocarcinoma, despite its benign-looking morphology, can exhibit aggressive behavior such as extraprostatic extension or metastasis.

Fine needle aspiration cytology is so rarely performed in the prostate that there is little chance to examine cytologic smears of prostate cancer or prostatic nodular hyperplasia. However, fine needle aspiration cytology still plays a major role in the detection of metastatic prostate cancer.<sup>7</sup> In addition to cytologic features, immunostaining for prostate specific antigen (PSA) and prostate acid phosphatase (PAP) is helpful for diagnosing metastatic prostate cancer. In a review of 50 cases of secondary prostatic adenocarcinoma, Mai et al emphasized immunostaining and did not describe unique detailed cytologic feature of metastatic prostatic adenocarcinoma, probably due to the variability of differentiation and architectural patterns. They found 12 cases that were not reactive to PSA or PAP, including small cell carcinomas, carcinomas with hormonal therapy, and poorly differentiated adenocarcinomas.<sup>7</sup>

When pseudohyperplastic patterns of adenocarcinoma are encountered in the metastatic work-up and no immunohistochemistry is available, the diagnosis may

be very difficult or even impossible as there are no cytological descriptions of pseudohyperplastic prostatic adenocarcinoma. Herein we describe a case of metastatic pseudohyperplastic prostatic adenocarcinoma. In the pulmonary aspirate of the present case, immunostaining was not possible because the aspirated material was very limited. Without information of prostate cancer history, a highly cellular smear but very bland architectural pattern and nuclear cytomorphology make diagnosis very difficult. Most aspirated samples were flat monolayered sheets without the three-dimensional clusters usually seen in epithelial malignancy. The smear showed a honeycomb pattern of evenly spaced tumor cells with monotonous, centrally located nuclei, ample amounts of cytoplasm, and distinct cytoplasmic borders. The irregular, long branches protruding from these flat sheets corresponded to elongated papillary infoldings of pseudohyperplastic adenocarcinoma. Together with en-profile views of tall columnar cells with basal nuclei seen in the border of larger sheets, the tumor cells were very similar to mucin-containing columnar cells in mucinous cystadenoma or adenocarcinoma.<sup>8</sup> The smear background was very clean without mucinous or other amorphous materials. Tumor tissue with tall columnar cells and a clear cytoplasm could also be differentiated. Clear cell carcinomas of low nuclear grade often show naked nuclei due to dissolution of cytoplasmic lipids by alcohol, and show single scattered cells as well as small clusters.<sup>9</sup> Benign clear cell tumors of the lung contain large polygonal or spindle-shaped cells and do not show glandular or luminal structures.<sup>10</sup>

At high power, the tumor cells showed distinct but not large or prominent nucleoli and evenly fine nuclear chromatin. The nuclear membrane was thin and delicate. In low grade prostatic adenocarcinoma, the presence of nucleoli is an important feature in distinguishing neoplastic glands from hyperplastic glands. However, some tumor cells in this case did not show distinct nucleoli. The primary prostatic adenocarcinoma also showed the same morphology. In previous

reports, nuclear features were more typical of carcinoma, but in the present case, the pseudohyperplastic component showing cytologic atypia focal in the prostatic biopsy. The rather bland nuclear morphology in the cytologic sample of pulmonary aspirate indicates that the aggressive behavior of this variant are not related to the cytologic appearance. The aggressive behavior of this tumor requires an intermediate grade classification.<sup>6</sup> Cytology in the prostate gland alone might not allow differentiation from benign nodular hyperplasia without immunostaining. It is very important to be aware of pseudohyperplastic prostatic adenocarcinoma in the metastatic work-up of unknown primary sites.

In summary, we describe an unusual cytology case of metastatic pseudohyperplastic prostatic adenocarcinoma in the pulmonary aspirate of a 75-year-old man. The presence of very large, flat, monolayered sheets without singly scattered cells or naked nuclei in the background, no associated necrosis or secretory materials, and elongated papillary branching, all reminiscent of benign nodular hyperplasia, can be cytologic feature of pseudohyperplastic prostatic adenocarcinoma.

## REFERENCES

1. Perez-Guillermo M, Acosta-Ortega J, Garcia-Solano J. The continuing role of fine-needle aspiration of the prostate gland into the 21st century: a tribute to Torsten Lowhagen. *Diagn Cytopathol* 2005; 23: 315-20.
2. Silletti JP, Gordon GJ, Bueno R, Jaklitsch M, Loughlin KR. Prostate biopsy: past, present, and future. *Urol* 2007; 69:413-6.
3. Humphrey PA, Kaleem Z, Swanson PE, Vollmer RT. Pseudohyperplastic prostatic adenocarcinoma. *Am J Surg Pathol* 1998; 22: 1239-46.
4. Levi A, Epstein JI. Pseudohyperplastic prostatic adenocarcinoma on needle biopsy and simple prostatectomy. *Am J Surg Pathol* 2000; 24: 1039-46.
5. Arista-Nasr J, Martinez-Benitez B, Valdes S, Hernandez M, Bornstein-Quevedo L. Pseudohyperplastic prostatic adenocarcinoma in transurethral resections of the prostate. *Pathol Oncol Res* 2003; 9: 232-5.
6. Eble JN, Sauter G, Epstein JI, Sesterhenn IA eds, Tumours of the Prostate; Acinar adenocarcinoma. In Tumours of the urinary system and male genital organs. Lyon : IARC Press; 2004. pp162-76.
7. Mai KT, Roustan Delatour NL, Assiri A, Al-Maghrabi H. Secondary Prostatic Adenocarcinoma: a cytopathological study of 50 cases. *Diagn Cytopathol* 2007; 35: 91-5.
8. Koss LG, Melamed MR. The prostate and the testis. In: Koss' diagnostic cytology and its histopathologic bases, 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. pp1266-72.
9. Zaman MB. The kidneys, adrenals and retroperitoneum. In: Koss LG, Melamed MR eds. Koss' diagnostic cytology and its histopathologic bases. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. pp1466-70.
10. Nguyen GK. Aspiration biopsy cytology of clear ("sugar") cell tumor of the lung. *Acta Cytol* 1989; 33: 511-5.
1. Perez-Guillermo M, Acosta-Ortega J, Garcia-Solano J. The continuing role of fine-needle aspiration of the prostate