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Mucinous adenocarcinoma: A case report from our practice

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Abstract

Background: Mucinous Adenocarcinoma of the Prostate (MACP) is a rare variant of prostate carcinoma, characterized by pools of extra-acinar mucin. Precise diagnosis is important due to nonspecific findings on imaging tests, the aggressive behavior and poor response to radiotherapy. The main point in MACP diagnosis is to rule out the adenocarcinomas, originating from the urinary bladder and colon.

Case report: A 57-year-old man presented to our clinic with urinary frequency, nocturia and voiding difficulties. Digital rectal examination revealed a slightly enlarged prostate, without palpable nodules. The initial serum PSA levels were 18.0ng/mL (normal 0-4 ng/ml). Twelve-core transrectal ultrasound-guided biopsy confirmed prostate cancer with Gleason score 8 (4+4). Up to 50% of the tumor lesion consisted of neoplastic glands with isolated cells, floating in mucinous material. The metastatic work-up, including CT scan and bone scintigraphy was negative and radical retropubic prostatectomy with lymph node dissection has been performed. Periodic Acid Schiff staining confirmed the presence of mucinous prostatic adenocarcinoma. Morphological examination was negative for lymph nodes metastases. The extraprostatic extension of the tumor and surgical margins were negative. Three years after surgery, patient's serum PSA remained undetectable, without recurrence.

Conclusion: We report this case due to the rarity of primary MACP and its challenging diagnosis. Although MACP may be associated with poor outcome, its proper diagnosis and treatment significantly contribute to favorable prognosis and patient survival.

Keywords

prostate cancer; mucinous adenocarcinoma; mucin

Abbreviations

MACP: Mucinous Adenocarcinoma; PSA: Prostate Specific Antigen; CT: Computed Tomography; TNM, NM: Classification of Malignant Tumors; MRI: Magnetic Resonance Imaging

Introduction

Mucinous Adenocarcinomas of the Prostate (MACP) are rare malignant tumors, characterized by the pools of extra luminal mucin, accounting less than 1% of all types of prostate cancer (PCa) [1]. Because 60 to 90% of PCa also secrete mucus, the diagnosis of primary MACP relies on the previously reported histologic criteria [2]. The diagnostic criteria for this tumor were based on the presence>25% of mucinous component of the tumor [3,4]. MACP is associated with increased levels of Prostate-Specific

Antigen (PSA), metastatic spread to bones and responds to hormonal therapy [3]. The infiltrating component in these cancers also contains lakes of mucin [4,5]. *Epstein and al*. divided MCAP into three groups i) Mucinous adenocarcinoma; ii) Primary signet-ring cell carcinoma; iii) Mucinous carcinoma with signet ring cells [6].

MCAP are associated with elevated PSA levels and respond well to hormonal therapy. In contrast, the signet-ring cell and mucinous carcinomas with signet ring cells do not respond to hormonal therapy. In addition, it was found that primary signet ring cell carcinoma and mucinous carcinoma with signet ring cells had poor outcome, compared with mucinous adenocarcinoma without signet ring cells [6].

Case Presentation

A 57-year-old man without history for malignant diseases, presented to our hospital with urinary frequency, nocturia and difficulties to void. Digital rectal examination revealed a slightly enlarged prostate (around 40 cc) without palpable nodules. The serum PSA was 18.0 ng/mL (normal range 0-4 ng/ml). Twelve-core transrectal ultrasound-guided biopsy demonstrated the presence of PCa with Gleason score 8 (4+4). Seven of the 12 cores contained acinar adenocarcinoma, occupying up to 25% of the prostatic tissue. In addition, 50% of the neoplastic glands contained cells, floating in a mucinous material. The metastatic work-up (CT scan and bone scintigraphy) was negative. The intraoperative frozen section of the lymph nodes and surgical margins were negative for metastatic disease. Open radical prostatectomy with bilateral pelvic lymph node dissection was performed. Radical prostatectomy specimens and the lymph nodes have been examined in a standard fashion. The prostatectomy specimen weighted 45g. Prostatic tissue was largely nodular with yellow areas, involving the posterior zone. Microscopically, the neoplastic proliferation was found in 40% of the prostate. Gleason was scored as 8/10 (4+4). In addition, pattern 5 was found in 2% of prostatic tissue. All pelvic lymph nodes were negative for metastases. The extra prostatic extension and surgical margins were also negative. The histological examination showed mostly acinar prostatic adenocarcinoma, consisting 40% of neoplastic glands and single cells, floating in abundant mucinous material, confirmed by a positive Periodic Acid Schiff (PAS) staining. The rest of the prostatic specimen showed Benign Prostatic Hyperplasia (BPH) with High-Grade intraepithelial Neoplasia (HGPIN). The final diagnosis was mucinous adenocarcinoma, pT2c N0M0 and Gleason score 8/10 (4+4), as shown in Figure 1.

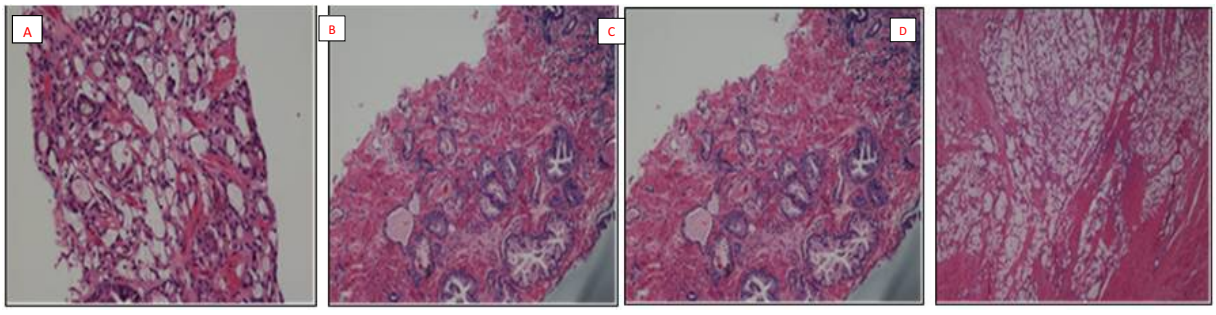

Figure 1: (A) Tru-cut biopsy specimens with abundant extracellular mucin more than 25% that defines the tumor as mucinous (H & E, x100). **(B)** The same biopsy with evidence of BPH and HGPIN (H & E, x 100). **(C)** Higher magnification shows mucinous adenocarcinoma with glandular fusion, Gleason score 8 (3+4). Pools of mucin with single cells floating in them areclearly visible (H & E, x200). **(D)** Radical prostatectomy specimen with vast areas of mucinous adenocarcinoma (H & E, x40).

The extensive postoperative metastatic work-up that included colonoscopy was negative; the stool test for occult bleeding with CEA antigen analysis were in normal ranges. Three years after surgery and close follow-up, patient has normal serum PSA levels with acid phosphatase within normal range.

Discussion

Samaratunga and al. have first described MACP in 1882[9] and since then, less than 200 cases have been reported [1]. The diagnosis of MACP relies on extra luminal pools of mucin found in more than 25% in prostatic tissue [2]. The mean age at the time of diagnosis is usually less than 60 years old. In overall, the pre-treatment PSA levels are between 4.0and 10.0 ng/mL and TNM is T1c, T2a or T2b [3–5]. Grading of MACP is controversial and some authors suggested scoring of the tumor based on the underlying architecture pattern, ignoring the extracellular mucin. Current recommendations for grading mucinous cancers are to grade the underlying architecture, based on extravasated mucin, essential criteria for the diagnosis of mucinous adenocarcinoma [7]. Recently updated grading of MACPs has been proposed based on the underlying architectural pattern, i.e. well-formed glands or Gleason 3; cribriform glands, or Gleason 4; single cells or Gleason 5, etc. 8 Most commonly, MACP are Gleason 8 (4+4) [4,9]. In recent study consisting of 143 cases with mucinous adenocarcinomas, the mean age was 61.4 y/o, and the mean preoperative PSA 7.8 ng/ml. Tumors in stage cT1 were81%, compared with these in cT2 (19%). The majority of mucin consisting carcinomas were with Gleason 4+3 (54.5%). In another study with 73 cases, mucinous component was found in more than25% [9]. Morphologically, MACP demonstrate mucoid or gelatinous cut surface and the light microscopy reveals pools of mucin in the stroma with groups of cells, forming acini. The presence of luminal mucin is a specific feature of these tumors. In addition, new data has been provided of the characteristics and distribution of mucin in both normal and malignant prostatic tissues [10,11]. The immunostaining in the benign tissues is positive for neutral mucins, whereas carcinomas contain sulphated type of sialic acidic mucin. Of note is that benign tissues do not secrete acidic mucin, while adenocarcinomas can produce in some extent. However, the colloid cancers secrete this type of mucin in significantly larger amounts [10]. Another study showed that mucin in MACPs is much more than the luminal mucin in the acinar carcinoma Gleason 3, demonstrating difference between both prostatic carcinomas [7]. Single cells, including signet ring forms, neuroendocrine and Paneth-like cells are also frequent findings in MACP. Immunohistochemically, MACPs are positive for Prostate Specific Antigen (PSA), Prostatic Acid Phosphatase (PAP) and Low Molecular Weight Cytokeratins (LMWCK). Pure MACPs are negative for Carcinoembryonic Antigen (CEA) and high molecular weight cytokeratins (HMWCK) [7]. Compared with MACP, the urothelial carcinoma is positive to HMVCK and CK7/20 and negative for PSA and PAP [5]. However, CT-scan and MRI used in MACPs were suggested as non-specific [12–15]. The progression and the outcome of MACP sare not fully understood [13]. *Epstein and al* have reported six cases of MACP with aggressive biological behavior and propensity to develop bone metastases [3]. Also, 12 cases with high-stagemucinous adenocarcinoma were treated with radiation, hormonal therapy or in combination, where the bone metastases were also common [17]. In contrast, *Osunkoya and al*. have reported a 5-year progression free risk of 97.2% of cases in a group of 47 patients with mucinous prostatic adenocarcinoma [20]. Diagnosis of MACP obligates torule out mucinous carcinoma, originating from the gastro-intestinal system and detailed medical history, endoscopy and imaging screening are important for the patient outcome. Genetic abnormalities also have been found in MACPs. Studies have shown ERG gene expression to occur in 50% of mucinous

adenocarcinoma [9,17]. Likewise, TMPRSS2: ERG fusion gene was identified in 83% of the seprostate cancers [18,19]. Furthermore, MUC 2 expression was identified in mucinous components of MACP [20]. *Osunkoaya and al*. showed that MACPs expresses PTEN in most cases [20]. Interestingly, the expression of PTEN in MACP was suggested as plausible factor possibly explaining the low aggressiveness of MCAP, compared with conventional adenocarcinomas of the prostate without extra luminal component [8,20].

Conclusion

We presented a rare case of mucinous adenocarcinoma, where we outlined the most important diagnostic features of MACP and specific diagnostic features of this tumor, which every urologist should keep in mind.

Acknowledgements

We dedicate this paper in memoriam to our colleague, friend and teacher Prof. Alexander Hinev, suddenly deceased in November 2017.

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