บทความพิเศษ

Pathologic Diagnosis of Prostatic Adenocarcinoma

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Prostatic adenocarcinoma is the most common malignancy in men in the United States and is the second most common cause of cancer death following lung cancer.[1] It was estimated that approximately 28,660 American men died of this tumor in 2008, while 186,320 new cases were detected.[2] In Thailand, it is among the three most common malignancies in male with an estimated incidence rate as high as 4.9 per 100,000.[3] It is now the most common cancer in men in Siriraj Hos-pital.[4] Latent prostate cancer incidentally found at the time of autopsy is also high, up to 80 % by age 80 years.[5]

Pathologically, the diagnosis of prostatic adenocarcinoma requires a combination of architectural, cytologic, and ancillary findings.[1,6] In the past, the prostate was divided into 5 lobes namely, anterior, middle, posterior, and 2 lateral lobes.[7] In 1988 McNeal introduced a different anatomic division. He devided the prostate into zones, namely peripheral zone (TZ), central zone and transition zone,[8] which was subsequently globally accepted since this zoning correlated better with the deseases of the prostate. The peripheral zone accounts approximately for 65% of normal prostatic volume and is prone to the development of inflammation and adenocar-cinoma,[9,10] while transition zone is responsible for the development of benign prostatic hyperplasia (nodular hyperplasia).[11]

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The most popular method of detection of the prostatic adenocarcinoma, both in early and advanced stages, is transrectal ultrasound-guided core needle biopsy. Introduction of the automatic spring-driver 18-gange core biopsy gun in the late 1980s has provided a simple and better way to obtain adequate prostatic tissue in the peripheral zone for histologic diagnosis. Routinely 12 cores of prostatic tissue are sampled in Siriraj Hospital. Transurethral resection specimens usually consist of prostatic tissue from transition zone and periurethral area. Parts of urethra, bladder neck, and anterior fibromuscular stroma might be included via this method. The central zone and peripheral zone are usually spared. Well-differentiated (low-grade) prostatic adenocarcinomas, which are frequently of small foci, are occasionally found in transition zone, and may be completely removed by this method. High-grade prostatic adenocarcinma found in transurethral resection chips usually represents invasion of the transition zone by peripheral zone tumor. Therefore, transurethral resection is not appropriate for detection of early carcinoma.

Grossly, identification of prostatic adenocarcinoma is of great difficulty or even impossible due to the prominent macroscopic features of nodular hyperplasia, a condition which affects men of the same age group. Some prostatectomics might show small foci of yellow-white tumor which are at least 5 mm. in greatest dimension. (Fig 1) These foci are usually firm in consistency due to desmoplastic reaction in stroma induced by tumor cells. Similar gross lesions may be caused by granulomas and prostatitis. Microscopically, abnormal architectural features can usually be detected at low-power to medium-power magnification and can lead to suspicion of cancer. Malignant acini are usually of small or medium-size and show irregular contours. Acinar size variation and varying spaces between acini are also helpful in diagnosis. Gleason grading system was created by Donale F. Gleason in 1966.[12,13] This system is generally accepted by most uropatho-logists world wide. In 2005, The International Society of Urological Pathology (ISUP) proposed a modified Gleason grading system in the conference on Gleason grading of prostatic adenocarcinoma.[14] An understanding of the Gleason grading system[15] is important in interpretation of small tumor foci.

It is well known that the outer layers of benign

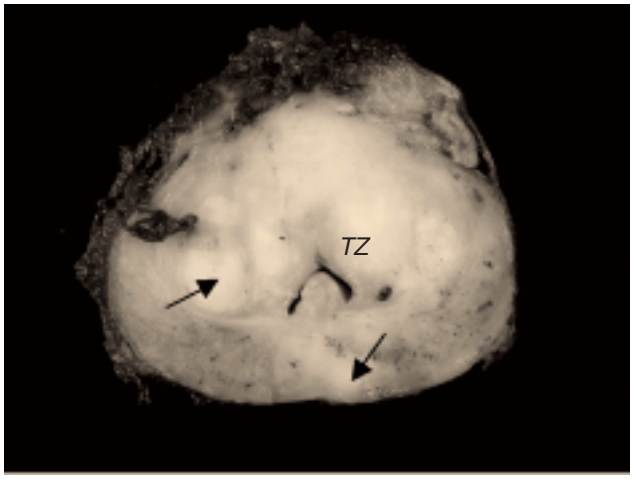

Fig 1. *Gross specimen of radical prostatectomy showing tumor nodules in peripheral zone (arrows) with extension to transition zone. (TZ)*

prostatic acini are lined by epithelial cells called "basal cells." The number of these cells decrease in high-grade prostatic intraepithelial neoplasia (PIN), and they are completely absent in prostatic adenocarcinma.[16,17] The basal cells may be difficult to identify in certain cases by routine hematoxylin- eosin stained sections. Monoclonal antibodies against them can be applied in doubtful cases, particularly in core needle biopsy (the clone 34βE12 is available in most pathology institutes. including Siriraj Hospital). (Fig 2)

Ancillary histologic features are very helpful to assure the diagnosis of prostatic adenocarcinma. Perineural invasion, mucinous fibroplasia (collagenous micronodule), glomerulation, mucin production (intraluminal and extracellular), microvascular invasion, and extra-prostatic extension are features confirming the diagnosis, particularly in needle core biopsy specimens. (Fig 3)[17-21]

Certain normal anatomic structures and embryonic rests can mimic prostatic adenocarcinoma and can cause problem in diagnosis, particularly in core needle biopsy specimens.17 These include seminal vesicles, ejaculatory ducts, Cowper's glands, paraganglionic tissue, mesonephric remnants, and ectopic prostatic tissue of the urethra. Some conditions, namely hyperplasia (benign epithelial hyperplasia, cribriform hyperplasia, clear cell hyperplasia, basal cell hyperplasia, and postatrophic hyperplasia), metaplasia (urothelial metaplasia and nephrogenic metaplasia), atrophic change, inflammation-induced atypia, radiation-induced atypia, adenosis, and selerosing adenosis can also cause confusion.

Androgen deprivation therapy may be applied in some patients with positive core needle biopsy before undergoing radical prostatectomy. Pathologic changes in such cases can make recognition and grading more difficult. Benign and malignant prostatic epithelia are both affected. Typically, acinar atrophy, loss of glandular architecture, nuclear and nucleolar shrinkages, nuclear hyperchromasia and pyknosis, and cytoplasmic enlargement and clearing are commonly present. (Fig 4) [22-24] To the author's experience, at least two ancillary findings can stand

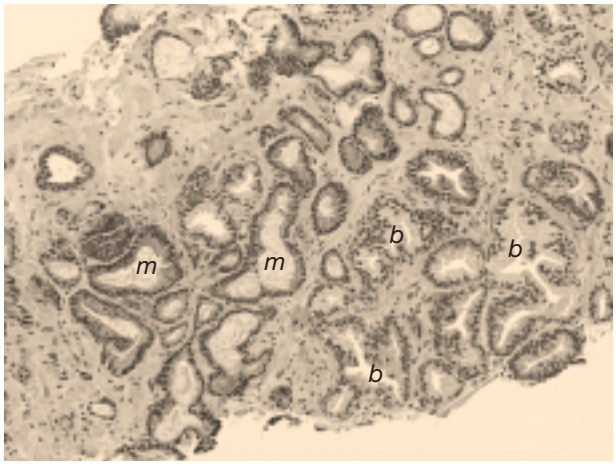

Fig 2A. *Microscopic features of malignant acini (m) showing abnormal arrangement and variation in acinar size. Benign acini (b) are also shown for comparison (H&E, x200).*

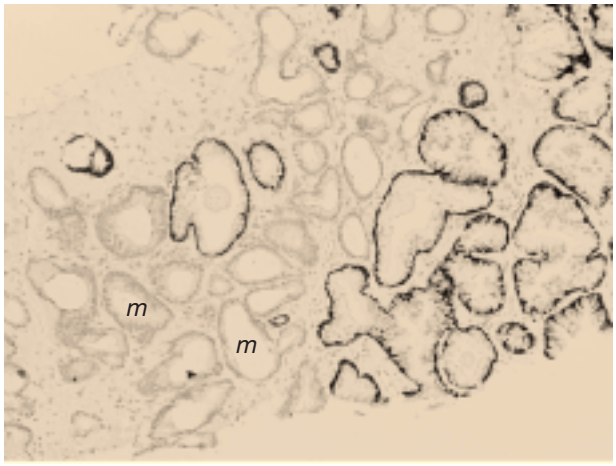

Fig 2B. *Same case showing absence of basal cells in malignant acini (m) by 34βE12 immunostaining. (34βE12 immunostain, x200).*

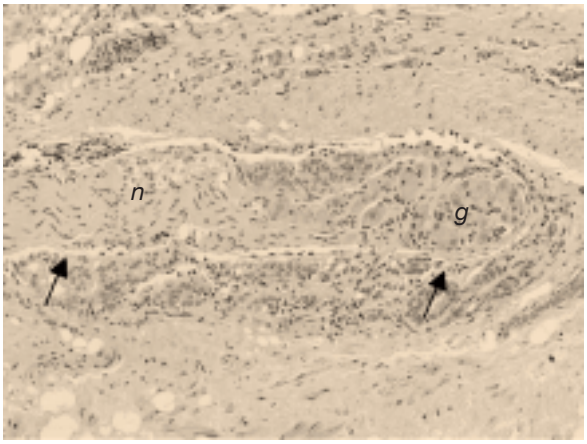

Fig 3A. *Perineural invasion of malignant acini (arrows). A neural ganglion (g) is present in continuation to the involved nerve fiber (n) (H&E, x200).*

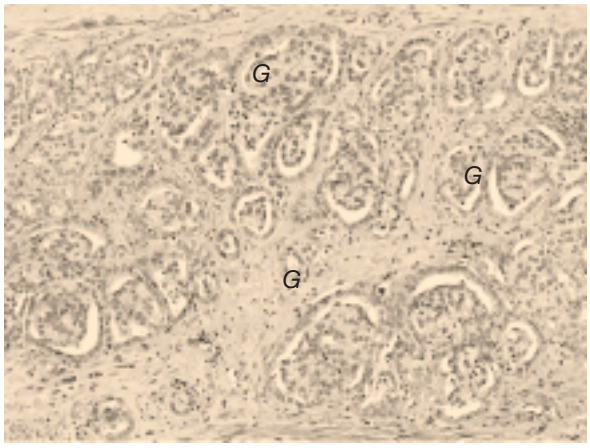

Fig 3B. *Glomerulation (G) of malignant acini (H&E, x200).*

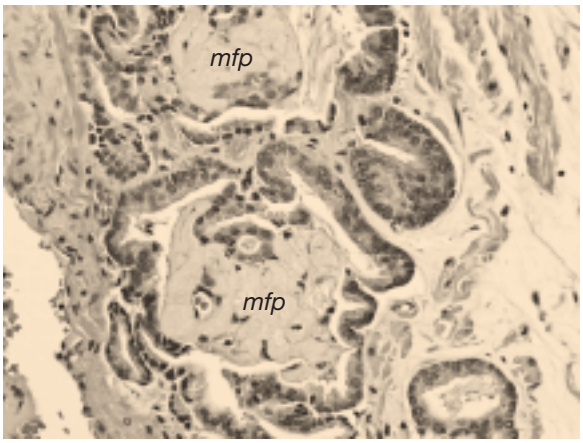

Fig 3C. *Mucinous fibroplasias (mfp) in malignant acini. Note acinophilic material in glandular lumens, only found in malignant glands (H&E, x400).*

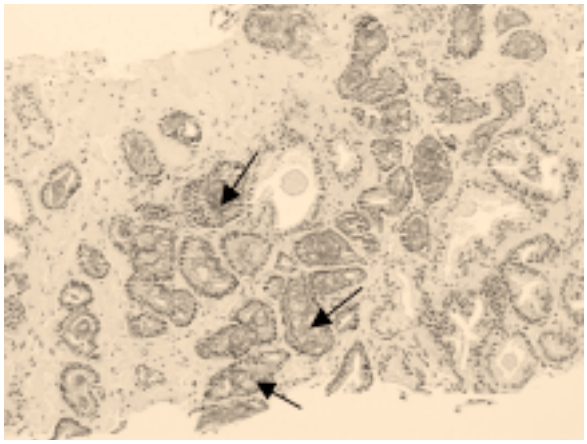

Fig 3D. *Mucin production seen as intraluminal mucicarmine positive secretion in glandular lumens (arrows) (mucicarmine, x200).*

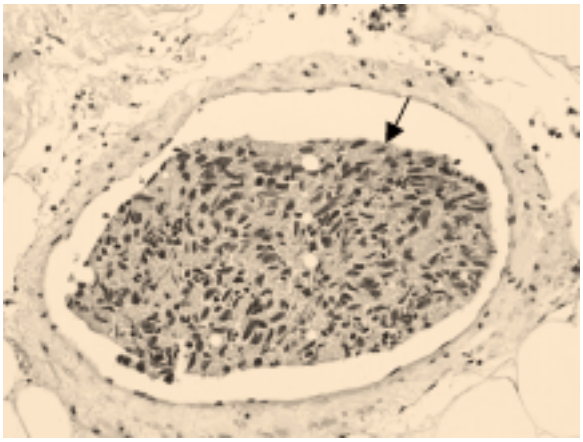

Fig 3E. *Microvascular invasion seen as a relatively large tumor embolus (arrow) in a lymphatic lumen (H&E, x400).*

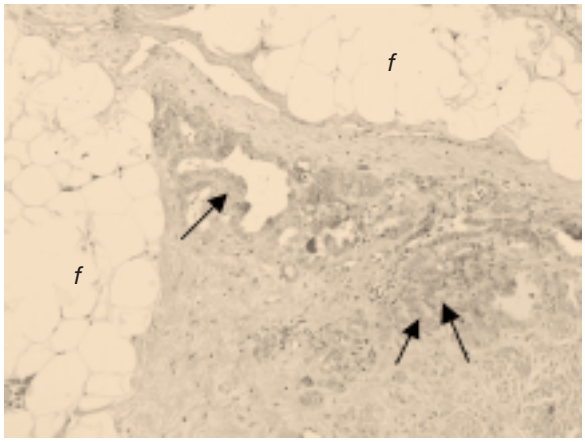

Fig 3F. *Extra-prostatic extension. Note malignant acini (arrows) in connective tissue among periprostatic fat (f) (H&E, x200).*

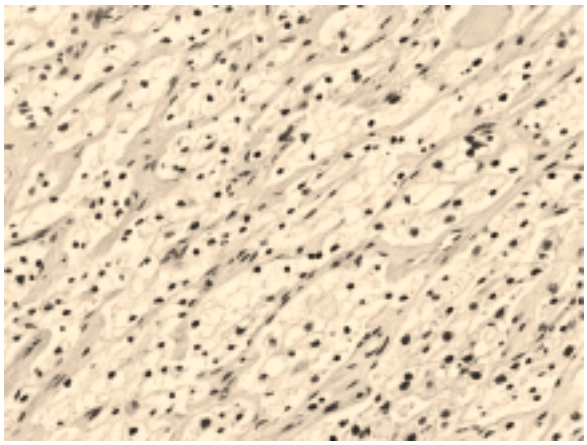

Fig 4A. *Malignant acini obtained from radical prostatectomy specimen with prior androgen deprivation therapy. Note nuclear shrinkage and cytoplasmic enlargement and clearing (H&E, x400).*

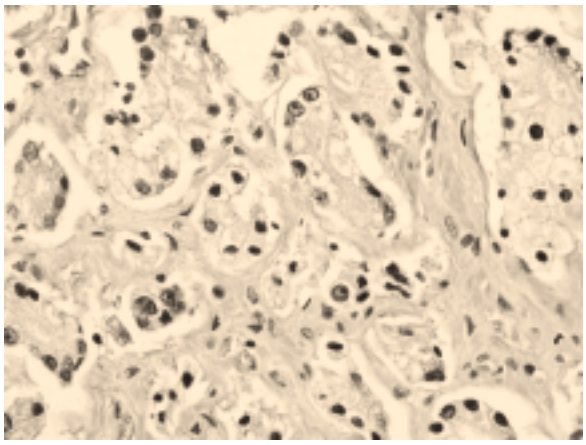

Fig 4B. *Nuclear and nucleolar shrinkages of malignant acini following antiandrogen therapy. (H&E, x600).*

antiandrogen therapy, and if present, are very useful to encourage the diagnosis. These include perineural invasion and mucin production (Fig 5). The therapy also affects non-neoplastic prostatic tissue, resulting in prominent acinar atrophy, decreased ratio of acini to stroma, squamous metaplasia, and stromal edema and fibrosis.[22] Grading of tumor is more reliable on previous core needle biopsy. Nevertheless, the attending pathologists should be informed about the treatment when examining radical prostatectomy specimens.

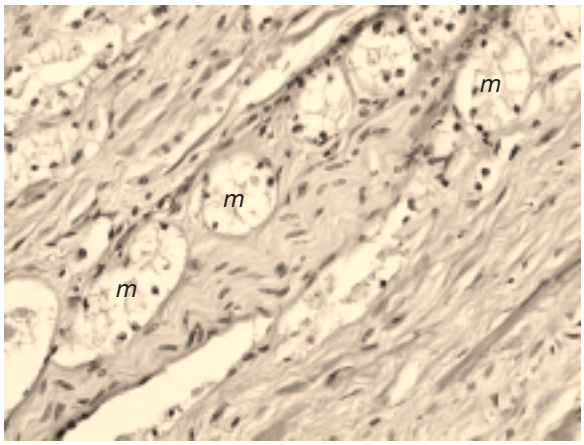

Fig 5A. *Perineural invasion by malignant acini (m) after antiandrogen therapy. Note nuclear shrinkage and cytoplasmic enlargement and clearing (H&E, x600).*

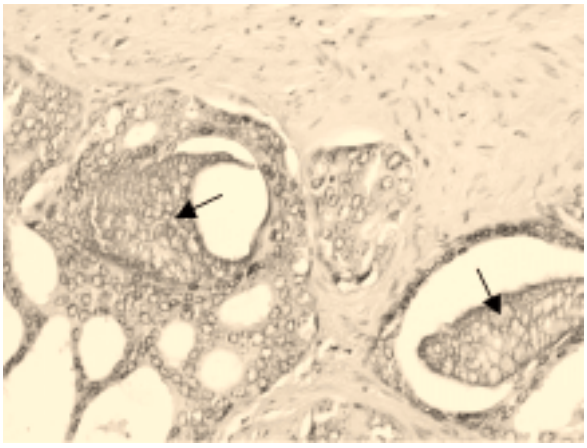

Fig 5B. *Intra-luminal mucin (arrows) in malignant acini after therapy. (muxicarmine stain, x600).*

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