Squamous cell carcinoma transformed from the prostatic adenocarcinoma with hormonotherapy: a case report and literature review

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Case Report

Keywords: Prostate, Squamous cell carcinoma, Adenocarcinoma, Hormonotherapy, Transformation.

Posted Date: April 11th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1527658/v1

Abstract

Background: Squamous cell carcinoma (SCC) of the prostate is a very rare and highly aggressive tumor, which is ineffective to multiple treatments and prone to metastasis, and has a worse prognosis than adenocarcinoma of the prostate. However, a transformation of prostatic adenocarcinoma into squamous cell carcinoma is rarer and may occur after hormonotherapy or radiotherapy. Hitherto, there are few cases in the world about the transformation from adenocarcinoma into squamous cell carcinoma after treatment. To our knowledge, our case is the first reported in China.

Case presentation: A 67-year-old man with metastatic adenocarcinoma of the prostate for 2 years was not suitable for radical prostatectomy due to the disease classified T4N1M1. Hormonotherapy using Luteinizing Hormone-Releasing Hormone (LHRH) analog (leuprorelin) and antiandrogen agent (bicalutamide) was started, and serum prostate-specific antigen (PSA) level gradually decreased to a nadir of 0.04ng/ml. After treatment of 2 years, he complained of worsening of lower urinary tract symptoms(LUTS), and then he underwent transurethral resection of the prostate (TURP). Histological analysis revealed there were poorly differentiated keratinizing squamous cell carcinoma in the most of cancer tissue. As of now, the patient has undergone docetaxel treatment, containing 2 times of systemic chemotherapy. The patient's general condition is currently good.

Conclusions: Prostatic adenocarcinoma transformed into squamous cell carcinoma after hormonotherapy is very rare. However, the serum PSA of this tumor is probably normal, PSA and the Gleason grading system are of limited value in the diagnosis of SCC, keratinization of histopathological examination enables its diagnosis. The transformation is subclinical. Hence, how to identify prostatic adenocarcinoma or SCC in prostate tissue needs a further investigation.

Background

Squamous cell carcinoma (SCC) of the prostate is an extremely rare tumor with aggressive nature, representing less than 1% of prostatic carcinomas[1]. Patients developing SCC has generally a worse prognosis than those with adenocarcinoma because it commonly metastasizes to the bone, liver, and lungs in an early time, and the median survival time is estimated to be 14 months[2]. It is worth noting that even in a metastatic SCC of the prostate, the serum prostate-specific antigen (PSA) may be within the normal range[3]. At present, the transformation of prostatic adenocarcinoma to SCC after hormonotherapy has been reported in the literature in a few cases. Here, we show a patient with SCC of the prostate transformed from the prostatic adenocarcinoma following 2 years of hormonotherapy.

Case Presentation

A 67-year-old man was admitted to the hospital for half a month of pain in the waist and hip, accompanied by lower urinary tract symptoms (LUTS). Laboratory examination showed the serum PSA level was 63.38ng/mL. Chest computed tomography (CT) scan revealed multiple small nodules lesions in both lungs. An abdomen and pelvis CT scan were also performed. There were several lymph node shadows in the right lower abdomen and abnormal high-density shadows in the lumbosacral vertebra and left hip, which were considered as tumor metastases. Prostatic magnetic resonance imaging (MRI) showed typical imaging features of prostate cancer (Fig. 1A, B). Unfortunately, his bone scan was positive (Fig. 1C). Subsequently, he underwent transrectal prostate biopsy and the Gleason score (GS) as assigned by standard 10–12 core biopsies was 9(4 + 5). the histological analysis revealed extensive acinar fusion, irregular glands with unclear outline and deficiency of basal cells in adenocarcinoma tissue (Fig. 2). No immunohistochemical (IHC) stain of prostatic adenocarcinoma was conducted at the time of analysis. Our patient was not suitable for radical prostatectomy due to the disease classified T4N1M1. Hormonotherapy using LHRH analogue (leuprorelin) and antiandrogen agent (bicalutamide) were started, and serum PSA level gradually decreased to a nadir of 0.04ng/ml. After a subsequent follow-up of 15 months, abdominal CT showed that his bladder was invaded by a solid lesion. For evaluation of the mass, MRI was performed and showed that the tumor of prostate extended to both seminal vesicles and bladder base (Fig. 3). 2 years after treatment, he complained of hip pain and worsening of LUTS. Then a thorough examination was carried out for him. The serum PSA level was 0.03ng/mL. Compared to those several months ago, the new Chest and abdomen CT showed no significant difference. The prostate MRI showed post-treatment imaging of prostate cancer (Fig. 4A, B). And then he underwent transurethral resection of the prostate (TURP). Histological

analysis revealed there were lots of poorly differentiated keratinizing squamous cell carcinoma accompanied by some neuroendocrine differentiation locally (Fig. 5A). Immunohistochemical staining displayed that almost all tumor cells were positive for p63(Fig. 5B), p40(Fig. 5C), and CD138. Ki67 was detected in about 70% of the tumor cells. His symptoms of the lower urinary tract were improved after TURP, but the prostatic adenocarcinoma was proved to transform into SCC. The patient started docetaxel treatment. So far, he had received 2 times of systemic chemotherapy. The patient's current general condition is fair.

Discussion

SCC of the prostate is a very rare and highly aggressive tumor, representing less than 1% of prostatic carcinomas[1, 3]. The age of onset of SCC is mostly about 40 to 80 years old, and the median survival time after diagnosis is estimated to be 14 months[4]. The clinical features of SCC of the prostate and adenocarcinoma of the prostate are quite different, and the SCC of the prostate of patient's symptoms are similar to those of advanced prostatic adenocarcinoma, including LUTS, acute urinary retention, and bone metastases, among which bone metastases are mainly osteolytic rather than osteoblastic, which can cause a pain associated with bone metastases[5]. As SCC of the prostate differs from adenocarcinoma in its therapeutic response and prognosis. It usually indicates a poor response to conventional treatment and a poor prognosis[6]. Because of the high level of malignancy, SCC of the prostate commonly metastasizes to other organs in an early time. However, the serum PSA may be at the normal range in SCC of the prostate. PSA and the Gleason grading system are not of high value in the diagnosis of SCC [7–9].

The etiology of SCC remains unclear. The origin may be the prostatic or bladder urethral squamous cell, prostatic acini metaplasia, or squamous metaplasia of a prostatic urethral primary tumor[4, 10]. Regarding the occurrence and progression of cancer, it is proposed that cancer stem cells with the ability of self-replication, multi-differentiation, and tumor formation are the origin, which can form pluripotent stem cells capable of multidirectional differentiation or metaplastic transformation of adenocarcinoma[11]. It suggested that the progress of SCC was possibly stemmed from a series of factors disabling columnar cells to produce the normal prostatic antigen, such as PSA and prostatic acid prophatase (PAP), whereas enabling them to produce keratin.[12]. Some reported that transformation of adenocarcinoma to SCC occurred secondary to radiation or endocrine treatment. And the transformation often occurs in high-grade prostatic adenocarcinoma[7, 8]. Similarly, the transformation occurring in our case belongs to this situation. Recently, Hubert et al.[13] detected a TMPRSS2-ERG fusion, among other genetic alterations, by comprehensive genomic profiling (CGP), supporting a diagnosis of metastatic SCC transformed from prostatic adenocarcinoma following androgen deprivation therapy (ADT).

As of now, there have been a few cases about prostatic adenocarcinoma transformation into squamous cell carcinoma through hormonotherapy with LHRH since Braslis et al[8] first reported in 1995. To our knowledge, our case is the first report in China. In 2004, Parwani et al[4] reported 33 cases of prostate cancer with squamous differentiation, 21 of which had a history of adenocarcinoma diagnosis before treatment. And of these 21 cases, a total of 9 had a history of hormonotherapy (8 cases treated with hormonotherapy alone and 1 case treated with hormonotherapy and radiation). And in 2019, Hamza et al[2] retrospectively analyzed more than 70 cases of prostate cancer with squamous differentiation. 40 of these cases were caused by the transformation of prostatic adenocarcinoma into SCC after radiation therapy (RT) or hormonotherapy. There were 8 cases of purely epidermoid carcinoma alone and 32 cases of adenosquamous carcinoma. Which above suggested that the transformation of prostatic adenocarcinoma into SCC may be associated with hormonotherapy. In addition, radiotherapy may also play an important role in transformation. Our patient was diagnosed with metastatic prostatic adenocarcinoma which transformed into SCC of the prostate after 2 years of hormonotherapy. Evidence revealed that there had been 6 cases of prostatic adenocarcinoma transforming into squamous cell carcinoma by hormonotherapy in the last decade. We reviewed these cases and our case in Table 1. Two of them underwent radiotherapy, 4 of these cases did not undergo radical prostatectomy but received hormonotherapy and eventually transformed into SCC of the prostate. However, the time of transformation from prostatic adenocarcinoma into squamous cell carcinoma was not yet clear. The Leuprorelin and bicalutamide for the treatment of our patient led to a decrease of the level of androgens in the blood, which may result in the

inability of the prostatic columnar cells to express PSA and PAP. while remaining the ability of the prostate to produce keratin facilitates transformation.

Table 1
Published cases about transformation of prostatic adenocarcinoma into SCC after hormonotherapy in the last 10 years

	Reference	*Year*	*Age (yr.)*	*Initial PSA(ng/ml)*	*GS*	*Radical prostatectomy*	*Radiotherapy*	*Hormonotherapy and therapy time*
1	Al-Qassim et al[4]	2014	65	84.5	4 + 5 = 9	No	No	LHRH analogue (Leuprorelin) 18 months
2	Lee et al[1]	2019	76	1.27	4 + 5 = 9	No	No	LHRH analogue (goserelin) and antiandrogenagent(bicalutamide) 7 months
3	Ichaoui et al[2]	2019	71	2.7	3 + 3 = 6	Yes	Yes	LHRH ananlogue(Triptorelin) 6 months
4	Dizman et al[14]	2020	76	44.7	4 + 4 = 8	No	Yes	CYP17 inhibitor and LHRH analogue(Leuprorelin) 3 years
5			60	9.9	5 + 4 = 9	Yes	No	LHRH analogue (Leuprorelin)and CYP17 inhibitor(Abiraterone) 2 months
6	Lau et al[13]	2020	68	N/A	3 + 4 = 7	Yes	No	LHRH analogue (Leuprorelin) and antiandrogen agent (bicalutamide) 8 months
7	Our case	2022	67	63.38	5 + 5 = 10	No	No	LHRH analogue (Leuprorelin) and Bilateral Orchidectomy 27 months

N/A, not mentioned in literature; PSA, Prostate specific antigen; GS, Gleason score; LHRH: Luteinizing Hormone Releasing Hormone.

Imaging diagnosis of SCC of the prostate is challenging because it is extremely scarce and lacks well-established imaging characteristics[1]. Currently, the treatment for primary SCC of the prostate is ineffective despite of a combination of surgical therapy, radiotherapy, and chemotherapy. For patients who have lost the opportunity for surgical therapy, a combination of chemotherapy and radiation therapy may be an effective treatment for SCC of the prostate. Biswas et al[15] reported a patient with primary SCC of the prostate staged as T4N1M0, who received chemotherapy regimen including Mitomycin C and 5-Fluoro-uracil (5FU) and low-dose radiotherapy. No progression was seen in the 27 months of follow-up. Onoda M et al[16] reported a case of locally advanced SCC of the prostate treated with a combination of docetaxel, cisplatin, and 5-fluorouracil chemotherapy and radiotherapy. The patient showed good responsiveness after treatment with no progression for 24 months of follow-up. Recently, Hanna K et al[17] reported a case of primary SCC of the prostate staged as T4N1M1. The patient was currently undergoing four cycles of adjuvant docetaxel and carboplatin. There is also no optimal treatment for SCC of the

prostate transformed from prostatic adenocarcinoma during hormonotherapy. Based on the pathological diagnosis and the imaging, our patient had experienced two cycles of adjuvant chemotherapy (docetaxel). Dizman N et al[14] conducted CGP on the squamous transformation of prostate adenocarcinoma, suggesting that CGP could play an essential role in clinical practice to identify the origin and targeted therapy of the squamous transformation.

Conclusions

Prostatic adenocarcinoma transforming into squamous cell carcinoma after hormonotherapy is really infrequent. However, the serum PSA of this tumor is probably normal. Although PSA and the Gleason grading system are of limited value in the diagnosis of SCC, keratinization of histopathological examination can help its diagnosis. The transformation is subclinical. The question on transformation from prostatic adenocarcinoma into SCC requires further research. we hope our case could be useful in the future.

Abbreviations

SCC
Squamous cell carcinoma
LHRH
Luteinizing Hormone Releasing Hormone
PSA
Prostate specific antigen
TURP
Transurethral resection of the prostate
CT
Computed tomography
MRI
Magnetic resonance imaging
LUTS
Lower urinary tract symptoms
PAP
Prostatic acid prophatase
CGP
Comprehensive genomic profiling
ADT
Androgen deprivation therapy
RT
radiation therapy
5FU
5-Fluoro-uracil
N/A
not mentioned in literature
GS
Gleason score.

Declarations

Ethics approval and consent to participate

Not applicable

Consent to publish

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Availability of data and materials

Data and records pertaining to this case are in the patient's secure medical records in the Qingdao Municipal Hospital. All searched data by literature review are included in this paper.

Competing interests

The authors declare no competing interests.

Funding

No funding support.

Authors' contributions

SZS and BJ were the patients' Urologists, reviewed the literature and contributed to manuscript drafting; SCH conceptualized the case report; XGH diagnosed the case by histopathology; CML diagnosed the case by imaging; ZJL revised and edited the manuscript. All authors read and approved the final manuscript.

Not applicable.

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References

1. Lee J: **Transformation of adenocarcinoma of prostate to squamous cell carcinoma following hormonal treatment: A case report and review of the literature**. Radiol Case Rep 2019, **14**(4):483–489.
2. Ichaoui H, Nasr SB, Gargouri F, Zribi A, Hermi A, Fendri S, Balti M, Ayari J, Khiari R, Msakni I *et al*: **Transformation of a prostatic adenocarcinoma into squamous cell carcinoma after luteinizing hormone-releasing hormone (LHRH) agonist and radiotherapy treatment**. Pan Afr Med J 2019, **34**:125.
3. Di Pietro C, Celia A, De Stefani S, Saredi G, Bianchi G: **Squamous cell carcinoma of the prostate**. Arch Ital Urol Androl 2006, **78**(2):75–76.
4. Parwani AV, Kronz JD, Genega EM, Gaudin P, Chang S, Epstein JI: **Prostate carcinoma with squamous differentiation: an analysis of 33 cases**. AM J SURG PATHOL 2004, **28**(5):651–657.
5. Malik RD, Dakwar G, Hardee ME, Sanfilippo NJ, Rosenkrantz AB, Taneja SS: **Squamous cell carcinoma of the prostate**. Rev Urol 2011, **13**(1):56–60.
6. Imamura M, Nishiyama H, Ohmori K, Nishimura K: **Squamous cell carcinoma of the prostate without evidence of recurrence 5 years after operation**. UROL INT 2000, **65**(2):122–124.
7. Al-Qassim Z, Mohammed A, Payne D, Stocks PJ, Khan Z: **Squamous cell carcinoma of the prostate following treatment with an LHRH-agonist: a rare case of transformation of adenocarcinoma of the prostate**. Cent European J Urol 2014, **67**(1):26–28.

8. Braslis KG, Davi RC, Nelson E, Civantos F, Soloway MS: **Squamous cell carcinoma of the prostate: a transformation from adenocarcinoma after the use of a luteinizing hormone-releasing hormone agonist and flutamide**. UROLOGY 1995, **45**(2):329–331.
9. Grignon DJ: **Unusual subtypes of prostate cancer**. Mod Pathol 2004, **17**(3):316–327.
10. Wernert N, Goebbels R, Bonkhoff H, Dhom G: **Squamous cell carcinoma of the prostate**. HISTOPATHOLOGY 1990, **17**(4):339–344.
11. Arva NC, Das K: **Diagnostic dilemmas of squamous differentiation in prostate carcinoma case report and review of the literature**. DIAGN PATHOL 2011, **6**:46.
12. Lager DJ, Goeken JA, Kemp JD, Robinson RA: **Squamous metaplasia of the prostate. An immunohistochemical study**. AM J CLIN PATHOL 1988, **90**(5):597–601.
13. Lau HD, Clark M: **Metastatic squamous cell carcinoma transformed from prostatic adenocarcinoma following androgen deprivation therapy: A case report with clinicopathologic and molecular findings**. DIAGN CYTOPATHOL 2020, **48**(12):E14-E17.
14. Dizman N, Salgia M, Ali SM, Wu H, Arvanitis L, Chung JH, Pal SK: **Squamous Transformation of Prostate Adenocarcinoma: A Report of Two Cases With Genomic Profiling**. Clin Genitourin Cancer 2020, **18**(3):e289-e292.
15. Biswas T, Podder T, Lepera PA, Walker P: **Primary squamous cell carcinoma of the prostate: a case report of a rare clinical entity**. Future Sci OA 2015, **1**(3):O18.
16. Onoda M, Sugimoto R, Uesugi N, Takayama M, Shiomi E, Kato R, Kato Y, Takata R, Omori S, Obara W: **Novel combination chemotherapy with radiotherapy for prostate squamous cell carcinoma**. Int Cancer Conf J 2017, **6**(1):25–28.
17. Hanna K, Lele SM, McCormick G, McMahon A, Hill B, Boyle SL: **Primary prostatic squamous cell carcinoma**. Urol Case Rep 2021, **34**:101478.

Figures

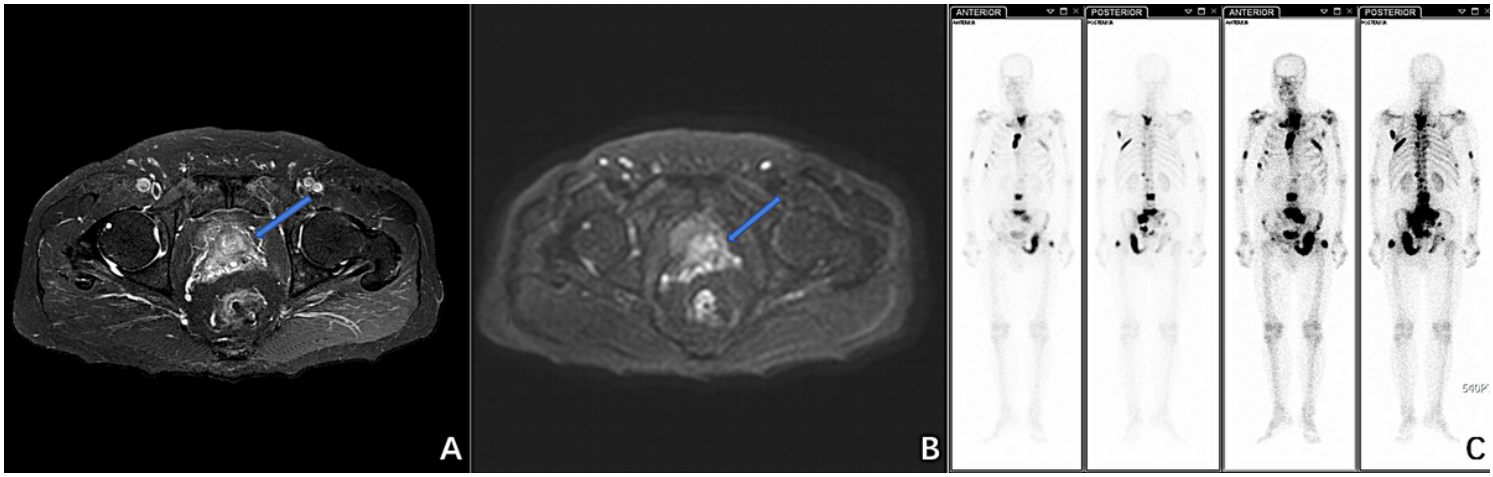

Figure 1

A Axial MRI (T2-weighted image) showing a mass lesion in the left peripheral zone. **B** Axial MRI (apparent diffusion coefficient) showing a mass lesion in the left peripheral zone. **C** Bone scintigraphy showing multiple metastases.

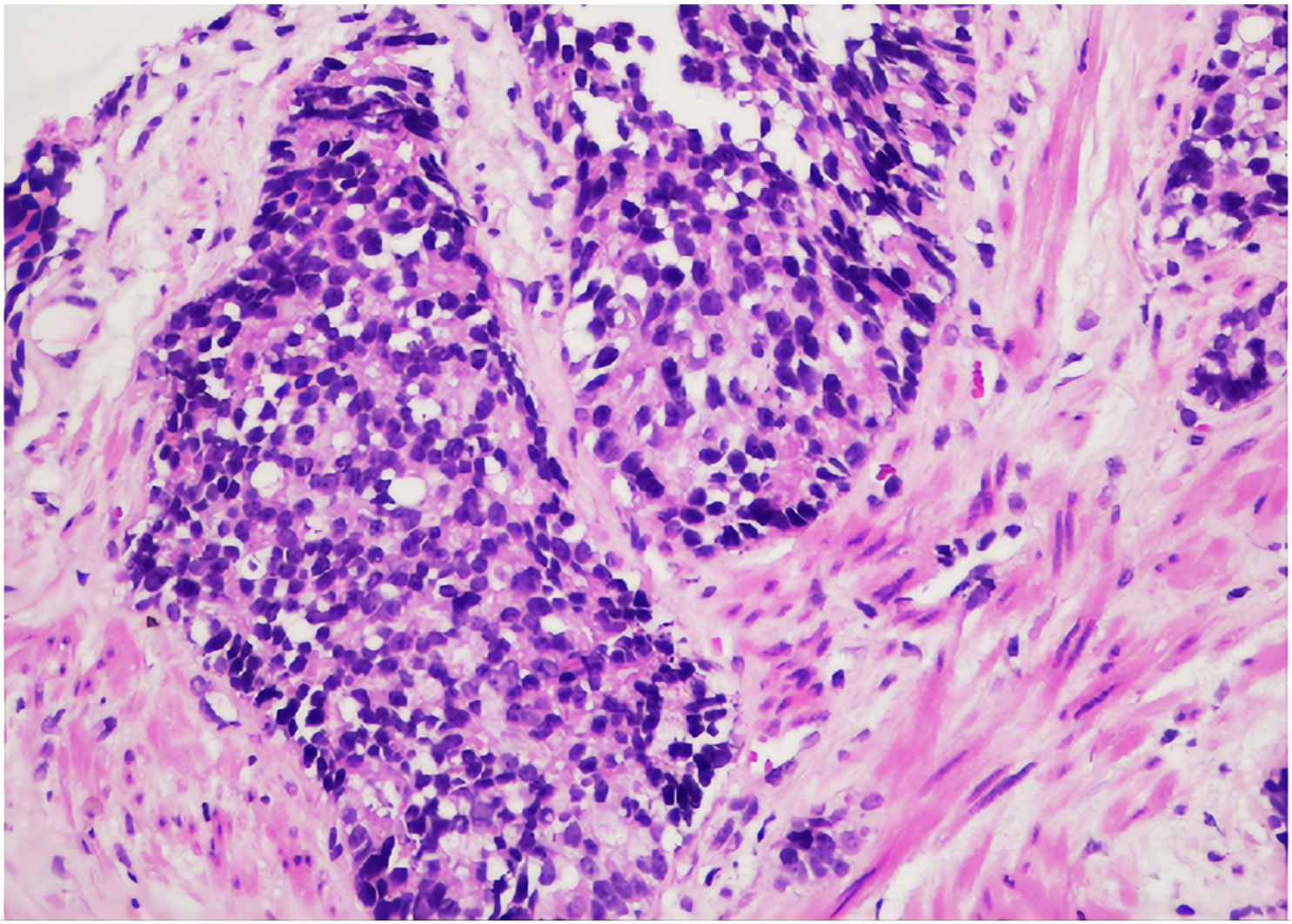

Figure 2

Initial biopsy form prostate showing acinar adenocarcinoma of Gleason 4 + 5 =9, the adenocarcinoma with extensive acinar fusion and irregular glands with unclear outline and the basal cells disappeared. (H&E, original magnification×100)

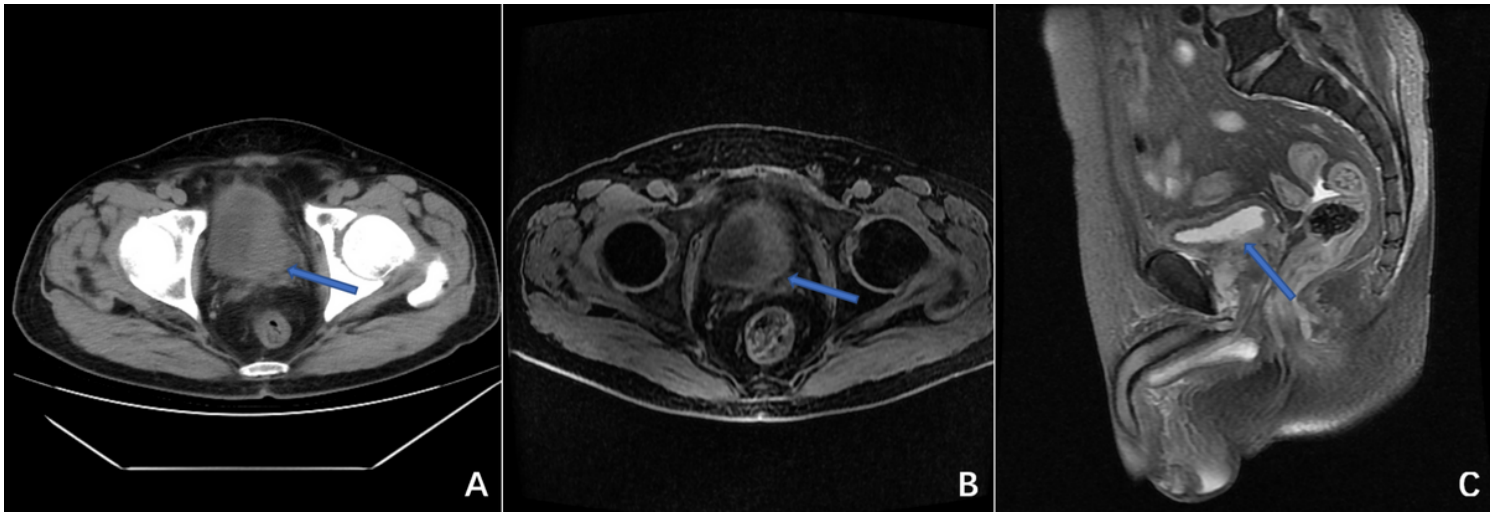

Figure 3

A Axial abdominal CT showing that the bladder was invaded by a solid lesion. **B** Axial MRI (T2-weighted image) showing a mass lesion in the left bladder. **C** Sagittal MRI (T2-weighted image) showing the mass of prostate extends to both seminal vesicles and bladder base.

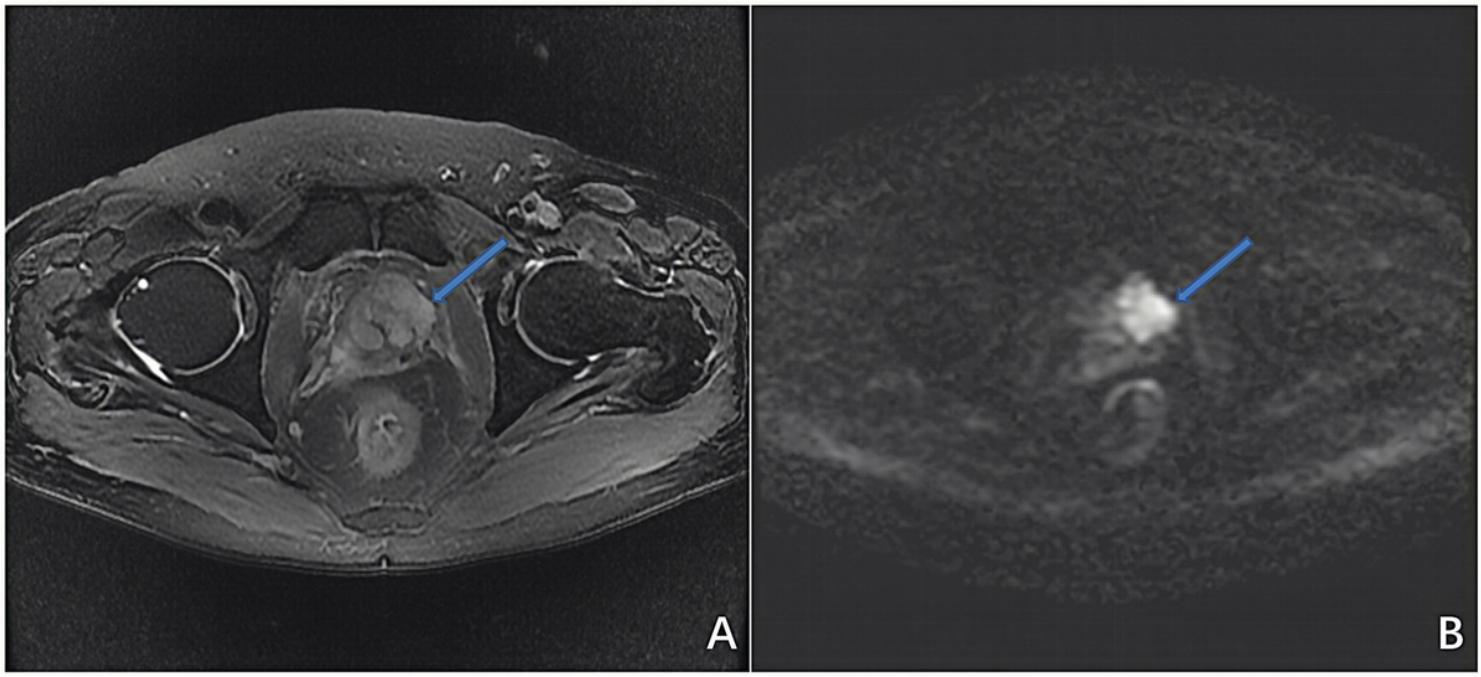

Figure 4

A Axial MRI (T2-weighted image) and B Axial MRI (diffusion weighted image) showing the mass lesion narrowed in the left peripheral zone.

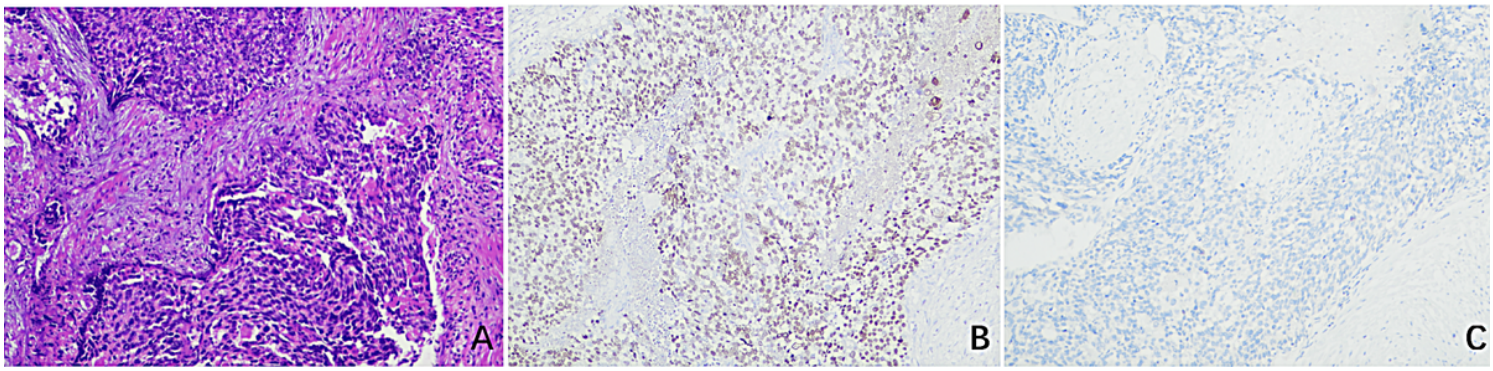

Figure 5

A Later transurethral resection of the prostate chips showing poorly differentiated keratinizing squamous cell carcinoma and with neuroendocrine differentiation in the local areas(H&E, original magnification×100). Immunohistochemical staining showed that tumor cells are positive for p63(**B**) and p40(**C**). (immunoperoxidase ×100).