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Case Report

Mistaken Metastasis: Radiation-Induced Rib Fracture Mimicking Malignancy on Computerized Tomography Case Report

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Keywords

Lung cancer · Bone metastasis · Cancer · Non-small cell lung cancer · Radiation therapy · Case report · Radiation-induced toxicity

Abstract

A 62-year-old woman with a 40-pack-year smoking history and severe chronic obstructive pulmonary disease with early-stage right upper lobe non-small cell lung cancer (NSCLC) was treated with stereotactic ablative radiotherapy (SABR). Two years after treatment, a surveillance computerized tomography scan showed lesions of the posterior 4th and 5th ribs including expansion of the medulla that was unusual and of concern for possible malignant infiltration. A follow-up magnetic resonance imaging (MRI) scan revealed these lesions to be healing fractures post-radiotherapy. Although generally well tolerated, SABR is known to produce inflammatory and fibrotic changes both in-field and in organs at risk, and rib fractures are a well-established adverse event. MRI has high diagnostic accuracy and sensitivity for rib fractures and was able to rule out malignant spread. This case demonstrates the need for regular follow-up following SABR for early-stage NSCLC, as well as the challenge of interpreting indeterminate post-SABR radiography findings.

Introduction

Stereotactic ablative radiotherapy (SABR – also known as stereotactic body radiotherapy) is an external beam radiation therapy method used to precisely deliver a potent dose of radiation to a target tissue. The use of SABR is recommended by international guidelines as

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standard curative treatment for patients with early-stage non-small cell lung cancer (NSCLC) who refuse or are unfit for surgery [1]. Although generally well tolerated, SABR may damage surrounding tissues, causing adverse effects such as chest wall toxicity and rib fractures [1, 2]. The acute inflammatory and late fibrotic changes caused by SABR in both target and adjacent tissues may manifest as indeterminate radiographic findings [1]. Guidelines from both the American Association for Thoracic Surgery and the National Comprehensive Cancer Network recommend post-SABR follow-up with regular surveillance computerized tomography (CT), but direction is lacking on how to proceed with further investigations in the setting of suspicious findings on initial CT imaging [3]. We report a case in which a radiation-induced rib fracture initially appeared to have a malignant component on CT, and review the utility of different diagnostic tools in this setting to accurately diagnose and avoid mistreatment.

Case Report

A 62-year-old female with a former 30-pack-year smoking history and severe chronic obstructive pulmonary disease was discovered to have a 10-mm right upper lobe nodule on chest X-ray during a routine respirology visit and confirmed on CT scan. Percutaneous biopsy of the lesion was not performed as it was high risk due to the patient's centrilobular emphysema. Over 9 months of surveillance, CTs showed growth to 15 mm as shown in Figure 1. PET scan was performed demonstrating avidity, with a standardized uptake value of 3.3. Given the high probability of malignancy and elevated risks of surgical excision given her respiratory function, the patient received SABR treatment with 54 Gy in 3 fractions, every other day (shown in Fig. 1). The patient underwent planning with contrast-enhanced 4D-CT, and GTV delineated on maximum inspiration and expiration sequences, forming an ITV. A 5-mm margin was utilized from ITV to PTV. The treatment plan met institutional planning constraints (chest wall <105% of prescription), though a portion of the chest wall did receive a maximum dose 54 Gy, a dose associated with high risk of rib fracture [4]. During initial follow-up CT imaging, a transient increase in tumor size was noted. Given resolution, the changes were felt to represent post-radiation fibrosis. Subsequent imaging confirmed good treatment response.

Two years following SABR, a surveillance CT scan exhibited the following concerning changes as reported by radiology: "interval change in the posterior right 4th and 5th ribs with expansion of the marrow cavity, associated with increased density particularly in the 5th rib and periosteal break in the 4th rib. Some of these appearances could represent radiation sclerosis, but expansion of the medulla is unusual and is of concern for possible malignant infiltration" (shown in Fig. 2). Clinically, the CT changes corresponded to the high-dose radiation treatment volume (shown in Fig. 1) and were suspected to be benign radiation-related post-treatment changes. Weighing the possibility of metastasis to the 4th and 5th ribs with the clinical suspicion of fracture, magnetic resonance imaging (MRI) of the chest was ordered. MRI revealed that 4th and 5th rib lesions corresponded to healing fractures (shown in Fig. 3). This was based on low T1 and increased T2 signal intensity, with minimal post-contrast enhancement, indicating callus formation. There was no evidence of an enhancing mass, communication between the lung lesion and adjacent ribs, or an underlying pathologic lesion within the ribs. As a result, MRI favored a diagnosis of healing fractures rather than metastatic spread. This impression was validated by further improvement on subsequent surveillance CT scans.

Regular surveillance CT scans in the 2 years following revealed no recurrence or spread of malignancy, or osseous lesions. Parenchymal post-radiation changes remained stable. The patient experienced minimal pain over the area of the rib fractures, managed adequately with

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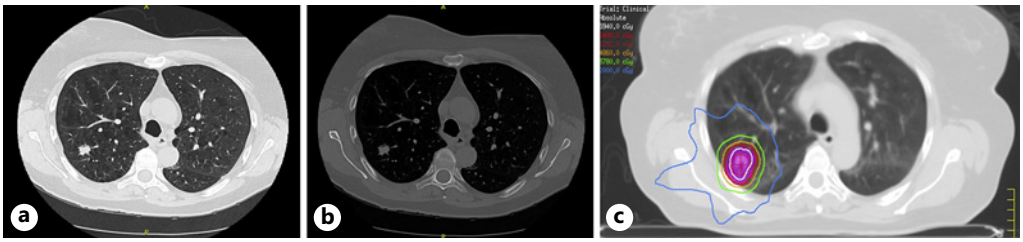

Fig. 1. Initial treatment: spiculated parenchymal-based nodule in posterior right upper lobe enlarging on CT thorax seen with lung window (**a**) and bone preset (**b**). **c** SABR was started after this CT showed mass enlargement to 1.5 × 1.1 × 2.5 cm with radiotherapy isodose lines in centigray from SABR treatment.

anti-inflammatory analgesics. A CT scan 23 months after the initial discovery of the fractures confirmed healing of the right 4th and 5th posterior rib fractures, and the patient continues with regular surveillance. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see www.karger.com/doi/10.1159/000528613).

Conclusion

This case highlights the diagnostic challenge of interpreting standard post-SABR radiographic findings following treatment of early-stage NSCLC. Differentiating between recurrent malignancy and post-radiation change is a significant challenge when evaluating post-treatment scans.

Guidelines recommend history, physical, and surveillance CT scans every 3–6 months for the first 3 years post-treatment, and continued follow-up to 5 years [5]. While optimal imaging frequency is unknown, early identification of local or regional recurrences may enable treatment with curative intent. In situations with indeterminate findings on imaging, effective diagnostic pathways are critical. Selecting the appropriate investigational modality can expedite appropriate next steps in treatment while limiting patient and system costs. In our case, a malignant finding would have necessitated further investigations and treatment in the form of local and/or systemic therapy [6]. Given the lack of diagnostic biopsy in this case (not uncommon in ES-NSCLC), deciding upon subsequent systemic therapies would have been challenging without confirmational biopsy, which could have subsequently exacerbated the rib fractures.

Local control with SABR in early-stage NSCLC is excellent, with rates between 85% and 95%, and rates of distant metastasis at 5 years post-treatment around 10% [7, 8]. SABR is known to cause fibrotic changes in radiated lung parenchyma and changes in adjacent structures, which may develop in mass-like patterns that mimic recurrent disease [3]. Given the low probability of metastatic spread of early-stage NSCLC and the location of the rib lesion adjacent to the high-dose region of radiation, the lesions were clinically suspected to be radiation-induced changes. Rib fractures are considered a relatively common adverse event following SABR, found in 7% of patients in a large pooled analysis [2]. However, some series have reported rates up to 55%, and rib fractures are felt to be more common with SABR than with conventional methods of radiotherapy [9, 10]. Predictors of rib fracture following SABR include a high total dose, high dose per fraction, short tumor-chest wall distance, female sex, and presence of pulmonary emphysema [9], all factors in our presented case. Although a common adverse effect of SABR, rib fractures are often asymptomatic and discovered

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Fig. 2. Findings on surveillance CT: CT thorax on June 7, 2019, revealed interval change in the posterior right 4th and 5th ribs with expansion of the marrow cavity (**a**), associated with increased density particularly in the 5th rib image 62 (**b**) and periosteal break in the 4th rib image 55 (**c**).

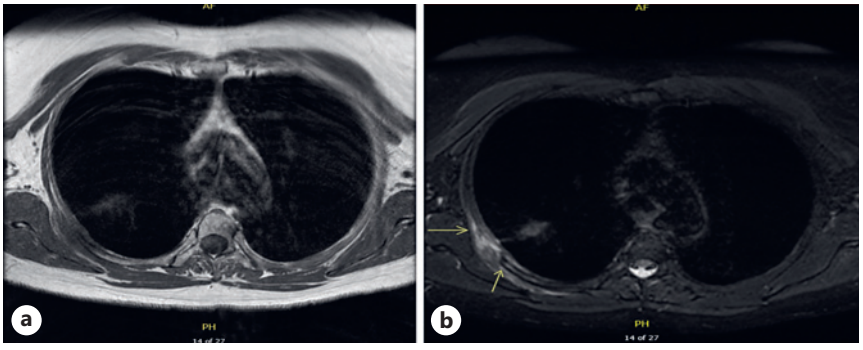

Fig. 3. MR chest: bone on September 9, 2019, showed abnormal signal changes involving the right posterior fourth and fifth ribs with what appear to be healing fractures using T1 (**a**) and T2 (**b**).

incidentally [4]. Fractures that are symptomatic are generally tolerable and can be managed adequately with analgesics, as in our case [4].

In cases with atypical findings, such as the high-density component causing expansion of the medullary cavity found in our case, guidance on best investigations to rule out malignancy is lacking [3]. Several imaging modalities have utility in diagnosing rib fractures, though mostly in the setting of traumatic injury. CT scans have a diagnostic accuracy and sensitivity rate of 57.14%, while MRI has superior accuracy (91.25%) and sensitivity (94.81%) [11]. Aside from excellent diagnostic capabilities, MRI avoids exposure to additional ionizing radiation, though timeliness of access and cost varies. In this case, the high level of soft tissue resolution provided added benefit in evaluating expansile component. Plain film X-ray and F-18 FDG PET/CT may also be useful, but have been found to have lower sensitivity and specificity [12, 13]. While PET/CT may have excellent malignant diagnostic qualities, its utility in our case may have been compromised given the small lesion and associated inflammation from fracture. Funded access and timeliness also vary by jurisdiction. Bone scintigraphy is highly sensitive in the detection of bone metastasis and fractures but is limited by specificity [14], and was likely to be avid in our case regardless of the correct diagnosis. Bone biopsy of the lesion can be useful in confirming malignancy; however, this procedure often poorly tolerated by patients and results may be non-specific if decalcification is required [15].

Our case adds to the growing literature characterizing the difficulty of interpreting radiographic findings on imaging following SABR treatment. Though post-radiation changes are common and malignant spread following SABR for early-stage NSCLC is uncommon, it is

nonetheless crucial to rule out disease recurrence or spread using additional imaging modalities such as MRI. Careful consideration of the relative advantages and disadvantages of each diagnostic modality including accessibility must be considered. We report the unusual case in which a rib fracture mimicked malignant spread on CT following SABR treatment for early-stage NSCLC and required follow-up MRI to reach an accurate diagnosis.

Patient Perspective

"After my treatment in 2017, I initially had no pain associated with my ribs. After 2 years I had some pain, occasionally significant, but did not last for long periods of time. On occasion it would start on days that I had been to the pool to exercise. Even now I still experience some slight rib pain which is managed well with anti-inflammatory tablets. I feel that the treatment I have been given has been effective; I live a full life at age 68 and am working in my own business 30 h a week. I am blessed that we have enough resources that I do not have to do any heavy housework. I am thankful for the medical care I have received."

Statement of Ethics

Ethics approval was not required for this case study. Written informed consent was obtained from participant for publication of the details of their medical case and any accompanying images. Ethical approval is not required for this study in accordance with local or national guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Supervision by D.P. Patient was under the care of D.P. Report was written by C.E.W. and A.M.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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