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## Case Report

# Transformation of adenocarcinoma of prostate to squamous cell carcinoma following hormonal treatment: A case report and review of the literature

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## ABSTRACT

Squamous cell carcinoma (SCC) of the prostate is a rare tumor with aggressive nature. This type of tumor has a poor response to conventional treatment and results in poor prognosis. Squamous differentiation or metaplasia may arise subsequent to endocrine or radiation treatment, but it is very rare. To date, a few cases have been reported in the literature. Due to its rarity, the radiologic findings of SCC of the prostate are not well established. We describe a case of SCC of the prostate developing in a patient with adenocarcinoma of the prostate following hormonal therapy. Furthermore, we review the imaging features of this rare disease across multiple imaging modalities.

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## Introduction

Squamous cell carcinoma (SCC) of the prostate is extremely rare, accounting for less than 1% of all cases of prostate cancer [1]. It generally carries a worse prognosis than adenocarcinoma because it commonly metastasizes early to the bone, liver, and lungs with an average survival of 14 months [2]. Serum prostate-specific antigen (PSA) commonly shows values within the normal range, even in a metastatic disease context [3].

To date, a few cases have been reported in the literature about tending to arise subsequent to endocrine or

radiation treatment with squamous differentiation or metaplasia [4,5]. Due to its rarity, the radiologic findings of SCC of the prostate are not well established. Herein, we describe a case of SCC of the prostate developing in a patient with adenocarcinoma of the prostate following hormonal therapy.

## Case report

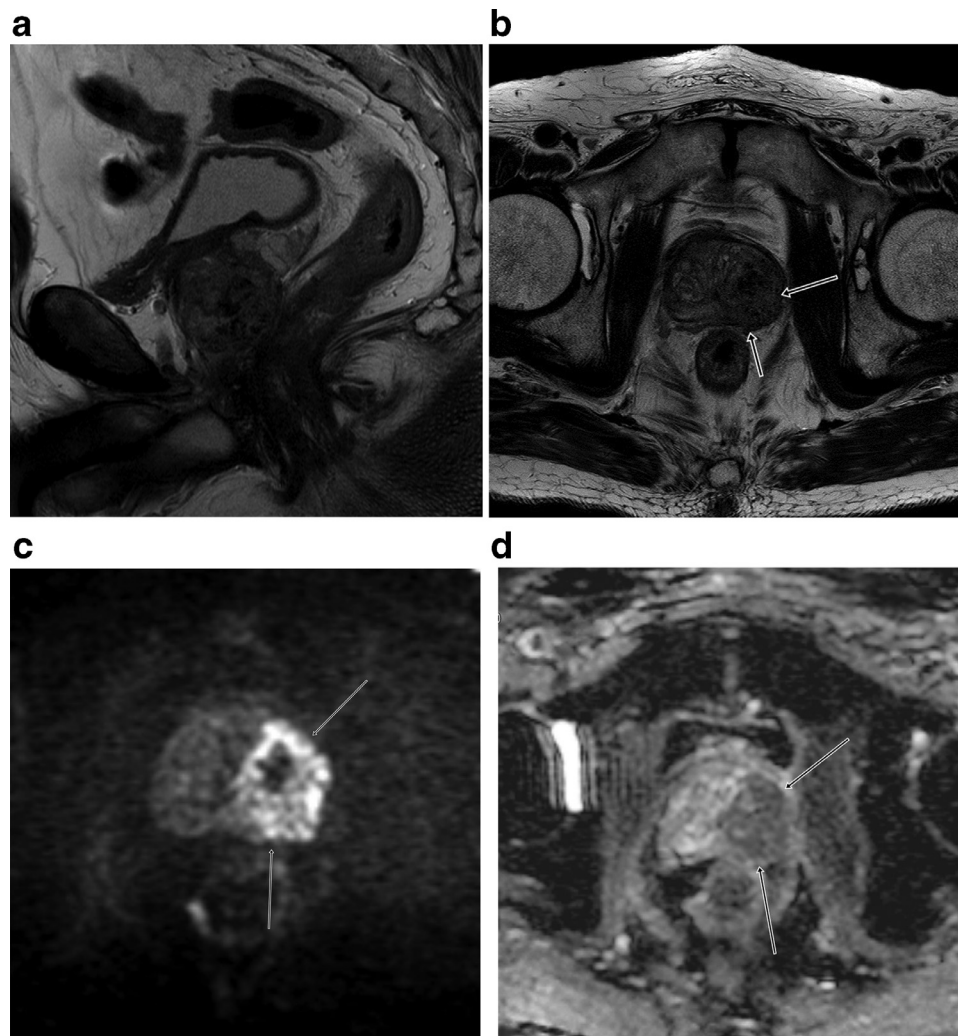
A 76-year-old male was referred to the clinic with incidental finding of multiple pulmonary nodules on chest X-ray.

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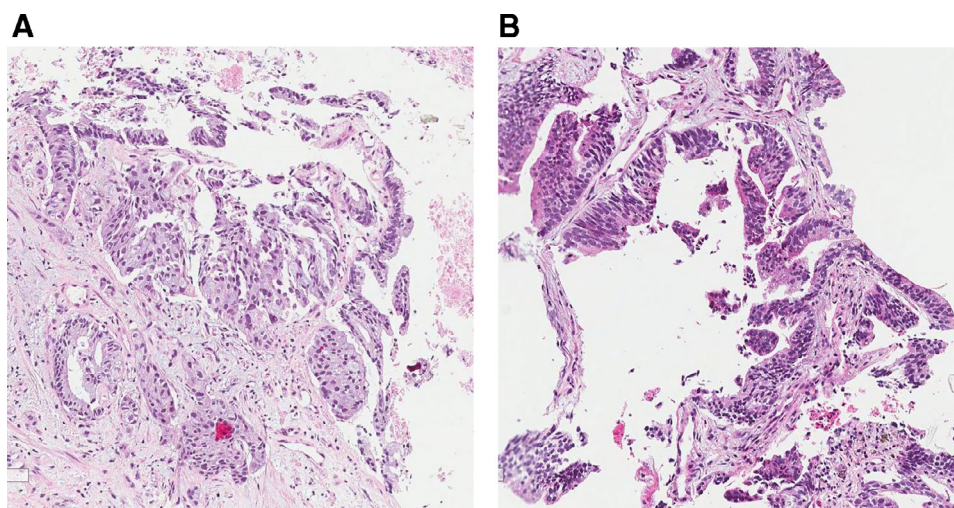


**Fig. 1** – Sagittal (A) and axial (B) T2-weighted MR images show diffuse low signal intensity in left peripheral and transition zone, associated with indistinct, irregular capsule (arrows). High-b value ( $b = 1500 \text{ s/mm}^2$ ) diffusion weighted MR image (C) shows a high signal intensity mass measuring 30 mm  $\times$  25 mm involving the left peripheral and transition zone with possible left posterolateral extracapsular extension (arrows). The apparent diffusion coefficient (ADC) map reveals (D) a mass with hypointensity (arrows).

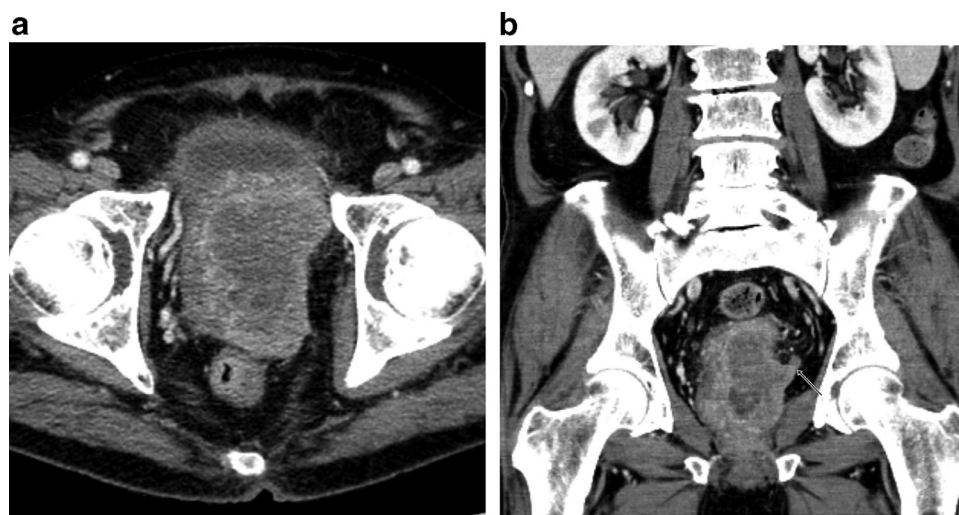
He underwent chest computed tomography (CT) scan, which showed multiple nodular lesions varying in size, in all lobes of both lungs. Abdomen and pelvis CT scan was also performed, and it showed an enhancing mass lesion in the left lobe of prostate gland in the portal venous phase. No enlarged lymph nodes could be detected at any abdominal site. On magnetic resonance imaging (MRI) of prostate, the boundary between the left peripheral and transition zone of the prostate was unclear. There was low signal intensity mass like lesion in left peripheral and transition zone, associated with indistinct, irregular capsule on T2-weighted image (Figs. 1A and B). Diffusion weighted image ( $b = 1500 \text{ s/mm}^2$ ) showed a high signal intensity mass measuring 30 mm  $\times$  25 mm involving the left peripheral and transition zone with possible left posterolateral extracapsular extension (Figs. 1C and D). Laboratory examination showed the serum PSA level was within the reference range (1.27 ng/mL, normal:

0–4 ng/mL). Subsequent transrectal ultrasound guided needle biopsy of the prostate was performed and a diagnosis of Gleason 4 + 5 adenocarcinoma of prostate. (Fig. 2A). Transthoracic needle aspiration was also done at the pulmonary nodule and the pathology from the nodule was consistent with adenocarcinoma, probably from prostate gland (Fig. 2B). A staging F18-fluorodeoxyglucose-positron emission tomography/CT (FDG-PET/CT) was performed, which revealed a hypermetabolic prostate mass in the left lobe with maximum standardized uptake value (SUVmax) 14.2. Multiple hypermetabolic pulmonary nodules were also seen. A bone scan was negative.

Hormonal treatment using LHRH analogue (goserelin) and antiandrogen agent (bicalutamide) were started, and serum PSA level gradually decreased to 0.03 during 5 months. Seven months after treatment, he complained worsening of urinary symptom.



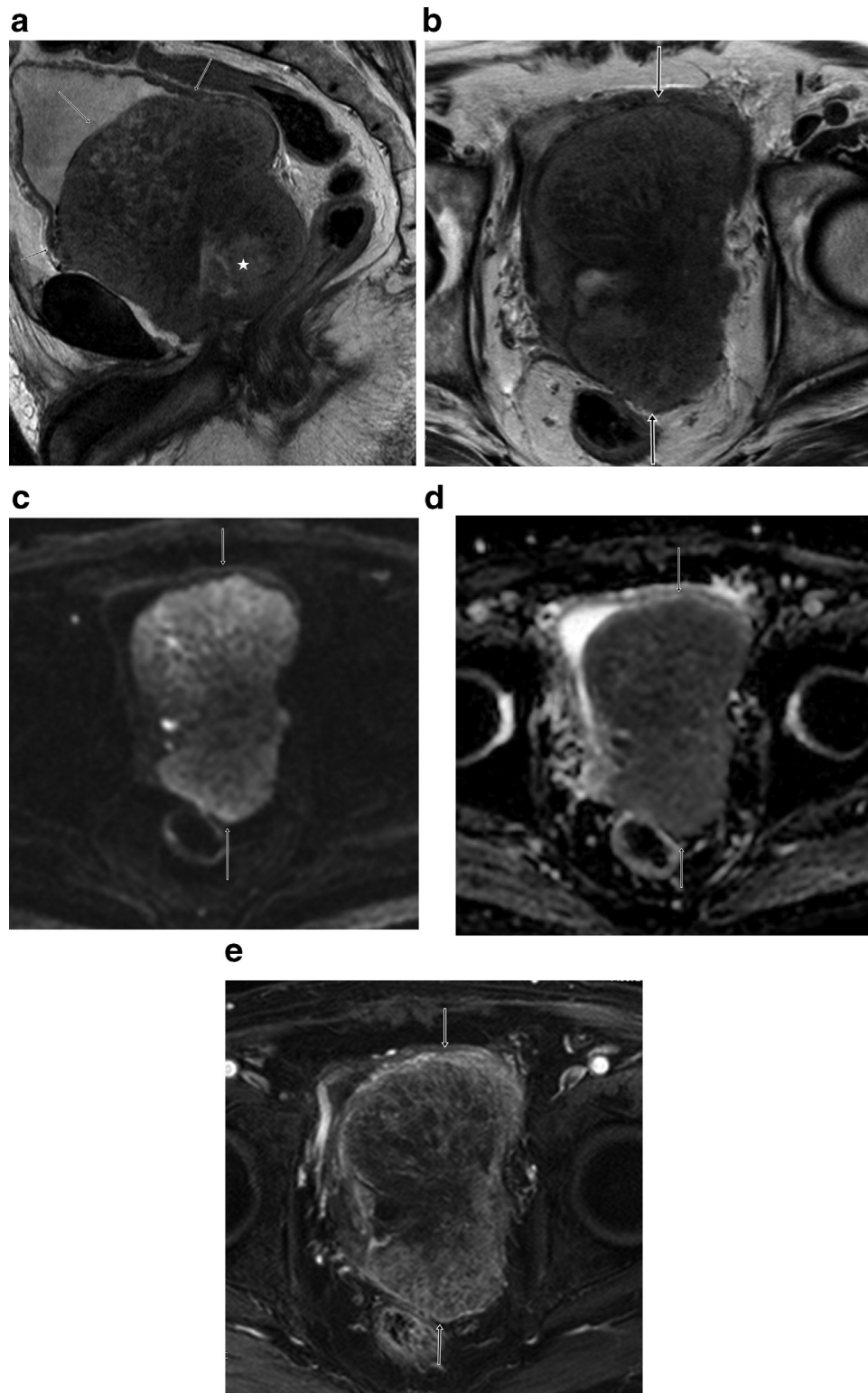
**Fig. 2** – Initial biopsy from prostate mass (A) showing acinar adenocarcinoma, Gleason 4 + 5 (score 9). The tumor is composed of poorly formed or irregular cribriform glands and individual cells with necrosis (H&E x 100). The specimen of lung biopsy (B) shows moderately differentiated adenocarcinoma, found to be AMACR positive and TTF-1 negative, consistent with adenocarcinoma, probably from prostate gland.



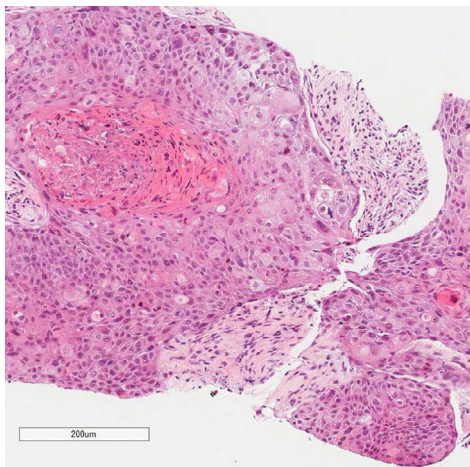
**Fig. 3** – Axial (A) and coronal (B) abdomen and pelvis CT scans show a heterogeneously enhancing, large mass involving the entire prostate in the portal venous phase. The mass extends posteriorly to both seminal vesicles, anteriorly to bladder base and left ureterovesical junction (arrow). No evidence of bone or lymph node metastases were noted.

Follow up abdomen and pelvis CT scan showed a large infiltrative neoplasm replacing the entire prostate with invasion to both seminal vesicles, bladder base and left ureterovesical junction in the portal venous phase (Figs. 3A and B). No evidence of bone or lymph node metastases was noted. For further evaluation of the mass, he underwent repeat MRI scan of prostate the following month. T2-weighted image demonstrated a large, infiltrative soft tissue mass, measuring 110 mm × 68 mm, involving entire prostate gland. The mass contained internal necrosis or cystic area and still showed extension to seminal vesicles and bladder base (Figs. 4A and B). Diffusion weighted ( $b = 1500 \text{ s/mm}^2$ ) showed the mass with inhomogenous high signal intensity (Fig. 4C). On ap-

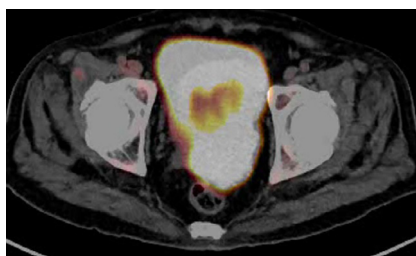
parent diffusion coefficient (ADC) map, the mass demonstrated markedly diffuse low signal intensity, suggesting restricted diffusion (Fig. 4D). On dynamic contrast enhancement MRI, the lesion showed early and persistent intense enhancement (Fig. 4E). On Chest CT scan, multiple pulmonary metastasis showed decrease in the size. Serum PSA level was still normal range ( $<0.03 \text{ ng/mL}$ ). He underwent a transrectal ultrasound guided prostate rebiopsy. The pathology was consistent with SCC in 11/12 cores (Fig. 5). There was no evidence of adenocarcinoma component in the prostate specimen. Cystoscopy ruled out a primary squamous cell cancer of bladder/urethra and anal/rectal regions, retrospectively. FDG-PET/CT scan was re-performed, which revealed a more



**Fig. 4** – Sagittal (A) and axial (B) T2-weighted MR images demonstrate a 110 mm × 68 mm large, infiltrative soft tissue mass involving entire prostate gland. The mass contains internal necrosis or cystic area (\* on A) and still shows extension to seminal vesicles and bladder base (arrow). Diffusion weighted ( $b = 1500 \text{ s/mm}^2$ ) image (C) showed the mass with inhomogeneous high signal intensity (arrow). On apparent diffusion coefficient (ADC) map (D), the mass demonstrated markedly diffuse low signal intensity, suggesting restricted diffusion (arrow). On axial contrast-dynamic scan (E), the mass showed avid and heterogeneous enhancement with areas of necrosis or cystic changes (arrow).



**Fig. 5 – Histologic section of prostate core needle biopsy. There is moderately differentiated squamous cell carcinoma characterized by presence of keratinization and abundant eosinophilic glassy cytoplasm. There was no evidence of adenocarcinoma component in the prostate specimen (H&E × 100).**



**Fig. 6 – On F18-fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) scan, increased FDG uptake was observed throughout the prostate extending to bladder base (SUVmax 27.89).**

hypermetabolic prostate mass in the left lobe (SUVmax 27.89) (Fig. 6)

Palliative radiation therapy was started, and his most recent CT scan, obtained 3 months after diagnosis, showed stable disease.

## Discussion

SCC of the prostate is a rare tumor with aggressive nature [1,2]. It usually occurs in the seventh decade of age with symptoms of urinary obstruction or pain related to bony metastasis [6]. It differs from common adenocarcinoma in its therapeutic response and prognosis. This type of tumor has a poor response to conventional treatment and resulting in poor prognosis [7]. Because of the rarity of this malignancy, the treatment is controversial. Various approaches including surgical intervention,

chemotherapy, and radiation therapy have been implemented without durable response [7–9].

The etiology of SCC is not fully understood. The origin is proposed to be pure prostatic origin such as prostatic or bladder urethral squamous cell, prostatic acini metaplasia, or squamous metaplasia of a prostatic urethral primary tumor [8–10]. Some reported transformation of adenocarcinoma to SCC occurred secondary to radiation or hormonal treatment [5,10]. As such malignancy can show extensive squamous metaplasia, it has also been hypothesized that it could derive from pluripotent stem cells capable of multidirectional differentiation or metaplastic transformation of adenocarcinoma [11]. Lager et al [12] reported SCC developed due to adverse stimuli affecting columnar cells causing them to express normal prostatic antigen such as PSA and prostatic acid phosphatase, although retaining the ability to produce keratin. It explained no elevated serum PSA in the patient with SCC, unlike prostate adenocarcinoma.

SCC developing after treatment with LHRH was first reported in 1995 by Braslis et al [4]. The patient treated with LHRH agonist (leuprolide and flutamide) for a high Gleason score adenocarcinoma. Squamous differentiation of prostate cancer can be encountered in pure form or associated with adenocarcinoma [11]. Most case reports of squamous transformation occurring after radiation or hormonal treatment tended to be associated with high grade adenocarcinoma, such as in our case [4,13]. Arva et al [11] reviewed 66 cases of prostate cancer with squamous differentiation, 27 (41%) were pure SCCs and 39 (59%) were associated with adenocarcinoma. Thirty five patients were initially diagnosed as having prostate adenocarcinoma with no squamous component and later developed squamous component following treatment. Seven of them (20%) had pure SCC, where in the remaining 28 cases (80%), the squamous component was associated with adenocarcinoma (adenosquamous carcinoma). They concluded that treated adenocarcinoma had a tendency to develop squamous transformation in association with adenocarcinoma. However, it is still unclear if SCC represents de novo malignancy or develops from adenocarcinoma following therapy.

To the best of our knowledge, a few cases of SCC have been reported to date in the English literature and there were only 6 cases including CT or MRI imaging finding. These imaging features are listed in Table 1. Ours is the first radiological case report of SCC of the prostate following hormonal treatment including CT and MRI finding.

For the 4 reviewed case reports, SCC of the prostate showed highly aggressive nature. In one case [14], a large infiltrative neoplasm replacing the prostate was observed. In another case [9], the mass demonstrated direct invasion of the bladder and left seminal vesicle. The penile metastasis, extensive pelvic lymphadenopathy, and bony metastasis were also observed. In the third [13] and fourth [15] cases, the lesions showed extracapsular extension and bladder base invasion, respectively. These features were very similar to our patient. CT and MR images showed a large infiltrative neoplasm with associated necrosis or hemorrhage that replaced nearly the entire prostate. We think that necrosis or hemorrhage might be explained as their rapid growth, which may help to distinguish SCC from usual adenocarcinoma. Furthermore,

**Table 1 – Imaging features of squamous cell carcinoma of the prostate.**

Reference	Year	Age (y)	Pathology	Imaging finding			
				CT	MR	Invasion	Metastasis
1 Okada et al [19]	2000	65	Primary SCC	Irregular hypodense mass on CT	A low SI mass with disruption of the transition & peripheral zone boundary	-	None
2 Malik et al [9]	2011	77	Primary SCC	N/A	A large infiltrative neoplasm replacing the prostate with inner necrotic/hemorrhagic portion	Invasion of bladder base, left SV	Pelvic LN Bone Penis
3 Wang et al [15]	2012	80	Primary SCC	A large neoplasm with heterogeneous enhancement in the prostate	N/A	Extension to bladder base	None
4 Dong et al [17]	2014	60	Primary SCC	N/A	A hyperintense mass lesion involving central zone on T2WI	-	None
5 Biswas et al [14]	2015	N/A	Primary SCC	A large mass replacing prostate	N/A	-	None
6 Abbott et al [13]	2016	67	SCC with adenocarcinoma	N/A	A hypointense mass involving peripheral zone on T2WI	Extracapsular extension	None

N/A = non available; SCC = squamous cell carcinoma; SV = seminal vesicle; T2WI = T2-weighted image.

the tumor showed markedly restricted diffusion which meant high cellularity. SCC of the prostate is thought to be more aggressive than typical prostate adenocarcinoma because of its extension beyond the prostate gland.

Due to high degree of malignancy, SCC of the prostate commonly metastasizes to the bone, liver, lungs, and lymph node [2]. In our patient, lung metastasis was noted at initial diagnosis. However, transformation to SCC of lung metastasis was unclear because transthoracic needle re-aspiration at the pulmonary nodule could not be performed due to small tumor size. In addition, the bony lesions are usually osteolytic rather than osteoblastic seen in adenocarcinoma of the prostate [16]. Malik et al [9] reported osseous metastasis of pelvic bone and sacrum, but the metastasis pattern was not noted. There were no bony metastases in this case.

There were a few case reports about FDG-PET/CT imaging of SCC. Strong FDG uptake throughout the prostate gland with SUVmax of 15.50 was reported by Dong et al [17]. Similarly, Gedik et al [18] reported high FDG uptake throughout SCC of the prostate gland and parailiac lymph node was noted with SUVmax values of 27.73 and 11.40, respectively. The author mentioned FDG affinity of SCC was different from adenocarcinoma. He suggested taking together the difference of origin between them and aggressive nature of SCC; this might result in high FDG uptake in the SCC of prostate and metastatic sites. In our patient, since high FDG uptake were noted in both initial adenocarcinoma and transformation to SCC, we could not evaluate the potential usage of FDG-PET/CT. However evaluation of disease extent may be useful.

Imaging diagnosis of SCC of the prostate is challenging because of its rarity and lack of well-established imaging characteristics. Differential diagnosis of a rapidly growing prostate mass with aggressive nature includes recurrent adenocarcinoma and small cell differentiation.

In summation, if rapidly growing prostate mass with aggressive nature is observed in the patient with history of radiation or hormonal treatment, radiologists should consider the possibility of squamous transformation of the prostate cancer, though it is exceedingly rare disease entity.

#### REFERENCES

- [1] Randolph TL, Amin MB, Ro JY, Ayala AG. Histologic variants of adenocarcinoma and other carcinomas of prostate: pathologic criteria and clinical significance. *Mod Pathol* 1997;10:612–19.
- [2] Moskovitz B, Munichor M, Bolkier M, Livne PM. Squamous cell carcinoma of the prostate. *Urol Int* 1993;51:181–3.
- [3] Okamoto T, Ogiu K, Sato M, Kaneko T, Suzuki Y, Tanji S, et al. Primary squamous cell carcinoma of the prostate: a case report. *Hinyokika Kyo* 1996;42:67–70.
- [4] 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;45:329–31.
- [5] 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 Eur J Urol* 2014;67(1):26–8. <http://doi.org/10.5173/cej.2014.01.art5>.
- [6] Mohan H, Bal A, Punia RP, Bawa AS. Squamous cell carcinoma of the prostate. *Int J Urol* 2003;10:114–16.
- [7] 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):122–4.
- [8] Wernert N, Goebbles R, Bonkhoff H, Dhom G. Squamous cell carcinoma of the prostate. *Histopathology* 1990;17:339–344.

- [9] Malik RD, Dakwar G, Hardee ME, Sanfilippo NJ, Rosenkrantz AB, Taneja SS. Squamous cell carcinoma of the prostate. *Rev Urol* 2011;13:56–60.
- [10] Parwani AV, Kronz ID, 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):651–7.
- [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;90:597–601.
- [13] Abbott DW, Kilari D, Senebottarath K, Iczkowski KA. Squamous cell carcinoma of the prostate with concomitant adenocarcinoma in the absence of prior androgen deprivation therapy. *Case Rep Clin Pathol* 2016;3(2):60–3.
- [14] 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(3):FSO18. <http://doi.org/10.4155/fso.15.16>.
- [15] Wang Y, Wang Y, Ma Y, Zhu B. Primary squamous cell carcinoma of the prostate. *Quant Imaging Med Surg* 2012;2(4):294–5.
- [16] Mott LJ. Squamous cell carcinoma of prostate: report 2 cases and review of the literature. *J Urol* 1979;121:833–5.
- [17] Dong A, Zuo C, Lu J, Wang Y. Squamous cell carcinoma of the prostate with strong FDG uptake on PET/CT. *Clin Nucl Med* 2014;39(7):650–2. <http://doi.org/10.1097/RLU.0b013e31829af937>.
- [18] Kara Gedik G, Yavas G, Akand M, Celik E, Sari O. Fluorodeoxyglucose positron emission tomography/computed tomography imaging of a patient with squamous cell carcinoma of prostate. *Case Rep Med* 2014;2014:860570. <http://doi.org/10.1155/2014/860570>.
- [19] Okada E, Kamizaki H. Primary squamous cell carcinoma of the prostate. *Int J Urol* 2000 Sep;7(9):347–50.