

CASE REPORT

Morphological characteristics of a mucinous adenocarcinoma of the prostate: differential diagnosis considerations

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Abstract

Mucoid adenocarcinoma of the prostate is a very rare variant, account less than 1% of prostatic adenocarcinomas. In this respect, the most common histopathological type of prostate cancer is acinar adenocarcinoma. Diagnosis of this variant is very important due to peculiarities: aggressive biologic behavior, poor response to radiotherapy. Although these tumors are not as hormonally responsive as acinar adenocarcinomas, some of them respond to androgen withdrawal. Before making a diagnosis of primary mucinous adenocarcinoma, is necessary to exclude an extraprostatic malignant neoplasia, especially from the bladder or bowel. We present the case of a male patient who suffered a transurethral prostatic resection surgery. Histopathological examination revealed malignant tumor cells floating in a pool of mucus or even acini mixed with signet ring cells. A particular aspect is that floating mucus cells have a non-papillary pattern similar to colloid carcinoma of the breast. The use of monoclonal antibody revealed positive immunoreaction of malignant cells for prostatic specific markers and excluded neoplastic invasion of the bladder or bowel carcinoma.

Keywords: prostate mucinous adenocarcinoma, mucin lakes, prostate specific antigen, carcinoembryonic antigen.

Introduction

Mucinous adenocarcinoma is an uncommon of prostate adenocarcinoma, whose treatment includes radical prostatectomy, radiotherapy and hormone therapy. Because 60–90% of malignant prostate cancers secrete mucus, the diagnosis of primary mucinous adenocarcinoma is based on histopathologic criteria. Mucinous adenocarcinoma diagnosis should be considered if the mucinous component is at least 25% of resected material. In addition, the chemical composition of mucin is different malignant mucinous neoplasia compared with that produced by normal tissue [1, 2]. Also, non-dilated gland that contain intraluminal mucin should not be labeled mucinous adenocarcinoma. Some prostate carcinoma may associate signet ring cells, although not containing intracytoplasmic mucin vacuoles. In order of make differential diagnosis, we must to remember that mucoid adenocarcinoma shows positive immunostaining for prostate specific antigen (PSA) and prostatic acid phosphatase (PrAP) but does not stain with carcinoembryonic antigen (CEA) [3].

Patient, Methods and Results

We present the case of a male patient (IF), 75-year-old, falling in the specific age group that manifests adenocarcinoma. He complained of hematuria, dysuria and polakiuria. Digital rectal exam revealed a slightly enlarged prostate. PSA has a value of 7 ng/dL. Patient's

medical history is insignificant. Chest X-ray and bone scan were negative. The excised material by transurethral prostatic resection surgery in the Department of Urology of Emergency County Hospital of Constanța, Romania, has identified a mucinous adenocarcinoma with a 4+4 Gleason score. The histopathological and immunohistochemical techniques were performed in the Clinical Service of Pathology, Emergency County Hospital of Constanța. The specimen was fixed in 10% formalin and included in five paraffin blocks. Sections of 5 μm were stained with Hematoxylin–Eosin and monoclonal mouse anti-human prostate specific antigen, clone ER-PR 8, isotype IgG1, kappa (Dako) and monoclonal mouse anti-human carcinoembryonic antigen (CEA), clone II-7, isotype IgG1, kappa (Dako) were applied. Microscopic images were taken with a Nikon camera using a Nikon Eclipse E600 microscope.

Endoscopic examination showed that prostatic urethra is lined by a whitish-translucent material. After transurethral resection of through urethra flowed gelatinous material. Macroscopic examination revealed the presence of multiple fragments with variable diameters, which measures overall 8/3.5/0.5 mm colored with translucent areas, low consistency.

Histopathological examination revealed that over 50% of tissue fragments presents mucin lakes (Figure 1), across which identify small malignant cells with cribriform and micro-glanduliform pattern with marked nuclear atypia (Figure 2). Some fragments provide

malignant cells with trabecular pattern and aspects of signet ring cells (Figure 3). The cells with signet ring pattern are due to intracellular accumulation of mucin compressing the hyperchromatic nucleus at the periphery. We also made a Periodic Acid Schiff (PAS) staining, which revealed pink colored mucus both intracellular in signet ring cells and (Figure 4). Areas of necrosis were identified extracellular into the mucin lakes. Microscopic diagnosis is mucinous adenocarcinoma of the prostate, Gleason score 4+4. To exclude an invasion from another level, it is recommended to complete investigations for assessing digestive tract.

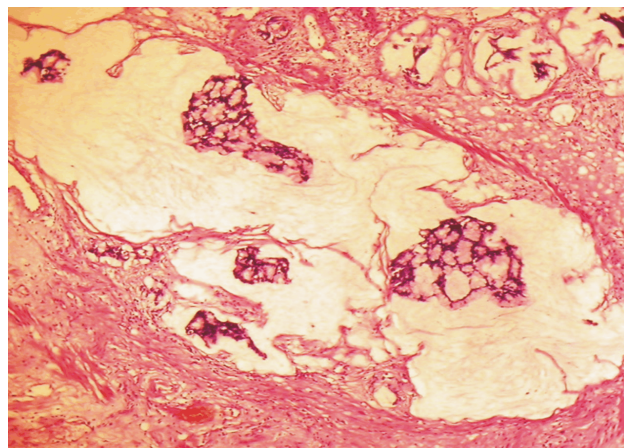


Figure 1 – Malignant glands floating in mucin lakes (HE stain, 100×).

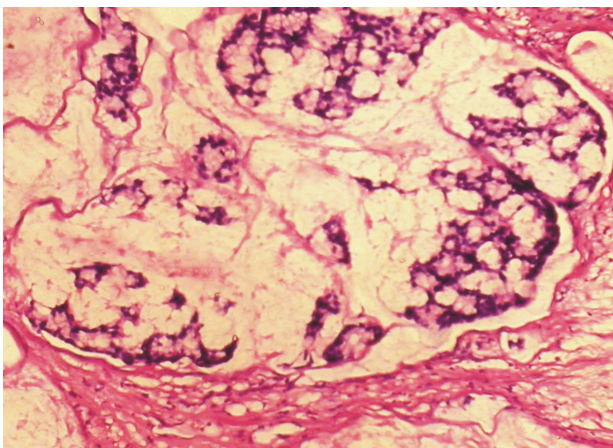


Figure 2 – Cribriform and microglanduliform disposition in mucinous areas (HE stain, 200×).

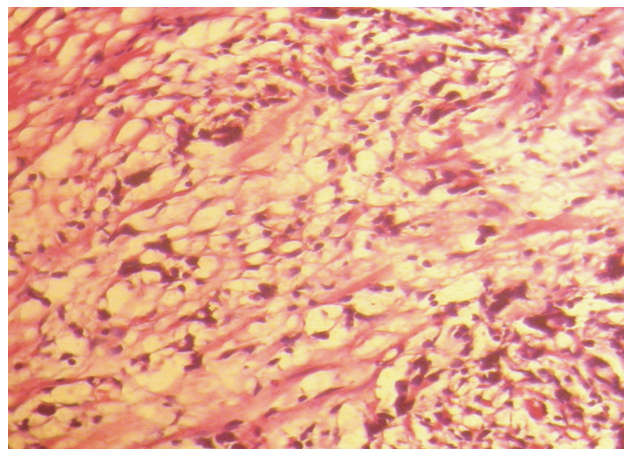


Figure 3 – Signet-ring cells appearance (HE stain, 200×).

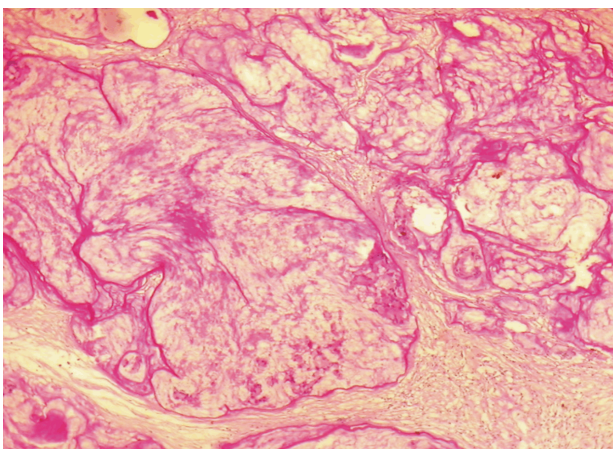


Figure 4 – Lakes of mucin dissecting stroma (PAS stain, 100×).

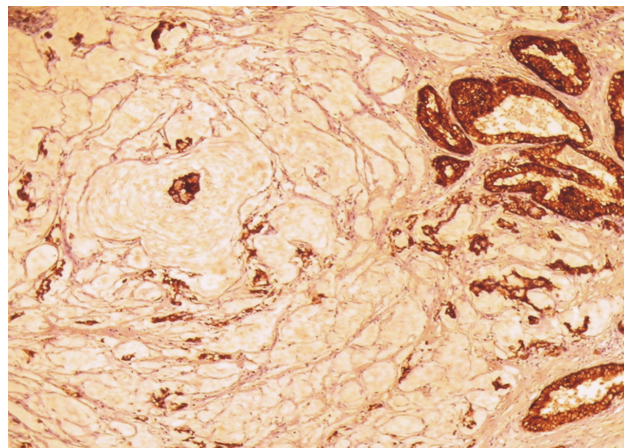


Figure 5 – Positive immunoreaction for PSA in prostatic epithelial cells, 100×.

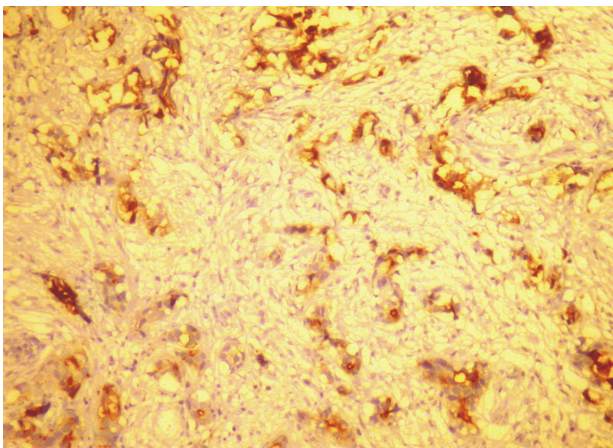


Figure 6 – Focal positive immunoreaction for PSA in signet ring population, 200×.

The patient was investigated to determine the origin of malignant cancers in the digestive system. Abdominal CT and colonoscopy did not reveal pathological processes at this level. Also, stool was negative for occult bleeding.

For diagnosis, the immunohistochemical methods were mandatory. Thus, application of monoclonal antibodies highlighted the following:

- positive reaction for PSA in all prostatic epithelial cell, including signet ring cells that reveal the origin from the prostate gland (Figures 5 and 6).
 - negative reaction for CEA (Figure 7).
- Radical prostatectomy was performed.

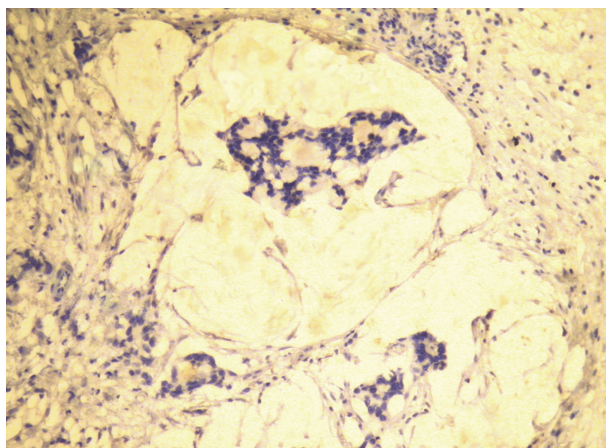


Figure 7 – Negative immunoreaction for CEA in malignant population, 200×.

Discussion

Since Boyd reported the first case of mucinous adenocarcinoma, in 1882, there were over 100 reported cases of primary tumors such [4].

Need for clear and precise definition criteria of this morphological entities often derived from their overstated in some reports. Problems regarding this pathology nomenclature stems from the fact that many cases of prostatic adenocarcinomas secrete mucus. Mucinous adenocarcinoma term should be used only when the amount of extracellular mucin is sufficiently large as to produce pools of mucus. If the mucin component occupies a reduced portion of the tumor, it will be called prostate adenocarcinoma with focal mucinous areas. According to this, mucinous adenocarcinomas of the prostate account for only 0.2–0.4% of prostatic carcinomas [5–8].

In the presence of an atypical glandular focus, the existence of extracellular mucin is diagnostic of carcinoma. Mucinous adenocarcinomas of the prostate are considered intermediate grade tumors and in mucinous areas usually predominant a cribriform pattern, being graded as Gleason 4. Gleason score in this case was 4+4, according to the 2005 *International Society of Urological Pathology Consensus Conference on Gleason Grading* [9]. Also, have been described mucoid adenocarcinomas characterized by the presence of glandular structures floating in mucus graded as Gleason pattern 3 [10].

According to the literature, only a small proportion of mucinous tumors are accompanied by positive signet ring cells in the mucin [11]. In one of these cases, carcinoma with signet ring cells comes from intestinal metaplasia of adjacent urothelium [12]. In our case, PAS staining revealed the presence of intracellular mucus. In primary signet ring cell malignant neoplasia of the prostate, the signet ring cells do not contain mucus and has a worse prognosis than mucinous carcinoma [13].

Distinction of mucinous adenocarcinoma must be done with metastasis arising from the bladder, urethra or colorectal origin. Have been described 15 cases of in situ and infiltrating mucinous adenocarcinoma arising

from prostatic urethra metaplasia and that invading prostate gland [14]. Subsequently there were three such cases described by other authors. An important criterion in distinguishing the two entities is that in adenocarcinoma of the prostatic urethra the typical glandular structures of acinar adenocarcinoma are not seen floating in the mucus. In some cases of adenocarcinoma of the prostatic urethra, mucin-containing signet cells were observed in the mucin lakes. Immunohistochemistry techniques demonstrate also the negativity to PSA and PSAP. In some cases these tumors showed positivity to high molecular weight cytokeratins as well as positive staining with cytokeratins 7 and 20 [15]. Tran KP and Epstein JI, in 1996, described two cases originating from the prostatic urethra, which were negative for prostate-specific antigen and prostate-specific acid phosphatase and positive for carcinoembryonic antigen [16].

In addition, mucinous adenocarcinoma of the prostate must be distinguished from an invasion of adenocarcinoma of the bladder. Differentiation is difficult because in some cases they can be positive to the PSAP. Some authors have described cases of bladder adenocarcinoma that show positive reaction to PSAP. The difference derives from the fact that bladder adenocarcinomas are focally positive to PSA and PSAP while prostate adenocarcinomas are diffusely positive. Other markers can be used in making the differential diagnosis, such as proPSA, prostein (p501S) and NKX3 but their usefulness remains to be demonstrated [17].

Regarding the differential diagnosis with colorectal mucinous adenocarcinomas, they mimic primary adenocarcinoma of the prostate usually. Prostate invasion by a mucinous adenocarcinoma of colonic origin is represented microscopically by lakes of mucus mixed or accompanied with tumor cells with acinar appearance, groups or isolated cells. Neoplastic proliferation infiltrates prostate tissue. It is advisable to corroborate the clinical data with history of colon cancer or endoscopic studies [18].

A primary tumor of the colon show negative reaction to PSA, positive reaction to CDX2 and CEA or positive nuclear beta catenin staining profile [19].

In the past, this type of tumor was considered less aggressive than typical adenocarcinoma that arises from the female portion of the prostate and not spread to bone. Once thought to not be associated with increased PSA values. However, some studies showed that mucinous adenocarcinoma of the prostate is biologically aggressive. Also, tend to develop bone metastases in advanced stages and is associated with increased levels of PSA [10]. In studies of Ro JY *et al.* [20], seven of the 12 patients died of tumor in five years and five of them lived in the next three years. In contrast, a recent study by Lane BR *et al.* [21] revealed a good prognosis for a group of 12 cases compared with a group of typical adenocarcinomas. It should be noted that in the latter study included patients received neoadjuvant hormonal therapy that could affect the return [20]. Other studies showed that mucinous adenocarcinoma treated by radical prostatectomy is not more aggressive than non-mucinous malignant neoplasia of the prostate [22, 23].

✉ Conclusions

Application of monoclonal antibodies has been extremely useful in establishing the origin of mucinous adenocarcinoma of the prostate. Managing patients with prostate mucinous adenocarcinoma is a challenge for all specialties involved in the diagnosis and treatment of this disease, mainly because of its features.

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