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Histopathological features of recurrent prostate adenocarcinoma after high intensity focused ultrasound (HIFU) focal treatment: A case report

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ABSTRACT

High-intensity focused ultrasound (HIFU) is a focal therapeutic approach for localised non-metastatic prostate cancer. We report a 53-year-old man who failed active surveillance of prostatic adenocarcinoma in the right lobe and underwent HIFU focal therapy. He experienced an outfield recurrence in the contralateral lobe thereafter and underwent salvage radical prostatectomy. We discuss the histopathological features in the salvage radical prostatectomy post HIFU treatment, its relationship to the outfield recurrence and the management.

Introduction

High-intensity focused ultrasound (HIFU) is a focal therapeutic approach for localised non-metastatic prostate cancer with effective outcome and lower probability of side effects.[1] HIFU therapy causes coagulative necrosis of the tumour by raising the local temperature while sparing surrounding organs in order to preserve urinary and sexual function.[2] Here we document the histological changes in the salvage radical prostatectomy of a patient who underwent focal-HIFU treatment for localised prostate cancer.

Case report

The patient presented in February 2019, aged 53, with serum total prostate specific antigen (PSA) level of 4.13 μg/L. (The chronological timeline of the patient's diagnostic and treatment journey is summarized in Fig. 1) The patient had no significant past medical history. Multi-parametric magnetic resonance imaging (MRI) prostate scan showed indeterminate diffuse bilateral peripheral zone lesions (Prostate Imaging Reporting and Data System, PIRADS 3), suggestive of a mild inflammatory process. Prostate volume was 21.9 ml. A transrectal ultrasound-guided biopsy of the prostate was performed, which showed adenocarcinoma of the prostate in tiny 1mm foci of Gleason 3 + 3 (grade group 1) in the right lobe (right apex lateral and right mid-gland medial, Fig. 2A–C). He was managed with active surveillance.

However, his total PSA increased from 4.13 μg/L (February 2019) to 4.53 μg/L (July 2019) and 6.2 μg/L (October 2019). In November 2019, he underwent focal HIFU therapy for prostate cancer, targeted on the localized lesions in the right apex and right mid-gland. Unfortunately, his follow-up was interrupted by the COVID-19 pandemic because he was working overseas outside Singapore. In Aug 2020, his total PSA increased to 10.27 μg/L. Another multi-parametric MRI scan showed contralateral left peripheral zone suspicious PIRADS 5 lesions. Prostate-specific membrane antigen positron emission computer tomography (PSMA PET-CT) scan showed a localised lesion within the prostate gland.

Subsequent MRI-ultrasound fusion guided biopsy showed locally recurrent cT2cN0M0 Gleason 3 + 4 prostate adenocarcinoma (PIRADS 5 lesion, grade group 2, Fig. 2, D). at the left peripheral zone and midline transitional zone at the apex anterior to the prostatic urethra (PIRADS 3 lesion, Gleason 3 + 3 (grade group 1, Fig. 2, E). The patient decided to undergo robotic salvage radical prostatectomy with bilateral pelvic lymph node dissection, which was done in Sep 2020. The histology showed prostatic acinar adenocarcinoma (pT2N0 Gleason 3 + 4, grade group 2) in the left lobe peripheral zone posteriorly and posterolaterally, extending into right lobe (Fig. 3A and B). Focal-HIFU treatment related changes were present in the right lobe posterior region, featuring stromal edema, hyalinization, fibrosis with neovascularization, corpora amylacea rimmed by foreign body type giant cells without glandular lining, hemosiderin laden macrophages and basal cell hyperplasia in the

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Chronological timeline of the patient's diagnostic and treatment journey

In February 2019, serum total prostate specific antigen (PSA) 4.13 μg/L, magnetic resonance imaging (MRI) prostate scan showed indeterminate diffuse bilateral peripheral zone lesions

↓ Needle biopsy of the prostate

Acinar adenocarcinoma of the prostate, 1mm, Gleason 3+3 (grade group 1) in the right lobe

↓ Active surveillance

July 2019: PSA 4.53 μg/L and October 2019: PSA 6.2 μg/L

↓ Focal High-intensity focused ultrasound (HIFU) therapy, November 2019

Aug 2020: PSA 10.27 μg/L, MRI: cT2cN0M0 prostatic cancer in the left peripheral zone and midline transitional zone at the apex.

↓ Needle biopsy of the prostate

Acinar adenocarcinoma of the prostate in the left peripheral zone Gleason 3+4 (grade group 2) and in midline transitional zone at the apex anterior to the prostatic urethra Gleason 3+3 (grade group 1)

↓ September 2020: Radical prostatectomy

Acinar adenocarcinoma of the prostate in the left lobe peripheral zone posteriorly and posterolaterally, extending into right lobe Gleason 3+4, (grade group 2), HIFU treatment related changes in the right lobe posterior region without viable tumour cells.

↓ Last follow-up in Jan 2021

Clinically well, PSA 0.015 μg/L

Fig. 1. Chronological timeline of the patient's diagnostic and treatment journey.

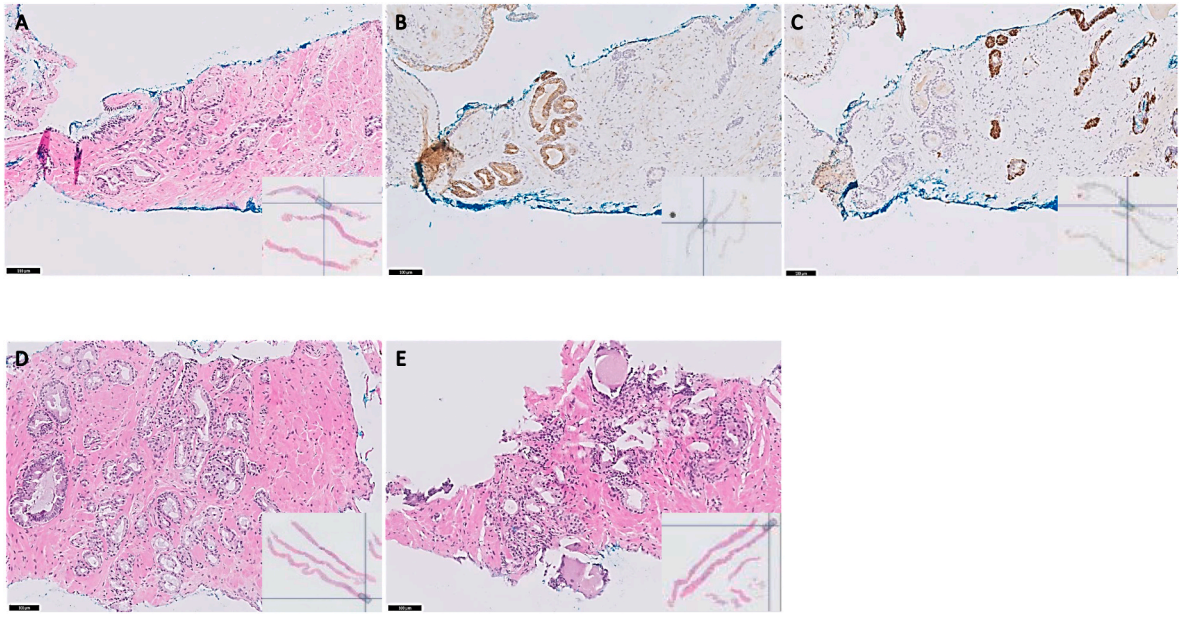

Fig. 2. (A) The initial needle biopsy shows a small focus Gleason 3 + 3 (grade group 1) prostatic acinar adenocarcinoma (Hematoxylin and eosin (H&E) at × 100 magnification, bar length: 100 μm). (B) The adenocarcinoma glands show cytoplasmic positivity for racemase (Immunohistochemistry × 100 magnification, bar length: 100 μm). (C) Absence of basal cell markers p63/high molecular weight cytokeratin around the adenocarcinoma glands (Immunohistochemistry × 100 magnification, bar length: 100 μm). (D) The second follow-up needle biopsy shows a Gleason 3 + 4 (grade group 2) prostatic acinar adenocarcinoma in the left peripheral zone (H&E, at × 100 magnification, bar length: 100 μm). (E) The second follow-up needle biopsy shows a Gleason 3 + 4 (grade group 2) prostatic acinar adenocarcinoma in right base (H&E, at × 100 magnification, bar length: 100 μm).

adjacent non-neoplastic glands are present (Fig. 3C–F). No viable tumour cells were seen in this region with prior focal-HIFU treatment.

The patient recovered well after the operation and serum PSA level was 0.015 μg/L in January 2021.

Discussion

HIFU focal therapy for prostate cancer can be used as primary treatment for localised disease in recent multicentre prospective studies, including treating clinically significant nonmetastatic prostate cancer.[1] HIFU is also an alternative for salvage therapy in localised relapse of

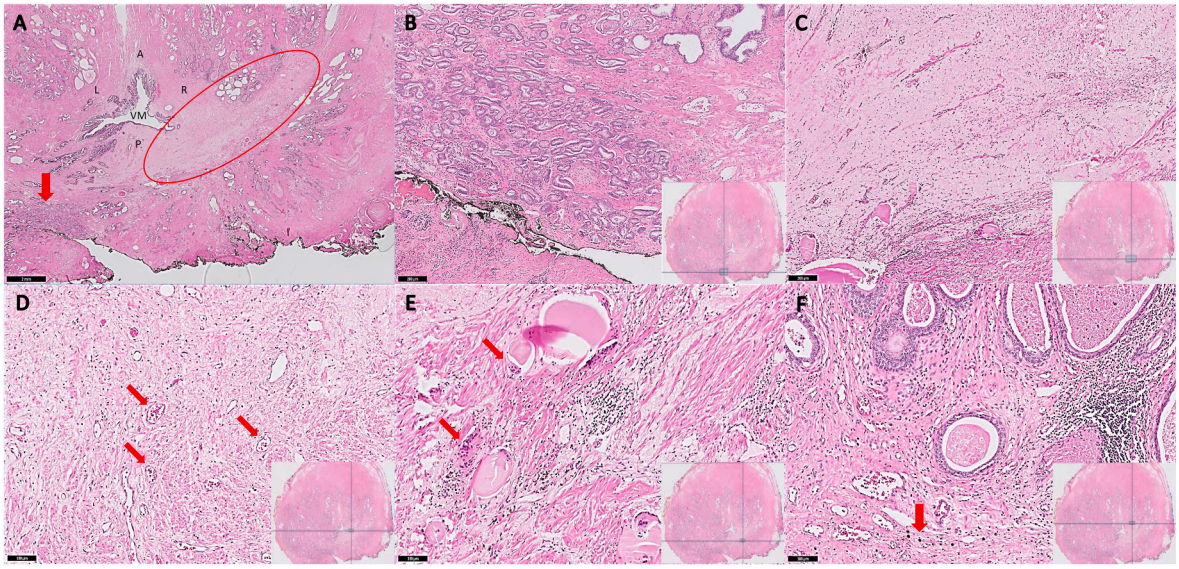

Fig. 3. (A) The radical prostatectomy shows acinar adenocarcinoma in the left lobe near the posterior surface (Red arrow) and the right lobe shows an area of hyalinised fibrosis, consistent with post high intensity focused ultrasound treatment changes (Red circled area) (Hematoxylin and eosin (H&E), VM: Verumontanum, A: Anterior, P: Posterior, L: Left lobe, R: Right lobe, at × 2 magnification, bar length: 2 mm). (B) The acinar adenocarcinoma in the left lobe shows Gleason 3 + 4 (grade group 2) pattern (H&E, × 50 magnification, bar length: 200 μm). (C) The post-HIFU treatment area in posterior right lobe shows fibrosis and edema without discernible viable adenocarcinoma glands (H&E, × 100 magnification, bar length: 100 μm). (D) An increased number of capillaries (Neovascularization, Red arrows) is present in the post-HIFU treatment area (H&E, at × 100 magnification, bar length: 100 μm). (E) Corpora amylacea without a glandular lining but instead rimmed by foreign body type multinucleated giant cells (Red arrows) are frequently seen in the post-HIFU treatment area (H&E, at × 100 magnification, bar length: 100 μm). (F) Basal cell hyperplasia with hemosiderin-laden macrophages (Red arrow) and chronic inflammation are present in the vicinity of the post-HIFU treatment area (H&E, at × 100 magnification, bar length: 100 μm).

prostate cancer following previous external beam radiotherapy.[2] In order to provide accurate pathological diagnostic and/or prognostic information in post-HIFU radical prostatectomy, pathologists require knowledge of the expected post-treatment histopathological changes, as has been established for radiation and hormonal therapy.

In our case, no viable tumour cells were identified within the treatment area which may indicate a satisfactory tumour response to focal HIFU therapy. The treatment related changes in the non-neoplastic tissue were mainly reactive and reparative in nature, such as stromal edema, hyalinization, fibrosis with neovascularization, corpora amylacea rimmed by foreign body type giant cells without glandular lining, hemosiderin laden macrophages and basal cell hyperplasia. There were no such changes seen in the adenocarcinoma in contralateral non-treated left lobe, suggesting that the tumour here was not subjected to the focal-HIFU treatment.

Previous study on histopathological findings of prostate adenocarcinoma in the radical prostatectomy specimens following focal-HIFU treatment included limited case number and the time interval in between the HIFU and radical resection was short.[3] Another study on biochemical failure after focal HIFU therapy reported 77% of such patients demonstrated positive prostatic adenocarcinoma on follow-up biopsies, but did not provide information on whether they were infield or outfield recurrences.[4] It also did not rule out potential sampling errors or any correlation with exact locations of core biopsies and previous MRI scan PIRADS lesions. However, tissue effects of HIFU did not impair pathologists' ability to detect and grade prostate adenocarcinoma in those post-HIFU biopsies. Our case concurs with reported post-HIFU histopathological findings, including the HIFU-treated area showing complete fibrosis without any evidence of residual carcinoma.

The value of serum PSA and multi-parametric MRI scans in predicting cancer recurrence showed sensitivity of about 14% after post-focal HIFU therapy and prostate biopsy was recommended as a better modality for routine follow-up.[5] Unfortunately, our patient's follow-up was disrupted by the COVID-19 pandemic and his PSA level was only obtained ten months post-treatment. The new focus of contralateral lobe adenocarcinoma shown on biopsy suggested an outfield recurrence, which was further supported by the radical prostatectomy findings.

In summary, we present histopathological changes of a case of focal-HIFU treatment of prostate adenocarcinoma followed by radical prostatectomy. The complete response with absence of residual cancer and associated treatment-related changes in the region of the biopsy-diagnosed prostatic adenocarcinoma support the efficiency of focal-HIFU therapy of localised prostatic cancer. The remaining cancer in the contralateral lobe together with increased PSA in the follow-up underscore the necessity of monitoring and surveillance following focal-HIFU prostate cancer treatment.

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Declaration of competing interest

Authors declare no conflicts of interest.

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