

Ductal Adenocarcinoma of the Prostate- from Endometriod Cancer to Today

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Abstract

Ductal adenocarcinoma of the prostate is a rare variety of the common acinar adenocarcinoma. It usually presents with obstructive symptoms and at cystoscopy is seen as an exophytic lesion at the area of the verumontanum. It accounts for less than 1% of all prostate cancers.

We present the case of a 53 year old male who was diagnosed with ductal adenocarcinoma of the prostate after undergoing elective transurethral resection of the prostate. Immunohistochemistry confirmed the nature of the tumour. The patient underwent a radical prostatectomy, however histopathology showed extensive extraprostatic extension.

Men with prostatic ductal adenocarcinoma have a worse prognosis than men with prostatic acinar adenocarcinoma thus, early diagnosis and aggressive management is indicated, even with low-volume metastatic disease.

Keywords: Ductal adenocarcinoma; Endometriod carcinoma; Prostate; Acinar

Introduction

Ductal carcinoma of the prostate is a relatively rare subtype of prostate cancer. First described almost 40 years ago, ductal prostate cancer was thought to have arisen from the prostatic utricle in the form of a mullerian ductal structure; however, immunohistochemistry studies have since shown that it arises from the prostatic ducts [1].

Ductal adenocarcinoma often involves the central ducts of the gland and may present as an exophytic papillary lesion in the prostatic urethra. The tumour presents in elderly men with haematuria or obstructive symptoms [2]. For this reason, they are often seen in Transurethral Resection (TUR) specimens and at Radical Prostatectomy (RP), and are less often found in needle biopsies.

Case Report

We present the case of a 53 year old male who was referred electively for a Transurethral resection of the Prostate (TURP) for significant lower urinary tract symptoms. His International Prostate Symptom Score was 26 out of 35. On examination, he had an enlarged, benign prostate with a volume of 64 cc on ultrasound. His PSA was 14.7 ug/L.

The patient then had a rigid cystoscopy and tri-lobar TURP. The histological examination of the prostate sections showed areas of cribriform growth patterns with cells tending to be columnar in shape. Immuno histochemical staining showed surrounding basal cells in

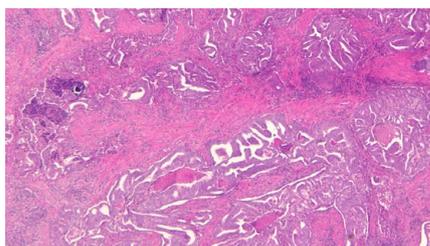
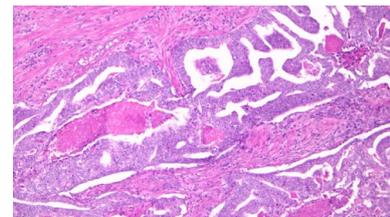


Figure 1: Ductal adenocarcinoma with cribriform growth pattern.



CT Scan pelvis: no evidence of extracapsular extension of tumour

Figure 2: Ductal adenocarcinoma with pseudostratified columnar epithelium and surrounding basal cells within cribriform structures. Stromal invasion of surrounding cells corresponding to Gleason's 4 and areas of comedo necrosis corresponding to Gleason's 5.

most of the cribriform structures. This confirmed a diagnosis of focal invasive ductal adenocarcinoma of the prostate (Figure 1 and 2).

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Staging CT revealed small hilar and mediastinal lymph adenopathy measuring up to 2cm in maximum diameter, suspicious for metastatic disease. Whole body bones scan showed no evidence of osteosclerotic metastatic disease.

The patient underwent a radical prostatectomy six weeks later. Histopathological examination of the prostate confirmed ductal adenocarcinoma with Gleason's score of 5+4=9. There was extensive extraprostatic extension and multifocal margin involvement. There was also extensive infiltration by tumour at the bladder neck and in both seminal vesicles. There were no lymph nodes identified in the specimen. A repeat CT Scan of the chest, abdomen and pelvis performed three months later revealed unchanged mediastinal and hilar lymph adenopathy. There was no enlarged pelvic lymph adenopathy. The patient's PSA at three (3) and six (6) months following surgery was 1.93 and 1.91 respectively. The patient was then referred to the radiation oncologist and a multidisciplinary team decision was made of continuing further treatment with External Beam Radio Therapy (EBRT) and Androgen Deprivation Therapy (ADT).

Discussion

Ductal adenocarcinoma of the prostate is a rare histological subtype accounting for 0.4-0.8% of prostate cancers in its purest form [3,4]. It occurs as a mixed tumour with the more common prostatic acinar adenocarcinoma up to 5% of all radical prostatectomy cases [3]. The incidence seems to be increasing, but the degree of ductal adenocarcinoma relative to acinar adenocarcinoma has decreased in recent years [5].

It was originally identified by Melicow and Pachter in 1967 and was initially thought to be a neoplastic proliferation of remnant paramesonephric tissue. It appeared histologically similar to endometrioid adenocarcinoma of the uterus and so was given the name endometrioid carcinoma of the prostate. This term was used until ultrastructural studies revealed that these tumours originate from the prostatic ducts and are now more correctly termed ductal adenocarcinoma [6].

Ductal adenocarcinoma of the prostate occurs most often in men between the ages of 60 and 80. Clinically, patients commonly present with obstructive or irritative symptoms or haematuria, which is consistent with the central location of these tumours around the verumontanum [7-9]. Cystoscopically an exophytic papillary lesion can sometimes be seen in the prostatic urethra at or near the verumontanum, which explains why the tumour is sometimes diagnosed post TURP [2].

Histologically, ductal adenocarcinomas of the prostate show a variety of architectural patterns, which may coexist such as papillary, cribriform, solid and glandular structures [1]. The two most common patterns are papillary and cribriform. Epstein suggested that ductal adenocarcinoma of the prostate behaved similar to Gleason's 8 (4+4) acinar prostate adenocarcinomas [4].

Prostatic ductal adenocarcinoma generally spreads in the same manner as the usual acinar adenocarcinoma, however, there is a greater propensity to spread to the testis and penis [9].

Most studies have demonstrated that ductal prostate adenocarcinoma has a more aggressive course than acinar prostate cancer [10]. Usually when diagnosed by prostate needle biopsy, more than half of the patients have high-volume disease with advanced pathologic staging and a shorter time to progression [2]. PSA levels may be normal even though prostatic ductal carcinoma cells express PSA. Morgan et al. reported that PSA levels were 30 % lower in ductal

cancers compared to acinar prostate adenocarcinoma and patients with ductal carcinoma were 2.4 times more likely to have a PSA below 4.0 ng/ml. They suggested that lower PSA levels may be due to the pattern of tumour growth within prostatic ducts resulting in increased levels of luminal PSA secretion and decrease levels of serum PSA [11].

In addition, Digital Rectal Examination (DRE) may be normal because ductal prostate adenocarcinoma tends to occur in the periurethral region of the gland. Because of DRE and PSA often being normal, ductal adenocarcinoma of the prostate is usually diagnosed at a later stage than the usual acinar prostate adenocarcinoma. The cohort SEER study done by Meeks et al. reported higher clinical stage pathology with ductal prostate adenocarcinoma compared to acinar prostate cancer (T3 or greater, 47% vs. 18%). The SEER study also reported similar rates of lymph node metastasis in ductal and acinar prostate cancer (3% vs. 1.8%), however, there was a threefold increase rate of metastasis in ductal prostate adenocarcinoma as compared to acinar prostate adenocarcinoma (11% vs. 4%) [5].

Most patients are managed by radical prostatectomy after tissue diagnosis. Tu et al. reported that more than 80% of men with ductal prostate adenocarcinoma have Gleason 8 or higher in their surgical specimen following radical prostatectomy [12]. Samaratunga et al. reported between 75% to 90% of men with ductal adenocarcinoma will have extraprostatic extension of tumour following radical prostatectomy [13]. Many also have positive surgical margins following surgical resection. Adjuvant radiotherapy following surgery is therefore thought to be useful in long-term local disease control [6].

Ductal carcinoma of the prostate tends to be hormone sensitive therefore, these patients may also benefit from Androgen Deprivation Therapy (ADT) [6]. Most patients with metastatic disease will be treated by ADT, either surgically by bilateral orchidectomy or medically via a GnRH agonist. For patients with hormone refractory ductal prostate cancer, chemotherapy may be considered. The TAX-327 trial highlighted the survival benefit of using intravenous docetaxel in patients with metastatic hormone refractory prostate cancer. This was typically administered every 3 weeks in combination with oral prednisolone 5 mg twice daily [14].

Meeks et al. in the cohort SEER study reported that the overall mortality was significantly worse in men with ductal prostate adenocarcinoma, almost threefold higher rate of death, as compared to acinar prostate adenocarcinoma. In addition, they reported that prostate-specific mortality was significantly worse for men with ductal prostate adenocarcinoma compared to acinar prostate adenocarcinoma [5]. Ductal prostate adenocarcinoma has a prostate-specific and overall mortality similar to a Gleason's 8 (4+4) acinar adenocarcinoma [5].

Conclusion

Ductal prostate adenocarcinoma is a rare form of prostate cancer. Men with ductal prostate adenocarcinoma are more likely to present with advanced disease and have a worse overall and prostate-specific mortality compared to the usual acinar adenocarcinoma. Therefore, men with ductal prostate adenocarcinoma should be counseled about the adverse features of this type of prostate cancer and may benefit from early and aggressive adjuvant therapies even with low volume metastatic disease.

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