MedCrave
Step into the World of Research
International Journal of Radiology & Radiation Therapy

Case Series
Open Access
CrossMark

Prostate-specific antigen bounce following radical prostatectomy and external beam radiotherapy: A case series

Abstract

Introduction: Localized prostate cancer (CaP) is often cured with radical prostatectomy (RP). To prolong PSA biochemical control, post-operative external beam radiotherapy (EBRT) can be given. PSA levels, however, can unexpectedly go through a bounce. When PSA readings don't go according to the prediction of the treating team, patients' expectations may not be met, and confidence can decrease. PSA bounce is not well described after RP followed by EBRT.

Methods: We present a series of six cases with no history of hormone therapy with a PSA bounce after RP followed by EBRT. Bounce was defined as any rise in PSA from previous that recovered without intervention. Analysis to find any common cause was done.

Results: Averages included patient age of 63 years; presenting PSA of 7; gland size of 44g; Gleason score of 7 and tumor volume of 3.1cc. On average they had 2 factors tha justified post-operative RT, the average nadir post RP was 0.14, 5 had salvage RT and had RT at an average of 38 months post RP. On average the bounce happened 10 months after RT, the average height of the bounce for 5 of 6 patients was 0.03ng/ml, the average duration for 5 of 6 patients was three months, 5 of 6 were stable on observation and 4 experienced second bounces at an average of 3 years after the first bounce which were all of lower amplitude than the first. No common thread in causality of the bounce was found except that the majority (5/6) had a PSA nadir that was still detectable post RP.

Conclusion: We suggest the treating team prepare patients for a possible bounce up front, especially those who do not nadir to undetectable post RP.

Keywords: prostate-specific antigen, prostatic neoplasms, radiotherapy, prostatectomy, anxiety, case reports

Volume 6 Issue 1 - 2019

Christina A Anthony,[1,2] Phillip Stricker,[3] David Ende,[3] Graham Coombes,[4] Gerald B Fogarty[1,5,6]

[1]Department of Radiation Oncology, St.Vincent's Hospital, Australia
[2]Department of Radiation Oncology, Westmead Hospital, Australia
[3]Department of Urology, St.Vincent's Hospital, Australia
[4]Department of Urology, Mater Hospital, Australia
[5]GenesisCare, St.Vincent's Hospital, Australia
[6]Faculty of Engineering, University of Technology, Australia

Correspondence: Gerald B Fogarty, Department of Radiation Oncology, St.Vincent's Hospital 438 Victoria Street Darlinghurst, Sydney, NSW, 2010, Australia, Tel +612 8302 5400, Fax +612 8302 5410, Email gerald.fogarty@genesiscare.com

Received: January 29, 2019 | **Published:** February 11, 2019

Abbreviations: CaP, carcinoma of prostate; Cc, cubic centimeters; Gms, grams; ECE, extra capsular extension; IHD, ischaemic heart disease; LN+, lymph node involvement; mar+, margin positive; MeSH, medical subject headings; Mm, millimeter; MRI, magnetic resonance imaging; ng/ml, nanograms per milliliter; Post op, post operative; PSA, prostate-specific antigen; PSMA, prostate specific membrane antigen–this abbreviation used usually as part of describing a [68Ga] gallium labelled prostate-specific membrane antigen ligand (PSMA) scan; RP, radical prostatectomy; RT, radiotherapy; SUV, standardized uptake value; SV+, seminal vesicle involvement; T2DM, type 2 diabetes; yrs, years

Introduction

Localized prostate cancer (CaP) is often cured with radical prostatectomy (RP).[1] Patients can then be followed with serial prostate-specific antigen (PSA) testing. PSA can reliably help in detecting progression.[2,3] To prolong PSA biochemical control, planned post-operative external beam radiotherapy (EBRT) can be given depending on the finding of high-risk histopathological findings,[4] or as early salvage for rising PSA.[5] PSA should nadir to undetectable after RP and EBRT.

PSA levels as they decline can unexpectedly go through a bounce. PSA bounce is a temporary, benign rise in PSA after RT, usually brachytherapy (BT), and to a lesser extent definitive EBRT, followed by a return to pre-bounce levels without treatment. The cause of the bounce is not known but has been associated with younger age in BT.[6] PSA bounce is not well described after RP followed by EBRT. Patients can become anxious when PSA levels don't perform as expected.[7] Confidence in the treating team can be impacted.

We present a series of cases of PSA bounce after RP followed by EBRT to try and find any common threads that can help the treating team prepare patients for a possible bounce.

Methods

The case notes of patients from the practice of a single radiation oncologist with a prostate cancer interest with a PSA bounce were reviewed. Bounce was defined as any rise in PSA from previous that recovered without intervention. The criteria for inclusion was that the patients had to have had a history of RP and follow-up EBRT for CaP but no hormone therapy. The notes were interrogated for any similarity in the cases.

Other factors were recorded including age, comorbidities, surgical and radiotherapy treatment details, PSA history including height and duration of bounce were found and tabulated.

A literature search with Medical Subject Headings (MeSH) search terms[8] of (radical prostatectomy), (radiotherapy), (Prostate-specific antigen) and (bounce) was conducted looking for similar series for comparison.

Results

Six cases of patients with RP for CaP, followed by EBRT with a PSA bounce but no history of hormone therapy were reviewed. Patients were treated between 2004 and 2015. All PSA biochemical tests were done by the same pathology provider. The cases are summarized below. Patient and tumour characteristics are tabulated in Table 1. Bounce and current situation characteristics are tabulated in Table 2. The literature search revealed no similar previous studies.

Table 1 Patient and treatment characteristics

Patient number	Age at RP; comorbidities	Presenting PSA ng/ml; gland size (gms); gleason score; tumour volume (cc)	High risk features	Post RP PSA nadir	RT - post op or salvage; months after RP; volume
1	54	2.7; 38; Gl 4+3=7; 0.3	none	<0.01	Salvage; 54; pelvis
2	64; T2DM IHD	unknown	unknown	unknown	Salvage; 144; fossa
3	57; Graves' disease	6.9; 40.9; Gl 4+3; 4.3	ECE, SV+	0.29	Salvage; 8; pelvis
4	65	6.9; 52;4+5; 4.5	ECE	0.17	post op; 3; pelvis
5	63	12; 45;3+4; 3.3	ECE; mar+	0.02	Salvage;12; fossa
6	73	6.3; 45; 4+3; 3.3	ECE; SV+;LN	0.22	Salvage; 4; pelvis
Average	63	7;44;7;3.1cc	2 factors	0.14	5 salvage; 38

ng/ml, nanograms per millilitre; RP, radical prostatectomy; PSA, prostate specific antigen; Gms, grams; Cc, cubic centimetres; T2DM, type 2 diabetes; IHD, ischaemic heart disease; ECE, extra capsular extension; SV+, seminal vesicle involvement; mar+, margin positive; LN+, lymph node involvement; Post op, post operative

Table 2 PSA Bounce characteristics and current situation

Patient number	RT to bounce (months)	Bounce height ng/ml	Bounce duration (months)	Current situation	Other information
1	2	0.04	3	Stable Observation at 0.04	
2	12	1.05	12	Stable Observation at 0.96	Bounce 2 at 12 months post RT
3	4	0.03	3	Stable Observation at 0.06	Bounce 2 at 14 months post RT
4	18	0.03	3	Stable Observation at 0.19	Bounce 2 at 3 yrs post RT
5	12	0.02	3	Stable Observation at 0.06	Bounce 2 at 7 yrs post RT
6	11	0.02	3	Systemic Therapy 3 years post bonce	At 2 years had RT
Average	10	0.03 Excluding 2	3 Excluding 2	Stable on observation	4 second bounces

RT, radiotherapy; yrs, years

Case summaries

Patient one had RP at 55 years of age with a 38-gm gland with 0.3cc tumour of Gleason 4+3=7 with no high-risk features. PSA went from 2.4ng/ml to undetectable (less than 0.01) at 6 weeks post operation. Thirty months later, it became detectable at 0.02. Twenty months later it was 0.06. PSMA scan showed positivity in the right seminal vesicle bed. He received RT, 66Gy in 33 fractions to a pelvic volume from prostatic fossa up to L5/S1 disc space at 54 months post RP. Six weeks after RT, PSA rose from 0.06 to 0.1, a bounce of 0.04, nadired to 0.01 at 12 months post RT, then 14 months later has increased to 0.04 and he is being currently observed.

Patient two had co-morbidities of Type 2 diabetes and ischaemic heart disease. He had RP for CaP at 64yrs, histopathological details are unknown. PSA had risen to 7.5ng/ml at 11 years, MRI showed a 10mm recurrence at the anastomosis. RT to prostatic fossa was given at 12 years. PSA nadired to 0.05 at 13 years then he had first bounce to 1.2 by 14 years with a negative PSMA scan. PSA then went to 0.77. One year later he had a second bounce to 1.02; and now 5 months later the PSA is 0.96 and he is being currently observed.

Patient three had Graves disease causing hypothyroidism. He had RP at 57 for CaP with gland weighing 40.9gms with volume of cancer of 4.3cc that was unifocal with Gleason 4+3=7 with 65% grade 4. He had risk factors of extracapsular extension of 1mm and bilateral seminal vesicle involvement. PSA at 6 weeks post op was 0.29ng/ml and 3 months later had a rise to 0.54. PMSA scan showed pelvic lymph nodes. Salvage node dissection showed 1/13 lymph nodes involved with a 10mm focus in left obturator node with no ECE. PSA then dropped to 0.11 after this surgery. Three months later PSA had risen to 0.16. He then had salvage pelvic RT 66Gy in 33 fractions at 8 months post RP. PSA dropped to 0.05 in four months but increased to 0.08 in six months later as bounce 1, dropping back to 0.05 three months later, then up to 0.07 as bounce 2 at 14 months, then down to 0.05 at another three months. PSA then back to 0.06 six months later where it remains a further 6 months later and he is being currently observed.

Patient 4 had RP at 65 for CaP with presenting PSA of 6.9ng/ml with a 52g gland with multifocal 4.5cc tumour of Gleason 9 with ECE bilaterally of 2mm. Post op PSA was 0.17 at 6 weeks, increasing to 0.21 by three months. He then had RT 66Gy in 33 fractions to pelvis, PSA nadiring to 0.01 at one-year post RT, then increasing to 0.04 as the first bounce at 18 months, then to 0.02 after three months, then up to 0.21 as the second bounce in 3 years post RP before decreasing to 0.19 three months later and he is being currently observed.

Patient 5 at 63 had RP for CaP with presenting of PSA 12ng/ml. He had a 45g gland, Gleason 3+4=7, with unifocal disease of 3.3cc with

Citation: Anthony CA, Stricker P, Ende D, et al. Prostate-specific antigen bounce following radical prostatectomy and external beam radiotherapy: A case series. *Int J Radiol Radiat Ther.* 2019;6(1):20–22. DOI: 10.15406/ijrrt.2019.06.00206

ECE up to 0.7mm; and a 6mm positive margin with grade 3 at margin and none of five lymph nodes involved. Post operative PSA went to 0.02 then rose to 0.03 in one year. He had salvage prostatic fossa RT. Post RT PSA went to 0.01. PSA rose to 0.03 in one year as first bounce then back to 0.2 for 2 years then to up to 0.08 as second bounce 2 over 5 years from RP. PSA went back to 0.06 after 3 months and he is being currently observed.

Patient 6 at 73 had RP for CaP with presenting PSA of 6.3ng/ml with a 43g gland with a 3.3cc multifocal cancer, Gleason 4+3=7, and ECE of up to 2mm. One of ten right sided lymph nodes was positive. None of eight left sided nodes were positive. Post operative PSA nadired to 0.22. By four months post RP it was 0.4. RT to pelvis was then given and eight months later PSA had fallen to 0.15. Three months later, eleven months after RT PSA rose to 0.17 as a bounce, settling to 0.10 three months later. 2 years later PSA was 0.34. PSMA scan showed paraaortic lymph nodes with SUV of 3.3 three months later. RT was given but PSA continued to rise to 0.79 three months later and he was referred for systemic therapy.

Discussion

Six cases of patients with RP for CaP, followed by EBRT with a PSA bounce but no history of hormone therapy were investigated and analysed. Analysis of the bounces revealed that,on average, the bounce occurred at an average of 10 months post EBRT, shorter than the 18 months seen in low dose rate BT (Kubo) . The average height of the bounce in 5 of 6 was 0.03ng/ml, the average duration of 5 of 6 was three months, 5 of 6 were stable on observation and 4 experienced second bounces at an average of 3 years after the first bounce, which were all of lower amplitude than the first.

On looking for similarities, no common cause of the bounce was found except that the majority (5 of 6) had a detectable PSA post RP. Only one had a history of an auto-immune disease and its treatment (Graves' disease). All were immune competent at the time of bounce. Only one needed further therapy to date, receiving RT for PSMA positive paraaortic nodes 2 years post bounce. He eventually needed systemic therapy 3 years post first bounce.

Expectations of prostate cancer patients can impact their cancer journey.[9] PSA bounce in BT is well described[10] and the treating team specifically advise patients about this, effectively managing the patient expectations. PSA bounce is not well described in EBRT, teams do not routinely advise patient about it and so an unexpected bounce after EBRT can be disconcerting for patients and difficult to distinguish from biochemical failure. Serial PSA readings over time are needed, as well as patience among all involved as the time course of the bounce plays out. When PSA readings don't go according to the prediction of the treating team, patient confidence can decrease. The subjective experience with this cohort was that the time of the bounce led to a decrease in confidence in the treating team. We suggest the treating team prepare patients for a possible bounce up front especially those who do not nadir to undetectable post RP.

Acknowledgments

None.

Conflicts of interest

The author declares that there is no conflicts of interest.

References

1. Bill-Axelson A, Holmberg L, Garmo H, et al. Radical Prostatectomy or Watchful Waiting in Prostate Cancer - 29-Year Follow-up. *N Engl J Med*. 2018;379(24):2319–2329.
2. Antonarakis ES, Zahurak ML, Lin J, et al. Changes in PSA kinetics predict metastasis- free survival in men with PSA-recurrent prostate cancer treated with nonhormonal agents: combined analysis of 4 phase II trials. *Cancer*. 2012;118(6):1533–1542.
3. Adhyam M, Gupta AK. A Review on the Clinical Utility of PSA in Cancer Prostate. *Indian J Surg Oncol*. 2012;3(2):120–129.
4. Pagano MJ, Whalen MJ, Paulucci DJ, et al. Predictors of biochemical recurrence in pT3b prostate cancer after radical prostatectomy without adjuvant radiotherapy. *Prostate*. 2016;76(2):226–234.
5. Thompson IM, Valicenti RK, Albertsen P, Davis BJ, Goldenberg SL, Hahn C, Klein E, Michalski J, Roach M, Sartor O, Wolf JS Jr, Faraday MM. Adjuvant and salvage radiotherapy after prostatectomy: AUA/ASTRO Guideline. *J Urol*. 2013;190(2):441–449.
6. Kubo K, Wadasaki K, Kimura T, et al. Clinical features of prostate-specific antigen bounce after 125I brachytherapy for prostate cancer. *J Radiat Res*. 2018;59(5):649–655.
7. Kobayashi M, Nukui A, Kamai T. Psychological impact of serial prostate-specific antigen tests in Japanese men waiting for prostate biopsy. *Int J Clin Oncol*. 2017;22(1):174–180.
8. https://www.nlm.nih.gov/mesh/
9. Xu J, Janisse J, Ruterbusch JJ, et al. Patients' Survival Expectations With and Without Their Chosen Treatment for Prostate Cancer. *Ann Fam Med*. 2016;14(3):208–214.
10. Bernstein MB, Ohri N, Hodge JW, et al. Prostate-specific antigen bounce predicts for a favorable prognosis following brachytherapy: a meta-analysis. *J Contemp Brachytherapy*. 2013;5(4):210–214.