False-Positive Findings on Bone Scintigraphy After MRI-Guided Stereotactic Ablative Radiotherapy for Osseous Oligometastasis.

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Research Article

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Abstract

Radical radiation therapy for oligorecurrent prostate cancer is considered to improve both overall and disease-specific survival. Therefore, accurate diagnosis by imaging is important when considering the indications for radiation therapy. We present a case of marginal recurrence of bone metastases from castration-resistant prostate cancer previously treated with radical radiation therapy, which could not be detected by bone single photon emission computed tomography/computed tomography (SPECT/CT) but could be diagnosed by 68Ga-prostate-specific membrane antigen positron emission tomography/computed tomography (68Ga-PSMA PET/CT). Bone SPECT/CT showed false-positive tracer uptake in the lesion previously irradiated. 68Ga-PSMA PET/CT scan showed no abnormal uptake in the previously irradiated lesion, but showed intense uptake in the newly developed metastasis near the irradiated site. 68Ga-PSMA PET/CT scan may be able to diagnose marginal recurrence after radiation therapy more accurately than bone SPECT/CT.

Introduction

Positron emission tomography/computed tomography (PET/CT) with ligands of the prostate-specific membrane antigen (PSMA) has been shown to be useful for initial staging of prostate cancer, assessment of biochemical recurrence, and detection of distant metastasis [1, 2]. For the detection of bone metastasis, PSMA PET was reported to have better sensitivity and specificity than bone scintigraphy [3]. Due to the high diagnostic accuracy for bone metastases, PSMA PET/CT plays an important role in the treatment of oligometastatic bone disease [4]. However, it is not known well whether PSMA PET can accurately diagnose the recurrence after radiation therapy for bone metastasis. Here, we report a case of oligometastatic prostate cancer who developed marginal recurrence of bone metastases previously treated with radical radiation therapy, which could not be detected by bone scintigraphy or bone single photon emission computed tomography/computed tomography (SPECT/CT) but could be diagnosed by 68Ga-PSMA PET/CT.

Case Report

A 64-year-old man with a history of high-risk prostate cancer (Gleason score 4 + 4 = 8; cT2aN0M0; prostate-specific antigen (PSA) level 9.29 ng/mL) was referred to our institution due to a slowly rising serum PSA level over 6 months. He had been treated with radical prostatectomy and whole pelvic radiotherapy 2 years previously, and receiving combined androgen blockade with leuprolide and bicalutamide. Since his PSA levels had been rising (PSA 1.866 ng/ml) in the setting of serum testosterone levels within the castrate range, he was diagnosed with castration-resistant prostate cancer (CRPC). Whole-body 99mTc-hydroxymethylene diphosphonate (HMDP) bone scintigraphy showed a solitary uptake in the right proximal humerus (Figs. 1a and 1b), but no other metastatic lesions were found on whole-body CT. Since radical local therapy for oligorecurrent prostate cancer is considered to improve both overall and cause-specific survival [5, 6], on-board MRI-guided stereotactic ablative radiotherapy (SABR) with a dose regimen of 35 Gy in 10 fractions was performed. His PSA level

decreased to 0.106 ng/ml 6 months after SABR, but began to increase continuously, so whole-body bone scintigraphy and SPECT/CT were performed when his PSA level reached 2.078 ng/ml. The bone scintigraphy (Figs. 2a and 2b) and SPECT/CT (Fig. 2c) showed solitary uptake of 99mTc-HMDP at the same site as the right proximal humerus which was previously treated with SABR. Although a slight accumulation was observed outside the previously treated site, CT showed no other bone metastases or metastases to other organs. MRI of the abdomen and pelvis was normal. In order to distinguish whether this biochemical recurrence was a relapse of the same bone metastases previously treated by SABR or newly developed metastasis, 68Ga-PSMA PET/CT was performed after obtaining informed consent.

68Ga-PSMA PET/CT showed no abnormal uptake in the previously irradiated lesion, but a new bone metastasis was found adjacent to the previously irradiated lesion (Fig. 3). The newly developed metastasis of the right humerus was hyperintense on short tau inversion recovery (Fig. 4a), diffusion-weighted imaging (Fig. 4b), and T1 mapping (Fig. 4c) compared to the previously irradiated site. Based on the MRI findings, we confirmed that the increased uptake of the right humerus detected by 68Ga-PSMA PET/CT was a newly developed metastasis of CRPC. Since whole-body 68Ga-PSMA PET showed no other abnormal uptake, salvage re-irradiation was performed using rotational intensity modulated radiotherapy system (TomoTherapy®, Sunnyvale, CA, USA) with 35 Gy in 10 fractions. His condition was uneventful during and after re-irradiation, and his PSA levels have been decreasing during the 6-month follow-up period.

Discussion

Radical radiation therapy for oligorecurrent prostate cancer is considered to improve both overall and disease-specific survival [5, 6]. However, there is no consensus on imaging modality to evaluate the indications for radical radiation therapy such as SABR. Recent report has shown the diagnostic utility of 177Lu-PSMA SPECT; however, 68Ga-PSMA PET is likely to be more useful because of the better spatial resolution and sensitivity of PET [7]. In this article, bone scintigraphy and SPECT/CT did not accurately detect the recurrent lesion. We considered that the first bone metastasis was osteoblastic metastasis, but the second bone metastasis was bone marrow metastasis rather than osteoblastic metastasis. Therefore, 99mTc-HMDP did not accumulate in the second metastasis, and abnormal accumulation was observed in the first osteoblastic metastatic lesion despite SABR was performed. On the other hand, in 68Ga-PSMA PET, the tracer specifically binds to the PSMA which is expressed in viable prostate cancer cells and the spatial resolution is better than SPECT [1–3, 7, 8].

There are several unique aspects in this article. First, 68Ga-PSMA PET may be superior to bone scan in evaluating the therapeutic effect after radiotherapy. As far as we know, this is the first report to evaluate the effectiveness of SABR by performing both bone SPECT/CT and 68Ga-PSMA PET/CT. We consider that 68Ga-PSMA PET may be a useful biomarker for assessing the therapeutic effect of SABR for osseous oligometastasis. Second, abnormal accumulation of 99mTc-HMDP on bone scintigraphy and SPECT/CT does not necessarily mean relapse when SABR is given to bone metastases. In a case of oligometastasis, local control of metastatic lesion is an important prognostic factor [4–6]. Therefore,

accurate assessment of the effectiveness of SABR is mandatory in considering re-irradiation or predicting prognosis. 68Ga-PSMA PET may become a useful biomarker for predicting the post-treatment course of oligometastasis.

There are several limitations in this study. First, the optimal timing of 68Ga-PSMA PET after SABR has not yet been determined. In addition, there are few well-documented reports on PSMA PET-guided SABR for oligometastasis of CRPC [9]. A large-scale prospective study may warrant the feasibility and effectiveness of PSMA PET-guided SABR. Second, a single case report cannot be generalized to others without further scientific validation, however, this is the first report showing that PSMA PET/CT helps diagnose marginal recurrence of bone metastases treated with SABR.

In conclusions, the implementation of PSMA ligand PET may substantially improve the diagnostic accuracy of detecting osseous oligometastasis even after SABR for metastatic CRPC.

Declarations

Funding:

Not applicable.

Conflicts of interest/Competing interests:

The authors declare that they have no conflict of interest.

Ethics approval:

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate:

Written informed consent was obtained from the patient.

Consent for publication:

Not applicable.

Availability of data and material:

Not applicable.

Code availability:

Not applicable.

Authors' contributions:

YH and ET contributed to the study conception and design. Material preparation, data collection and analysis were performed by YH and ET. The first draft of the manuscript was written by YH. All authors read and approved the final manuscript.

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Figures

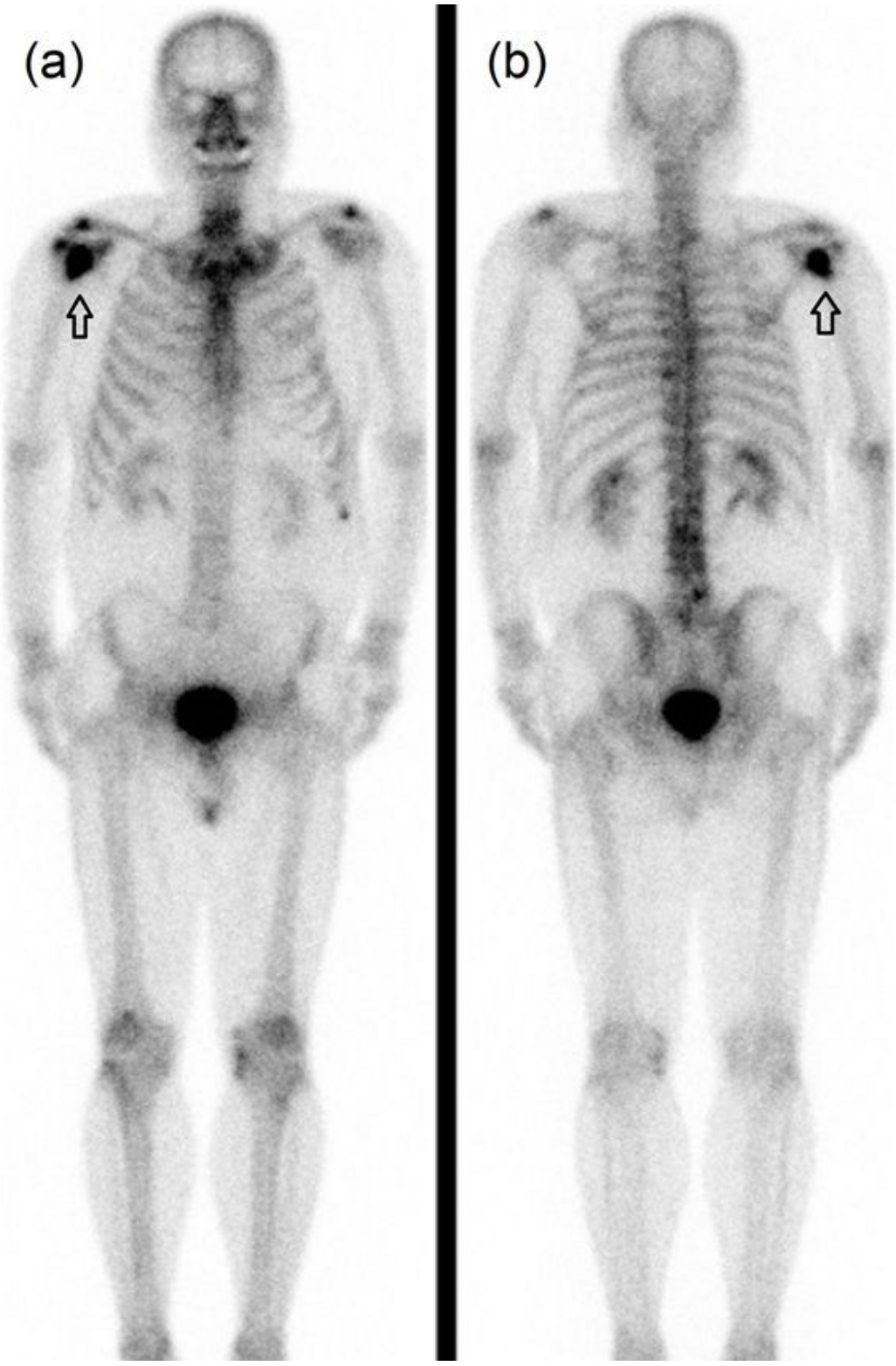

Figure 1

Whole-body 99mTc-hydroxymethylene diphosphonate (99mTc-HMDP) bone scintigraphy before stereotactic ablative radiation therapy (SABR). Anterior (a) and posterior (b) views of planar bone scan showed increased activity in the right proximal humerus (arrows).

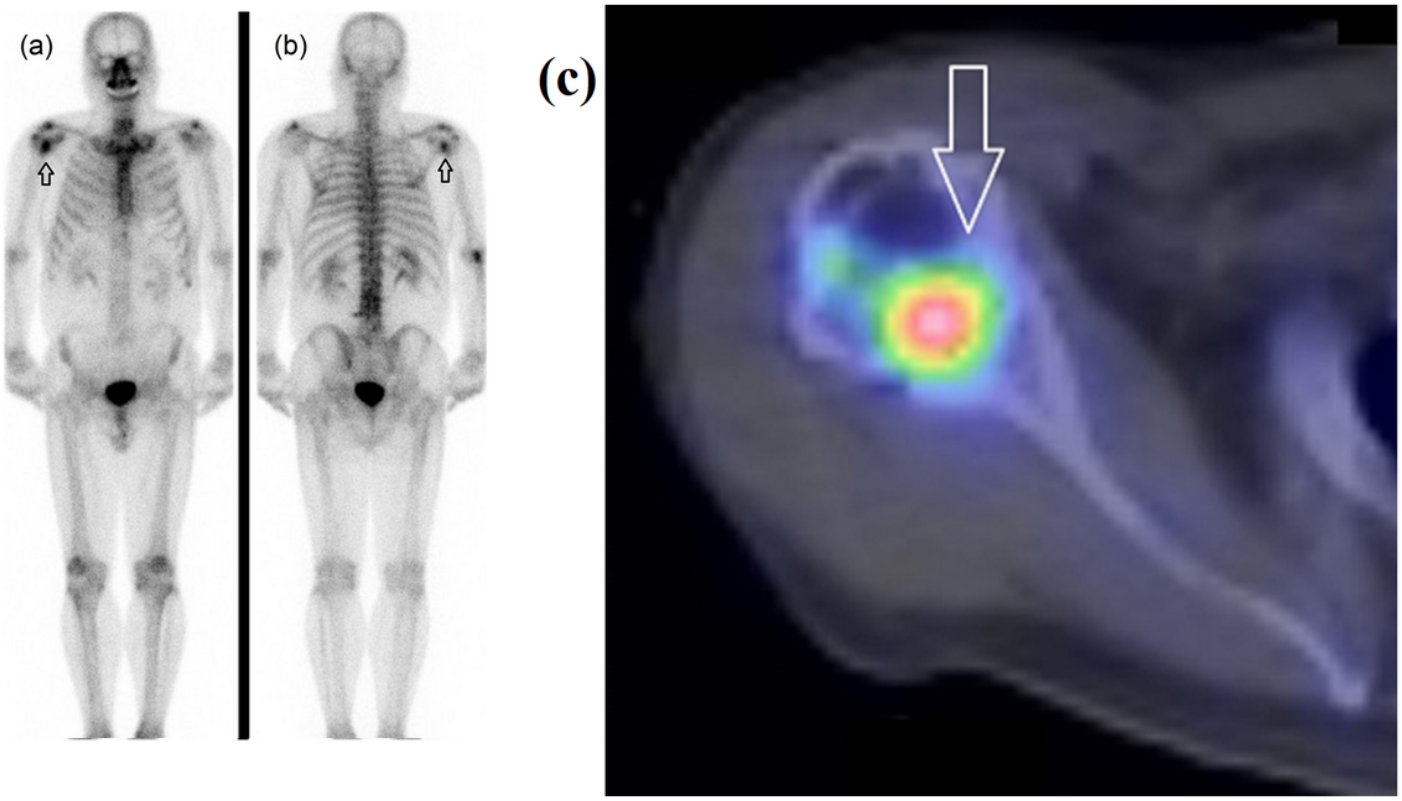

Figure 2

Whole-body 99mTc-HMDP bone scintigraphy and single photon emission computed tomography/computed tomography (SPECT/CT) after SABR. Anterior (a) and posterior (b) views of planar bone scan showed increased activity in the right proximal humerus (arrows). The bone scintigraphy shows focal tracer uptake at almost the same site as before SABR. (c) SPECT/CT revealed increased uptake of 99mTc-HMDP adjacent to the scapulohumeral joint (arrow).

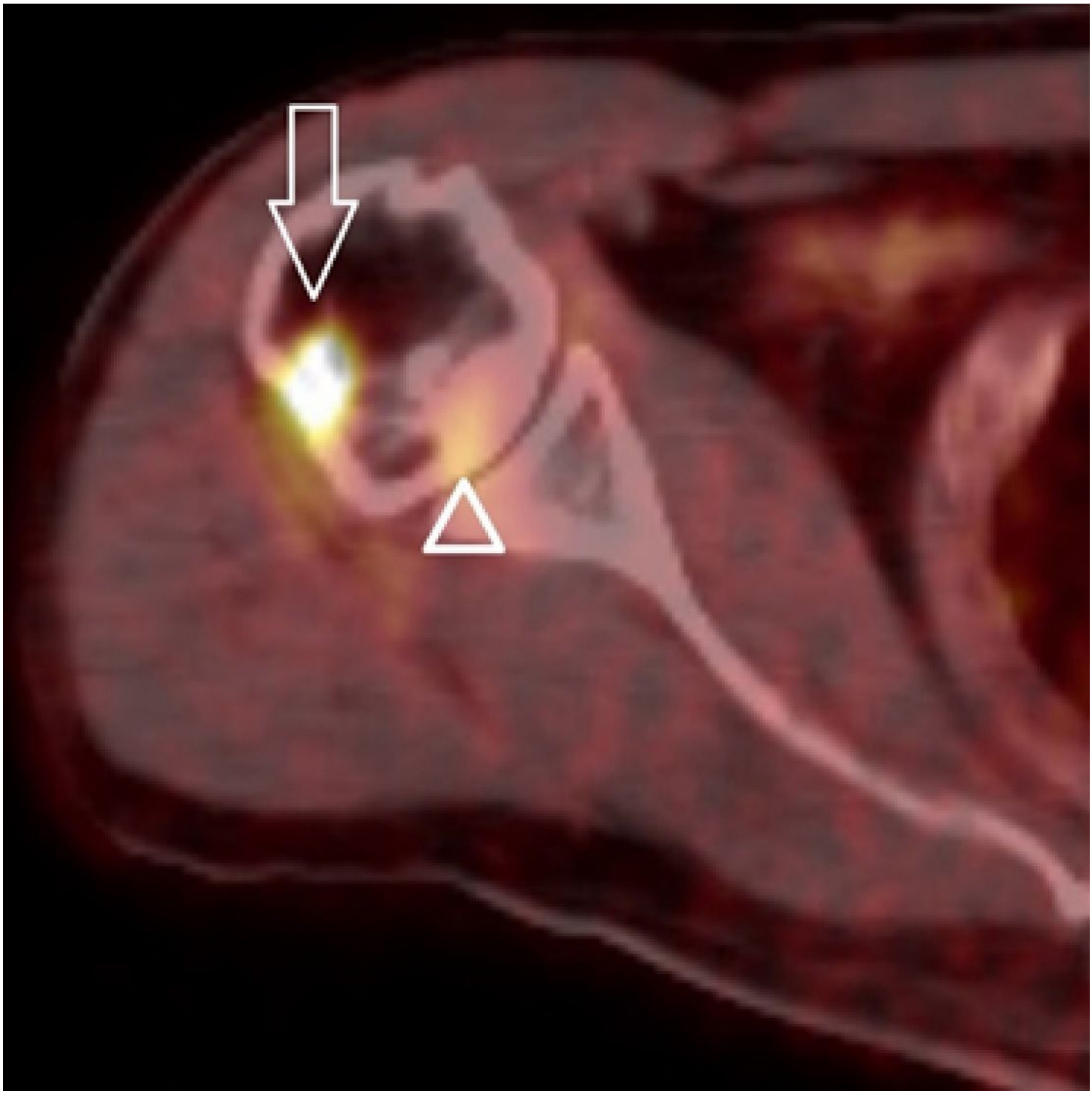

Figure 3

68Ga-prostate-specific membrane antigen positron emission tomography/computed tomography (68Ga-PSMA PET/CT) after SABR. 68Ga-PSMA PET/CT scan showed no abnormal uptake in the irradiated lesion (arrowhead), but new bone metastasis (arrow) was detected adjacent to the previously irradiated lesion.

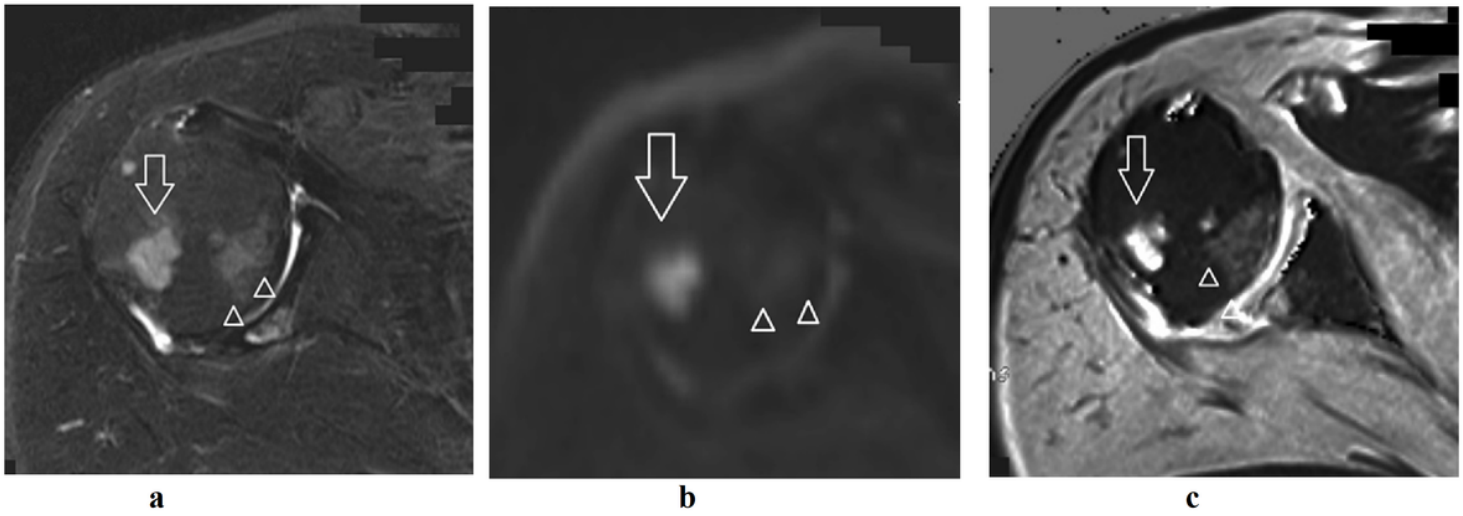

Figure 4

MRI of the right humerus after SABR. The newly developed metastasis (arrow) was hyperintense on short tau inversion recovery (a), diffusion-weighted imaging (b= 800 sec/mm^2) (b), and T1 mapping (c) compared to the previously irradiated lesion (arrowheads).