

Lymph Node Response in a Patient With Metastatic Castration-resistant Prostate Cancer Treated With Radium-223

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Clinical Practice Points

- Bone metastasis is a prevalent complication and a major cause of death among patients with metastatic castration-resistant prostate cancer (mCRPC). Radium-223, an α -emitter that selectively targets bone tumors, is a promising treatment choice for mCRPC patients with bone metastases.
- Recent preclinical evidence has suggested that radium-223, despite its short range of radiation, might lead to regression of tumors at distant sites, potentially through induction of immunogenic responses. A similar abscopal effect has occasionally been reported in patients undergoing local radiotherapy.
- In the present case report, serial gallium-68 (^{68}Ga) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) scanning showed consistent disease responses of both metastatic lymph nodes and bony metastases in a mCRPC patient treated with radium-223.
- It is worth investigating whether the potential abscopal effect is associated with the ultimate overall survival advantages in mCRPC patients receiving radium-223. The potential synergistic effect of radium-223 and immunotherapies is another key direction for future research.
- A ^{68}Ga -PSMA PET/CT scan could help assess disease response to radium-223 and serve to guide subsequent local ablative therapy for nonresponding tumors.

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Introduction

A substantial proportion of metastatic castration-resistant prostate cancer (mCRPC) patients develop bone metastases, which are a main cause of death and other skeletal-related complications.^{1,2} One of the promising treatment options for mCRPC patients with bone metastases is radium-223, a targeted α -emitter that selectively binds to areas of increased bone turnover in bone metastases and emits high-energy, short-range (< 100 μm) radiation, leading to a strong and highly localized cytotoxic effect.³⁻⁶ Its efficacy and safety were established in the ALSYMPCA (a phase III study of radium-223 dichloride in patients with symptomatic hormone refractory

prostate cancer with skeletal metastases) trial⁷ and verified in a number of real-life studies.⁸⁻¹⁰

Given the highly bone-seeking nature and localized radiation effect of radium-223, it is not expected to act on carcinomas in soft tissue. However, preliminary evidence has suggested that radium-223 might lead to regression of tumors at distant sites,¹¹⁻¹³ possibly through induction of adaptive immune responses.^{11,13} This abscopal effect has been reported for local radiotherapy (RT) in a number of cases.¹⁴⁻¹⁸

The present report details the case of persistent tumor responses in the lymph nodes, as shown by dual-tracer gallium-68 (^{68}Ga) prostate-specific membrane antigen (PSMA) positron emission tomography/computed tomography (PET/CT) imaging results, in a mCRPC patient with bone metastases treated with radium-223.

Case Report

A 79-year-old man with prostate adenocarcinoma, stage pT2N0, Gleason score 3 + 4, underwent radical prostatectomy in 2004, followed by salvage RT to the prostate bed because of biochemical

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Table 1 Functional Parameters Shown by ⁶⁸Ga-PSMA PET/CT Scans

Site	Aug 5, 2016 (Baseline)			Mar 29, 2017 (After ²²³ Ra ^a)			Change From Baseline (SUV _{max} %)	Aug 21, 2017 (5 mo After ²²³ Ra)			Change From Baseline (SUV _{max} %)	Remarks
	LD (mm)	PD (mm)	⁶⁸ Ga-PSMA (SUV _{max})	LD (mm)	PD (mm)	⁶⁸ Ga-PSMA (SUV _{max})		LD (mm)	PD (mm)	⁶⁸ Ga-PSMA (SUV _{max})		
Bone lesions												
S2	11.2	7.5	5.3	Resolved			-100.0	NA	NA	NA	NA	
Left lateral 7th rib	11.8	7.4	3.9	Resolved			-100.0	8.2	7.4	5.8	+48.7	
T6	19.8	16.5	63.5	11.7	10.5	3.2	-95.0	15.7	12.6	1.4	-97.8	Pre- ²²³ Ra pRT ^b
Manubrium	15.0	13.7	64.0	9.3	6.1	5.1	-92.0	6.2	5.1	4.7	-92.7	
C2 right lamina	18.0	11.1	79.5	11.2	7.5	10.2	-87.2	9.8	6.3	3.0	-96.2	Pre- ²²³ Ra pRT ^b
Right posterior 9th rib	22.1	12.3	39.2	16.5	12.4	7.1	-81.9	16.8	13.2	7.3	-81.4	
Lesion around right 6th costal cartilage	10.5	7.4	5.2	10.5	9.2	4.8	-7.7	10.6	3.7	6.0	+15.4	
Left clavicle	11.4	9.1	5.5	10.3	9.2	5.1	-7.3	7.8	6.4	4.3	-21.8	
S1 right-side lesion	10.5	7.4	10.6	11.7	10.5	17.6	+66.0	9.4	6.7	7.0	-34.0	Post- ²²³ Ra SBRT ^c
Left humerus	12.6	7.0	6.0	11.4	8.4	11.7	+95.0	9.0	5.4	6.2	+3.3	Post- ²²³ Ra SBRT ^c
Lesion around left 5th costal cartilage	12.5	6.3	19.6	19.3	12.4	43.7	+123.0	7.7	5.9	23.4	+19.4	Post- ²²³ Ra SBRT ^c
Lymph node lesions												
Lymph node at right iliac bifurcation	17.3	11.7	46.4	20.4	17.3	20.6	-55.6	12.3	7.9	9.4	-79.7	
Left internal iliac node	10.3	9.2	20.4	9.6	8.7	10.9	-46.6	8.7	5.4	2.7	-86.8	
Left internal mammary node at 1st intercostal space	19.8	11.4	90.9	19.9	14.9	52.0	-42.8	17.8	11.3	50.7	-44.2	
New bone lesions found Aug 21, 2017												
Right lateral 1st rib	NA	NA	NA	NA	NA	NA	NA	15.0	10.5	1.5	NA	
Left posterior 3rd rib	NA	NA	NA	NA	NA	NA	NA	5.5	5.3	1.8	NA	
T3 right transverse process	NA	NA	NA	NA	NA	NA	NA	15.6	6.7	1.7	NA	
Lesion around right 6th medial costal cartilage	NA	NA	NA	NA	NA	NA	NA	6.4	4.2	3.1	NA	
Left posterior ilium	NA	NA	NA	NA	NA	NA	NA	6.4	4.2	2.1	NA	

Abbreviations: ⁶⁸Ga = gallium-68; LD = longest diameter; NA = not available; PD = diameter perpendicular to LD; PET/CT = positron emission tomography/computed tomography; PSMA = prostate-specific membrane antigen; pRT = palliative radiotherapy; ²²³Ra = radium-223; SBRT = stereotactic body radiotherapy; SUV_{max} = maximum standardized uptake value.

^aRadium-223 treatment, 6 injections completed; first injection was on Oct 24, 2016 and the last injection on Mar 10, 2017.

^bpRT was completed in Aug 2016 (ie, 2 months before ²²³Ra administration).

^cSBRT was given from April to May 2017 (ie, 1 month after completion of ²²³Ra treatment).

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