Annals of Diagnostic Pathology 27 (2017) 7–13

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Macrocystic ductal adenocarcinoma of prostate: A rare gross appearance of prostate cancer

Fumiyoshi Kojima [a], Hiroyuki Koike [b], Ibu Matsuzaki [a], Yoshifumi Iwahashi [a], Kenji Warigaya [a], Masakazu Fujimoto [a], Kazuo Ono [c], Youji Urata [d], Yasuo Kohjimoto [b], Isao Hara [b], Shin-ichi Murata [a,*]

[a] Department of Human Pathology, Wakayama Medical University, 811-1, Kimiidera, Wakayama 641-8509, Japan
[b] Department of Urology, Wakayama Medical University, 811-1, Kimiidera, Wakayama 641-8509, Japan
[c] Department of Diagnostic Pathology, Japanese Red Cross Wakayama Medical Center, 4-20, Komatsubaradori, Wakayama 640-8558, Japan
[d] Department of Diagnostic Pathology, Japanese Red Cross Kyoto Daiichi Hospital, 15-749, Honmachi, Higashiyama, Kyoto 605-0981, Japan

ARTICLE INFO

Keywords:
Prostate
Ductal adenocarcinoma
Cystic
PIN-like
Macrocystic
Cystadenocarcinoma

ABSTRACT

Macroscopic cyst-formation by prostatic adenocarcinoma, herein referred to as macrocystic prostatic adenocarcinoma (MPA), is extremely rare. To date, no studies of prostate cancer performed based on gross cystic appearance have been reported. MPA can include various diseases, one of which is cystadenocarcinoma. Several cases of ductal adenocarcinoma exhibiting a macrocystic appearance have recently been reported; however, the histological and clinicopathological characteristics of MPAs have yet to be characterized and established. Therefore, we aimed to determine the histological and clinicopathological characteristics of MPA, via a multi-institutional investigation. We discovered five patients with MPA out of 1559 treated patients (0.32%); all cases were ductal adenocarcinomas. MPA was found to have three growth patterns: Two cases showed a prevalence of exuberant papillary proliferation with a fibrovascular core in the macroscopic multilocular cysts. Two others predominantly exhibited multilocular cysts lined by flat epithelium with foci of low papillae, and the fifth had a cystic lesion with intracancerous necrosis. Three of the cases showed extraprostatic invasion; however, none of the patients experienced recurrence during the follow-up period. Each predominant growth pattern tended to exhibit unique clinicopathological characteristics with respect to serum prostate specific antigen level and tumor size and location. In conclusion, we demonstrated that MPA is a ductal adenocarcinoma that is composed of intracystic exuberant papillary proliferation and flat proliferation with foci of low papillae, both of which might exhibit different clinicopathololgical appearances.

1. Introduction

Prostatic carcinoma is one of the highest-incidence malignancies and a top cause of cancer-related deaths among men, especially in industrialized countries such as Japan and Western countries. Clinical diagnosis of prostatic carcinoma is established using serum prostate-specific antigen (PSA) levels, digital rectal examination, transrectal ultrasonography, and biopsy. Prostatic carcinoma is usually detected as a solid, hard mass on transrectal ultrasonography and/or digital rectal examination. The majority of prostatic carcinomas are acinar adenocarcinomas, although some rare variants have also been reported [1].

Macroscopic cyst-formation by prostatic adenocarcinoma is an extremely rare condition that exhibits an unusual appearance on urological examinations. Herein, we refer to prostatic adenocarcinomas that form macrocystic appearances as macrocystic prostatic adenocarcinomas (MPAs). To date, no case series of MPAs based on their gross appearance have been reported. MPA can include various diseases, one of which is cystadenocarcinoma [2-9]. Most cystadenocarcinomas are reported in Japan [3-5,7]. Cystadenocarcinoma involves multilocular cysts with papillary proliferations and Roman arch structures lined by stratified columnar cells. Its diagnostic criteria and prognosis remain unclear owing to its rarity. Additionally, several cases of ductal adenocarcinoma presenting a macrocystic appearance have recently been reported [9-12]. Ductal adenocarcinoma, a variant of prostatic adenocarcinoma, usually presents with a macroscopically solid, non-cystic appearance as well as microscopically proliferated papillary and cribriform structures composed of tall columnar cells with a pseudostratified nucleus. Typical ductal adenocarcinoma often shows aggressive behavior and results in poor overall survival that is similar to that observed with acinar adenocarcinoma with a grade group 4.

In this study, we aimed to determine the histological and clinicopathological characteristics of MPA through a multi-institutional investigation.

* Corresponding author.
E-mail address: smurata@wakayama-med.ac.jp (S. Murata).

http://dx.doi.org/10.1016/j.anndiagpath.2016.12.002
1092-9134/

Table 1
Primary antibodies used for immunohistochemistry in this study.

Antibody	Clone	Source	Dilution
P63	4A4, mouse monoclonal antibody	Dako, Tokyo, Japan	1:200
CK-HMW	34bE12, mouse monoclonal antibody	Dako, Tokyo, Japan	1:200
AMACR	rabbit monoclonal antibody	Dako, Tokyo, Japan	1:500
PSA	ER-PR8, mouse monoclonal antibody	Dako, Tokyo, Japan	1:100
ERG	EP111, rabbit monoclonal antibody	Nichirei, Tokyo, Japan	ready-to-use
PAX8	rabbit polyclonal antibody	Proteintech, Tokyo, Japan	1:200
MUC6	CLH5, lyophilized mouse monoclonal antibody	Leica, Tokyo, Japan	1:200

Abbreviations: *CK-HMW*, cytokeratin high molecular weight; *AMACR*, alpha methylacyl CoA racemase; *PSA*, prostate specific antigen; *ERG*, erythroblast transformation-specific-related gene; *PAX8*, paired box 8; *MUC6*, mucin-6.

2. Materials and methods

2.1. Study design

We reviewed macroscopic findings of 1559 surgically resected prostatic adenocarcinomas treated at three institutions in Japan between 2004 and 2015. We retrieved five MPAs from the pathology archives of these hospitals, and obtained clinical data from the patients' medical records.

2.2. Histological and immunohistochemical examinations

We examined formalin-fixed, paraffin-embedded, and hematoxylin-eosin (HE)-stained tissue samples, prepared from whole specimens of resected prostates under light microscopy. Additionally, we performed immunohistochemical staining using standard procedures with a Nichirei Histostainer (Nichirei, Tokyo, Japan). The primary antibodies used in this study are listed in Table 1. Antigen retrieval was performed using a citrate buffered warm bath (pH 6) using the following antibodies: p63, CK-HMW, AMACR, PAX8, and MUC6. We also pretreated the samples in heat processor solution (pH 9, Nichirei, Tokyo, Japan) for ERG. The institutional ethical review board of our institution approved this study (No. 1758).

3. Results

3.1. Clinical features

We found five cases of MPA from among 1559 resected prostatic adenocarcinomas (0.32%) (Table 2). The patients were between 64 and 77 years of age, with an average age of 70.8 years. Serum PSA levels ranged from 2.27 to 105.43 ng/mL. In all cases, postoperative serum PSA levels were below 0.03 ng/mL. Preoperative needle biopsy examinations were performed, but definitive pathological diagnoses of adenocarcinoma were not achieved in two cases (patients 1 and 2) until specimens were obtained via transurethral resection. None of the patients experienced recurrence during the follow-up period of 6–76 months (average: 42.6 months).

3.2. Histological findings

3.2.1. Macroscopic findings

The tumor sizes ranged between 1.0 and 5.0 cm; those of patients 1 and 2 were located in the periurethral region (Fig. 1) and central zone, respectively, while those of patients 3, 4, and 5 (Figs. 2 and 3) were in the peripheral zone. The tumor of patient 1 invaded the urinary bladder (Fig. 1). The lesions in the others patients localized in the prostate (Figs. 2 and 3). The tumors of patient 1 and 2 included intracystic nodules; the cyst of patient 2 contained a bloody fluid. The tumor of patient 5 resembled a hematoma (Fig. 3).

3.2.2. Microscopic findings

The histological findings of all MPAs were consistent with ductal adenocarcinoma. Two MPA cases (patients 1 and 2) showed a predominance of papillary proliferation with a fibrovascular core in the macroscopic multilocular cysts, as well as exuberant proliferation occupying the cystic space (Fig. 1). The tumors in two other cases (patients 3 and 4) formed macroscopic multilocular cysts with a flat luminal surface as well as foci of low papillary growths with a fibrovascular core (Fig. 2). The MPAs of patients 3 and 4 did not have exuberant papillary proliferation; patient 3 had a small area of papillary growth similar to that of patients 1 and 2 (Fig. 2). The final case (patient 5) was ductal adenocarcinoma with intracancerous necrosis and a hemorrhaging cystic lesion (Fig. 3). Two cases (patients 1 and 3) showed acinar adenocarcinoma, grade group 1 (Gleason score 3 + 3 = 6), but were separately distributed and distant from each other. However, patient 5 exhibited intermingled ductal and acinar adenocarcinoma, grade group 5 (Gleason score 4 + 5 = 9; mixed acinar and ductal adenocarcinoma), where the former occupied 40% of the area of the carcinoma.

All MPA cases were composed of amphophilic tall columnar cells with enlarged oval nuclei showing pseudostratified alignment. These nuclei showed increased fine granular chromatin and enlarged nucleoli (Fig. 4A). The cyst-lining cells showed atypia that was similar to that of the papillary region (Fig. 4B); some cysts were lined by foamy cytoplasmic cells (Fig. 4C). In patient 5, viable ductal component cells showed a

Table 2
Clinicopathological findings of macrocystic prostatic adenocarcinoma.

Case	1	2	3	4	5
Age (years)	75	68	77	70	64
Preoperative PSA (ng/mL)	105.43	31.62	2.27	8.6	14.48
Postoperative PSA (ng/mL)	0.02	<0.01	<0.01	<0.01	<0.01
Site	periurethra	CZ	PZ	PZ	apex
Size (cm)	5.0 × 4.0 × 3.0	4.0 × 3.0 × 4.0	2.0 × 1.0 × 2.5	1.0 × 0.5 × 0.5	1.0 × 1.0 × 1.5[a]
Histological growth characteristic	exuberant pap	exuberant pap	flat with foci of low papilla	flat with foci of low papilla	necrosis
Grade group (Gleason score)	4 (4 + 4 = 8)	4 (4 + 4 = 8)	4 (4 + 4 = 8)	4 (4 + 4 = 8)	5 (5 + 4 = 9)
pT	4	3b	3a	2a	3a
EPE (location)	urinary bladder	seminal vesicle	periprostatic tissue	–	periprostatic tissue[b]
RM	–	–	–	–	+[c]
Grade group (Gleason score) of combined acinar adenocarcinoma	1 (3 + 3 = 6)	–	1 (3 + 3 = 6)	–	5 (4 + 5 = 9)
Follow-up (month)	15	73	6	43[d]	76

Abbreviations: *PSA*, prostatic specific antigen; *PZ*, peripheral zone; *CZ*, central zone; *pap*, papillary; *EPE*, extraprostatic extension; *RM*, resection margin.
[a] The size was of the ductal adenocarcinoma component of the mixed acinar-ductal adenocarcinoma.
[b] Acinar component invaded into the extraprostatic tissue.
[c] Th resection margin was positive in the acinar component.
[d] Case 4 was lost follow-up.