Miscellaneous Rare Tumours of the Prostate Gland

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CHAPTER 1

ADENOCARCINOMA OF THE PROSTATE GLAND: A PREAMBLE OVERVIEW INTRODUCTION TO MISCELLANEOUS RARE TUMOURS OF THE PROSTATE GLAND

BLURB

Adenocarcinoma of the prostate gland is the most common type of cancer of the prostate gland. Nevertheless, there are other rare types of malignant neoplasms of the prostate gland which clinicians should know about. In order to understand various features of rare types of prostate cancer, it is important for all clinicians to have a clear understanding of the more common adenocarcinoma of the prostate gland. The ensuing article has detailed out various aspects of adenocarcinoma of the prostate gland.

ABSTRACT

Carcinoma of the prostate gland is the most common non-cutaneous cancer in men, which gives the diagnosis and staging of this cancer great medical and public interest. Even though adenocarcinoma of the prostate gland could be slow growing, the disease, nonetheless, accounts for more than 10% of cancer-related deaths in males, with tens of thousands of men dying of prostate cancer each year. Apart from pure adenocarcinoma of the prostate gland, which is the most common sub-type of prostate cancer, other cell-types of prostate cancer which portend aggressive clinical and biochemical behaviour and associated with poor prognosis do exist. Diagnosis of these rare types of prostate cancer at times had tended to be delayed or misdiagnosed. Furthermore, some of these cell types of rare prostate cancer are not associated with raised levels of serum prostate specific antigen (PSA) unlike the more common pure adenocarcinoma of the prostate gland. Diagnosis of these rare subtypes of prostate cancer

requires utilisation of various types of antibodies for immunohistochemistry staining studies, usually not used for the diagnosis of pure adenocarcinoma of the prostate gland. The treatment options for the majority of rare sub-types of prostate cancer is different from the treatment options for pure adenocarcinoma of the prostate gland. The ensuing chapters in the book have detailed out extensively the manifestations, diagnostic features, treatment, as well as outcome of these rare tumours. Recommendations regarding research, as well as development of new and effective medicaments for the treatment of these rare tumours that would ensure the patients remain alive for longer periods, would be advised. Meanwhile, all clinicians need to know a lot about the more common pure adenocarcinoma of the prostate gland before learning about the rare sub-types of prostate cancer. This chapter has been devoted to the presentation of a background preamble of information on pure primary adenocarcinoma of the prostate gland.

INTRODUCTION

Adenocarcinoma of the prostate gland is the most common type of prostate cancer that afflicts men all over the world. Nevertheless, there are rare types of prostate cancer which tend to be reported sporadically through out the world. Before learning and updating knowledge about rare types of prostate cancer, it would be important that clinicians are up to date with their bird's eye view information and knowledge about adenocarcinoma of the prostate gland.

Prostate cancer is stated to be the most common non-cutaneous cancer in men, making the diagnosis and staging of this cancer of great medical and public interest [1]. Even though prostate cancer could be slow growing, the disease, nonetheless, has been iterated to account for more than 10% of cancer-related deaths in males, with tens of thousands of men dying of prostate cancer each year [1].

Screening for adenocarcinoma of the prostate gland, with testing for serum prostate specific antigen (PSA) level assessment and sometimes digital rectal examination (DRE), could identify asymptomatic cases and enable early diagnosis of the neoplasm. Nevertheless, there is controversy regarding screening for prostate cancer. Testing for serum PSA levels would not help identify a number of the rare sub-types of prostate cancer.

The ensuing documentation contains an overview about adenocarcinoma of the prostate gland as a preamble to the book on rare malignant tumours

of the prostate gland, which have been narrated in detail in the subsequent chapters of the book.

KEY WORDS: Adenocarcinoma of prostate; Prostate cancer, Common type; Rare type; Screening; Serum prostate specific antigen; Prostate biopsy; Digital rectal examination; Histopathology; Immunohistochemistry; Molecular and cytogenetics studies; Hormonal treatment; Radiotherapy; Chemotherapy; Recurrence; Metastases.

AIM

To review and update the literature generally on prostate cancer.

METHOD

Internet data bases were searched including Google; Google Scholar; Yahoo; and PUBMED. The search words that were used included: prostate cancer; adenocarcinoma of prostate; carcinoma of prostate; and prostatic cancer. Thirty-five (35) references were identified which were used to write up the overview preamble documentation on adenocarcinoma of prostate and prostate cancer general information.

OVERVIEW OF ADENOCARCINOMA OF PROSTATE GLAND

Definition/general statements [2]

- Adenocarcinoma of the prostate gland is the most common malignancy of the prostate gland [2].
- Adenocarcinoma of prostate gland does originate from prostatic secretory epithelium [2].

Essential features of adenocarcinoma of the prostate gland [2]

- It has been pointed out that clinical and radiology imaging features are neither sensitive nor specific for confirmation of the diagnosis of adenocarcinoma of the prostate gland [2].
- Adenocarcinoma of the prostate gland has often been diagnosed based upon pathology examination of non-targeted needle biopsies investigating raised serum prostate specific antigen (PSA) levels in men [2].

- It has been pointed out that absence of basal cell layer is a pathognomonic histological feature of adenocarcinoma of the prostate gland [2].
- It has been iterated that: pathognomonic diagnostic features of adenocarcinoma of the prostate gland, include the following: circumferential perineural invasion, glomerulations and collagenous micronodules (mucinous fibroplasia) [2].
- It has been stated that other histopathology examination features of adenocarcinoma of the prostate gland include the following: pathological features: infiltrative architecture, nucleolar prominence, amphophilic cytoplasm and some intraluminal contents (crystalloids, blue mucin, pink amorphous material) [2].

Terminology

The terminologies that have been utilised for adenocarcinoma of the prostate gland has been summated as follows: [2]

- Prostate cancer
- Prostate adenocarcinoma
- Subtypes of prostatic adenocarcinoma include: acinar adenocarcinoma, ductal adenocarcinoma, atrophic adenocarcinoma, pseudo-hyperplastic adenocarcinoma, microcystic adenocarcinoma, foamy gland adenocarcinoma, mucinous adenocarcinoma, signet ring variant of adenocarcinoma, pleomorphic giant cell adenocarcinoma, sarcomatoid adenocarcinoma

Epidemiology

The epidemiology of adenocarcinoma of the prostate gland have been summated as follows: [2]

- Adenocarcinoma of the prostate gland is the second most common cancer and second leading cause of cancer related death in American men [3].
- Ninety-two percent (92%) of United States of America (U.S.A) cases of adenocarcinoma of the prostate gland tend to be diagnosed in men who are older than 55 years, and 19.5% in men who are older than 75+ years [3].
- It has been stated that adenocarcinoma of the prostate gland is found at autopsy in 40% of men who are more than 60 years of age. [4]

- It has been iterated that incidental adenocarcinoma of the prostate gland has been reported in about 25% of cystoprostatectomies which has been undertaken for the treatment of urinary bladder cancer [5].
- It has been iterated that globally, highest age standardised rates of adenocarcinoma of the prostate gland have been documented in Oceania, North America, Europe [6].
- It has been pointed out that lower rates of adenocarcinoma of the prostate gland have been documented within developing countries. Which might be due to different screening programs and diagnostic pathways [2].
- It has been documented that there is a higher incidence of adenocarcinoma of the prostate gland in men of African heritage [6].

Sites

The sites of adenocarcinoma of the prostate gland have been summated as follows: [2]

- Majority of adenocarcinomas of prostate gland are multifocal [7].
- 75% to 80% of adenocarcinomas of the prostate gland are found within the posterior/posterolateral peripheral zone of the prostate gland [2].
- About 13% to 20% of adenocarcinomas of the prostate gland are found within the transition (periurethral) zone [8] [9].
- It has been iterated that most clinically significant adenocarcinomas of the prostate gland arise within the peripheral zone that is sampled by needle biopsies [2].
- It has been iterated that transition zone adenocarcinoma of the prostate gland is associated with favourable pathology features and better recurrence free survival [10].
- It has been iterated that adenocarcinoma of the prostate gland less frequently involves the anterior prostate most likely due to inadequate sampling using standard biopsy approach [11].

Pathophysiology [2]

The pathophysiology of adenocarcinoma of the prostate gland has been summated as follows: [2]

- Germline variants can increase risk of adenocarcinoma of the prostate gland.
- Somatic mutations in genes such as *ERG, ETV1/4, FLI1, SPOP, FOXA1, IDH1, PTEN, TP53, MYC, CDH1* has been documented in individuals who had been afflicted by adenocarcinoma of the prostate gland [12] [13].
- The most common somatic genomic rearrangement which has been reported in individuals afflicted by adenocarcinoma of the prostate gland is fusion of the androgen regulated gene *TMPRSS2* with a member of the *ETS* transcription family [13].

Aetiology [2]

The aetiology of adenocarcinoma of the prostate gland has been summated as follows: [2]

- Obesity increases the risk of adenocarcinoma of the prostate gland [14].
- Nonmodifiable risk factors for the development of adenocarcinoma of the prostate gland include the following: age, race and family history: [15]
    - Genetic susceptibility to adenocarcinoma of the prostate gland has been linked to African heritage [15].
    - Increased risk for the development of adenocarcinoma of the prostate gland is stated to exist with first degree relatives who have prostate cancer [15].
    - *BRCA2* mutations has been stated to increase the risk by 5-fold; *BRCA2* associated cancers has been iterated to occur at a lower age and have worse survival outcomes [13] [16].
    - Additional germline variants associated with increased cancer risk has been stated to occur in *HOXB13* [13].
    - Increased risk for the development of adenocarcinoma of the prostate gland has been reported in association with Lynch syndrome [17].
- Numerous single nucleotide polymorphisms (SNPs) that have a low to moderate effect on risk / progression of adenocarcinoma of the prostate gland has been identified [18].

- It has been documented that high levels of IGF1 may confer increased risk for the development of adenocarcinoma of the prostate gland [19].

Clinical features [2]

The manifestations of adenocarcinoma of the prostate gland, has been summated as follows: [2]

- Adenocarcinoma of the prostate gland is generally asymptomatic unless locally advanced or metastatic [2].
- Adenocarcinoma of the prostate gland is often diagnosed pursuant to investigation of non-specific lower urinary tract symptoms [2].
- Digital rectal examination (DRE): the prostate gland may feel normal or may be enlarged/asymmetrical/hard/have a palpable nodule present [2].

Diagnosis [2]

The diagnosis of adenocarcinoma of the prostate gland has been summated as follows: [2]

- Generally, adenocarcinoma of the prostate gland is diagnosed by pathology examination of systematic transrectal ultrasound guided prostate biopsy specimens [2].
- Trans-perineal needle biopsies of the prostate gland are increasingly being used as the biopsies tend to be associated with lower risk of infection [2].
- Pre-biopsy MRI scan of the prostate gland, followed by systematic biopsies supplemented with targeted biopsies from any radiological abnormality, leads to better identification of clinically significant prostate cancer than systematic prostate biopsy alone [20].
- Incidental prostate cancer has sometimes tended to be diagnosed in transurethral resection of prostate (TURP) specimens. [2]
- Immunohistochemistry with basal cell markers (HMWCK, p63) and AMACR are used to establish the diagnosis in equivocal cases [2].

Laboratory tests [2]

The ensuing iterations have been made about laboratory tests in adenocarcinoma of the prostate gland: [2]

- Raised serum PSA prompts clinicians to investigate for adenocarcinoma of the prostate gland [2].
- Different serum PSA cutoffs have been used to prompt the undertaking of prostate needle biopsy [2].
- It has been iterated that age specific cutoffs, PSA velocity (rate of change in PSA over time) and PSA density (PSA per unit prostate volume - ng/mL/cc), may increase sensitivity and specificity of PSA testing [2] [21].
- It has been pointed out that U.S.A. Preventative Services Task Force (USPSTF) has recommended against serum PSA based screening for prostate cancer in men who are 70 years old and older and that: [2]
    - For men aged 55 - 69 years, the undertaking of periodic PSA based screening should be an individual choice.
    - Screening in this age group offers a small potential benefit of reducing the chance of death from prostate cancer in some men; however, many men will experience potential harm [21].
- American Urological Association (AUA) does not recommend PSA screening in men under age 40 years or in men aged 40 - 54 years at average risk: [2]
    - For men age 55 - 59 years, shared decision making is desirable.
    - For men aged 70 years and over or men with < 10 - 15 -year life expectancy, PSA screening is not recommended [22].
- It has been stated that a potential urine biomarker for prostate cancer is PCA3 [2] [13].

Radiology description [2]

Summations which have been made regarding radiology imaging in adenocarcinoma of the prostate gland include the following: [2]

- Ultrasound scan (USS) generally is used to guide prostate biopsies; prostate cancer may appear hypoechoic but USS is neither sensitive nor specific [2].
- Multiparametric MRI scan is commonly used for local tumour staging; and it may also be used to identify abnormalities for targeting during prostate biopsy [2].
- MRI scan abnormalities are generally reported using either PI-RADS (Prostate Imaging - Reporting and Data System) or Likert score [2].
- CT scan is utilised to identify metastatic disease in lymph nodes [2].
- Isotope Bone scan is utilised to detect bony metastases in prostate cancer [2].
- PET / CT scan is utilised to detect micro-metastatic disease in selected patients, such as men with raised serum PSA levels after treatment [2].

Prognostic factors [2]

Summations which have been made regarding prognostic factors associated with adenocarcinoma of the prostate gland include the following: [2]

- Biopsy results: tumour extent (mm or percentage core involvement), grade (Gleason score and grade group), perineural invasion, extra-prostatic extension [2].
- Radical prostatectomy specimen findings: tumour size, Gleason score and grade group, stage, margin status [2].
- Cribriform morphology and intraductal carcinoma associated with invasive prostate cancer are adverse prognostic indicators [2] [23].
- Small cell carcinoma component is associated with aggressive behaviour and treated differently [2].
- Some expert groups recommend incorporating intraductal component into the Gleason score while others recommend reporting it separately in a comment [2] [24] [25] [26].

Treatment [2]

Summations which have been made regarding treatment in adenocarcinoma of the prostate gland include the following: [2]

- Pre-operative risk stratification of primary adenocarcinoma of the prostate gland is based upon serum PSA, clinical stage, biopsy parameters (tumour extent, grade, cribriform morphology, intraductal carcinoma, perineural invasion) [2].
- Primary treatment options are based upon pre-operative risk stratification including the ensuing: [2]
    - Active surveillance
    - Focal therapy (cryotherapy, high intensity ultrasound)
    - Radical prostatectomy
    - Brachytherapy
    - External beam radiotherapy
    - Hormone therapy (e.g., luteinizing hormone releasing hormone [LHRH] analogues, antiandrogens)
    - Orchidectomy (rare in contemporary practice)
    - Chemotherapy (for metastatic disease)
- Postprostatectomy options: [2]
    - Generally, PSA monitoring and early salvage therapy if rising serum PSA
    - Less commonly adjuvant therapy for high stage disease or margin positivity

Macroscopy gross description [2]

Summations which have been made regarding gross examination of specimens of adenocarcinoma of the prostate gland include the following: [2]

- Adenocarcinoma of prostate gland is often grossly inapparent [2].
- Adenocarcinoma of prostate gland may form a cream mass [2].

Microscopic (histopathology examination) description [2]

Summations which have been made regarding microscopy examination of specimens of adenocarcinoma of the prostate gland include the following: [2]

- Gleason grading is based on the architecture of the tumour. [2]
- Gleason grades represent a morphological spectrum from well-formed glands (pattern 3), to increasingly complicated glandular proliferations (pattern 4), to almost no glandular differentiation (pattern 5) [2] [27].

- Glandular crowding and infiltrative growth pattern tend to be visualised [2].
- Nuclear enlargement, and nucleolar prominence tend to be visualised [2].
- Round generally monomorphic nuclei tend to be visualised [2].
- Amphophilic cytoplasm tends to be visualised [2].
- Mitoses tend to be visualised [2].
- Apoptotic bodies tend to be visualised upon microscopy examination in specimens of adenocarcinoma of the prostate gland [2].
- Stromal desmoplasia tends to be seen during microscopy examination of specimens of adenocarcinoma of the prostate gland [2].
- Intraluminal contents: crystalloids, pink amorphous secretions, and blue mucin are visualised during microscopy examination of specimens of primary adenocarcinoma of the prostate gland [2].
- Glomerulations, collagenous micronodules (mucinous fibroplasia) tend to be visualised during microscopy examination of specimens of adenocarcinoma of the prostate gland [2].
- Demonstration of absence of basal cell layer in specimens of adenocarcinoma of the prostate gland has been stated to generally require immunohistochemical confirmation [2] [28].

Cytology examination description [2]

Summations which have been made regarding cytology examination of specimens of adenocarcinoma of the prostate gland include the following: [2]

- It has been iterated that urine cytology for detecting prostate cancer has a very low sensitivity [2] [29].
- It has been iterated that urine cytology is not utilised clinically in the diagnosis of prostate cancer [2].
- It has been documented that fine needle aspiration (FNA) of metastatic prostate cancer to a lymph node may show microacinar complexes/cell clusters/single cells with fragile cytoplasm and prominent nucleoli [2] [30].

Positive stains

Summations which have been made regarding positive immunohistochemistry staining studies in adenocarcinoma of the prostate gland include the following: [2]

Adenocarcinoma of prostate tumour cells tend to exhibit positive staining upon immunohistochemistry staining studies to the following tumour markers: [2]

- **PSA**
- **NKX3.1**
- **AMACR** (P504S, racemase)
- **Prostein** (P501S)
- **PSMA**

Rare tumours may have aberrant expression of:

- p63 [2] [31] [32]

Negative stains [2]

Summations which have been made regarding negative immunohistochemistry staining studies in adenocarcinoma of the prostate gland include the following: [2]

Adenocarcinoma of prostate tumour cells tend to exhibit negative staining upon immunohistochemistry staining studies to the following tumour markers: [2]

- **CK7**
- **CK20**
- High molecular weight cytokeratins **(34 beta E12, CK5, CK5/6**)
- **p63**
- **CDX2**
- **GATA3**
- **TTF1** [31]

Molecular/cytogenetics description [2]

Summations which have been made regarding molecular/cytogenetics features associated with adenocarcinoma of the prostate gland include the following: [2]

- Prostate cancer is stated to be a heritable disease. [2]
- A family history of a first degree relative with prostate cancer is stated to increase the risk of developing prostate cancer by 2-fold [2] [33].
- 30 - 40% of familial risk for the development of adenocarcinoma of the prostate gland has been stated to be due to genetic factors [2] [33].
- Genetic factors associated with the development of adenocarcinoma of the prostate gland has been iterated to include highly penetrable rare variants and more common low to moderate risk variants [2] [33].
- It has been stated that highly penetrant variants of adenocarcinoma of prostate gland occur in *BRCA2* and *HOXB13* [2].
- It has been stated that over 280 SNPs have been identified as prostate cancer risk factors [2] [33].
- It has been iterated that for most SNPs, the molecular mechanism of prostate cancer association is generally unknown, as they occur in noncoding regions of the genome [2] [33].
- It has been stated that in adenocarcinoma of the prostate gland cases, somatic mutations do occur within genes such as *ERG, ETV1/4, FLI1, SPOP, FOXA1, IDH1, PTEN, TP53, MYC, CDH1* [2] [33] [34].
- It has been documented that most common somatic genomic rearrangement that occurs in cases of adenocarcinoma of the prostate gland, is fusion of the androgen regulated gene *TMPRSS2* with a member of the *ETS* transcription family [2] [33].
- It has been stated that somatic mutation profiles of prostate cancer are associated with clinical and pathological outcomes and: [2].
    - There are 7 major subtypes, which are defined by either specific gene fusions of *ETS* transcription family members (*ERG, ETV1, ETV4* and *FLI1*) or mutations (*SPOP, FOXA1, IDH1*) [2] [35].
- It has also been stated that different subtypes have different molecular profiles, for example: [2] [35]

- *ETS* subset (59% of cases) are enriched in *PTEN* mutations.
- *SPOP* mutant subset (11%) of cases have distinct somatic copy number alteration profiles, including deletions of *CHD1*, 6q, and 2q.

❖ Radical prostatectomy: Pathology examination features and grading scoring in specimens of primary adenocarcinoma of the prostate gland have been summated as follows: [2]

- Histological tumour type: acinar adenocarcinoma [2]
- Gleason score: [2]
  - Primary Gleason grade: 3
  - Secondary Gleason grade: 3 [2]
  - Tertiary Gleason grade (< 5%): is not applicable. [2]
  - Gleason score: 3+3=6 [2]
  - Grade group: 1 [2]
- Location of dominant tumour: right apex [2].
- Extra-prostatic extension: not identified [2].
- Bladder neck: not involved [2].
- Seminal vessels: not involved [2].
- Margin status: not involved [2].
- Lympho-vascular invasion: not identified [2].
- Regional lymph node status: [2]
  - Number of nodes examined: 9
  - Number of positive lymph nodes: 0
- Primary tumour: pT2 pN0 [2].

Differential diagnoses [2]

Summations which have been made regarding the differential diagnoses of primary adenocarcinoma of the prostate gland include the following: [2]

❖ Benign prostate tissue: [2]

- Pale cytoplasm
- Corpora amylacea
- No other intraluminal contents
- Basal cell marker immunoreactivity

❖ Prostatic atrophy: [2]

- Lobular architecture

- Scant cytoplasm
- Basal cell marker immunoreactivity

❖ **Adenosis: [2]**
- Lobular architecture
- Basal cell marker immunoreactivity (often scattered)

❖ **Atypical small acinar proliferation (ASAP)**: [2]
- Small size
- Lack of significant cytological atypia, including a lack of macro-nucleoli

❖ **High grade prostatic intraepithelial neoplasia**: [2]
- Less architectural atypia
- Maintained basal cells

❖ **Post-atrophic hyperplasia**: [2]
- Some glands atrophic
- Basal cell marker immunoreactivity (often scattered)

❖ **Partial atrophy**: [2]
- Atrophic glands with abundant lateral pale cytoplasm
- Irregularly distributed nuclei
- Basal cell marker immunoreactivity (often scattered)

❖ **Radiation atypia: [2]**
- Glandular atrophy
- Nuclear irregularity and pleomorphism
- Atypical stromal cells
- Basal cell marker immunoreactivity

❖ **Urothelial carcinoma: [2]**
- Nuclear irregularity and pleomorphism
- Hyaline dense eosinophilic cytoplasm
- Desmoplastic stromal reaction
- Immunoreactivity for urothelial markers (**GATA3, CK7, p63,**)
- No expression of prostatic immunomarkers (**PSA, PSAP, NKX3.1**)

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CHAPTER 2

SPECIMENS: PIN-LIKE ACINAR ADENOCARCINOMA OF THE PROSTATE GLAND

BLURB

Adenocarcinoma of the prostate gland is the most common prostate gland malignant neoplasm that afflicts individuals all over the world. Nevertheless, it is important for all clinicians and patients to know that other types of malignant lesions of the prostate gland are sporadically reported throughout the world. PIN-like adenocarcinomas of the prostate gland are rare tumours of the prostate gland that are typified by crowded, and often, cystically dilated glands, that architecturally simulate high-grade prostatic intraepithelial neoplasia and which are lined by malignant pseudo-stratified columnar epithelium. The ensuing article has detailed out features of PIN-like adenocarcinoma of the prostate gland, that clinicians should know about, to enable them to appreciate the differences between this rare tumour and the more common adenocarcinoma of the prostate gland.

ABSTRACT

PIN-like adenocarcinomas of the prostate gland are rare tumours of the prostate gland that are typified by crowded, and often, cystically dilated glands, that architecturally simulate high-grade prostatic intraepithelial neoplasia and which are lined by malignant pseudo-stratified columnar epithelium. Overall, PIN-like carcinoma tumours tend to be limited in size, not advanced in stage, and not associated with high-grade cancer upon radical prostatectomy, and they do demonstrate low rates of Gleason pattern 4 and TMPS-ERG rearrangement. The tumours tend to be graded as Gleason 3+3 = 6. Diagnosis of PIN-like ductal adenocarcinoma of the prostate gland has tended to be diagnosed following pathology examination of specimens of the prostate gland, which had been obtained from prostate biopsy specimens, trans-urethral resection of prostate gland

specimens or prostatectomy specimens. Cases of PIN-like adenocarcinoma of the prostate gland that are diagnosed would tend to be localised tumours that would portend an indolent biological behaviour with no subsequent development of metastasis; however, if the PIN-like adenocarcinoma of the prostate gland is associated contemporaneously with a synchronous acinar ductal adenocarcinoma or another variant subtype of prostate cancer, then the prognosis would be dependent upon the synchronous prostate cancer. The symptoms of PIN-like carcinomas of the prostate gland tend to be non-specific and the diagnosis has tended to be incidental findings. Because of the low-grade, localised, small-size of PIN-like ductal carcinomas of the prostate and the fact that metastasis development of metastasis has not been reported in association with the pure form of the tumour, a patient who has been diagnosed with a pure form of the tumour could be managed by active surveillance initially, which would therefore preserve the prostate gland. In addition, pure PIN-like adenocarcinoma of the prostate gland can be managed by all treatment options, some of which include: active surveillance, hormone treatment, radiotherapy, prostatectomy, cryotherapy, irreversible electroporation, radiofrequency ablation of the tumour, selective prostate artery angiography, and super-selective embolisation of the branch of the prostate artery, supplying the prostate cancer with regular follow-up assessments of the treated patients. Longer term studies will be necessitated in order ascertain further information related to PIN-like adenocarcinoma of the prostate gland.

KEY WORDS: PIN-like acinar ductal carcinoma of prostate; Biopsy of prostate; Incidental; Trans-urethral resection of prostate; Prostatectomy; Indolent behaviour; Gleason 6+6; Active surveillance; Serum prostate specific antigen; Histopathology; Microscopy; Immunohistochemistry; Molecular and cytogenetics studies; Cytology.

INTRODUCTION

Kaur et al. [1] stated the following:

- Prostatic ductal adenocarcinoma is an aggressive morphological sub-type typified by pseudostratified, tall columnar epithelium with variable architectural patterns.
- It has been stated that conventional ductal carcinomas which are composed of papillary and cribriform patterns behave clinically like Grade Group 4 acinar tumours of the prostate gland and they are frequently associated with high grade acinar carcinomas [2].

- Genomic analyses had demonstrated that ductal and acinar adenocarcinoma likely have a common origin when both morphologies are present [3] [4].
- Ductal foci accrue additional alterations leading to frequent activation of targetable pathways such as PI3K- or WNT-signalling, based upon early or late divergence from coincident acinar foci [4] [5].
- It has been previously demonstrated that *TMPRSS2-ERG* gene fusions and PTEN loss are less common in ductal carcinoma compared to acinar adenocarcinoma [3] [6].
- Ductal carcinomas also have frequent pathogenic germline alterations of DNA repair genes, congruent with their aggressive clinical behaviour and which indicated that some may respond to immunotherapy [7] [8].
- Prostatic intraepithelial neoplasia (PIN)-like ductal carcinoma, is a rare tumour, typified most commonly by cystically dilated glands lined by pseudostratified columnar epithelium with flat and tufted architecture simulating high-grade prostatic intraepithelial neoplasia (PIN) but lacking basal cells. This entity was first reported by Hameed and Humphrey with an incidence of 1.3% in biopsies [9]. In seminal early studies, these tumours had been referred to as or were termed "PIN-like ductal" due to the overlapping cytological features with conventional ductal adenocarcinoma [10]. Though molecular characterisation has been limited, their institution reported that PIN-like ductal carcinomas do have lower rates of ERG expression and PTEN loss, similar to what is visualised in conventional ductal carcinoma [6] [11].
- Clinically, nevertheless, PIN-like ductal carcinomas do behave relatively indolently, similar to Grade Group 1 acinar tumours, in stark contrast to the aggressive clinical course which had been reported for the majority of conventional ductal carcinomas [10] [11].

Considering that not many cases of PIN-like carcinoma of the prostate gland have been reported in the literature, it would be envisaged that majority of clinicians globally would not have encountered a case of this tumour before. This article on primary PIN-like adenocarcinoma of the prostate gland has been divided into two parts: (A) Overview, which has discussed the general overview aspects of PIN-like ductal carcinoma of the prostate gland; and (B) Miscellaneous narrations and discussion from

some case reports, case studies and studies related to Primary PIN-like adenocarcinoma of the prostate gland.

AIM

To review and update the literature on PIN-like ductal carcinoma of the prostate gland.

METHODS

Internet data bases were searched including: Google; Google Scholar; Yahoo; and PUBMED. Search words that were used included: PIN-like ductal carcinoma of prostate; PIN-like adenocarcinoma of prostate; prostatic PIN-like adenocarcinoma. Fourteen (14) references were identified which were used to write the article which has been divided into two parts: (A) Overview which has discussed the general overview aspects of PIN-like ductal carcinoma of the prostate gland and (B) Miscellaneous narrations and discussion from some case reports, case studies and studies related to primary PIN-like adenocarcinoma of the prostate gland.

[A] OVERVIEW

Definition/general statements [12]

- It has been iterated that PIN-like adenocarcinoma is a subtype of prostatic adenocarcinoma which exhibits prostatic intraepithelial neoplasia (PIN) type architecture with single and separate glands that display tufted, flat, or micropapillary growth and often cystic glandular dilatation [9] [10] [11].
- It has been stated that the neoplastic glands simulate PIN with pseudostratified epithelium but without basal cells and frequently with glandular crowding

Essential features

The essential features of the prostate gland in PIN-like adenocarcinoma of the prostate gland has been summated as follows**: [12]**

- PIN-like adenocarcinoma of the prostate gland can simulate high grade PIN, but unlike high grade PIN, the glands could be crowded or cystically dilated and of critical importance. PIN-like glands completely lack basal cells [12].