A Rare Presentation of Interstitial Lung Disease in a Follow-up Patient with Breast Carcinoma

Lithika M Lavanya¹, T. R. Arulponni²*

¹Department of Radiation Oncology, Mysore Medical College and Research Institute, Mysore, Karnataka, India
²Department of Radiation Oncology, Ramaiah Medical College, Bengaluru, Karnataka, India

Abstract

Breast cancer is the most common malignancy in women. The incidence is increasing in developing countries. Adjuvant radiation reduces ipsilateral breast tumor recurrence and, in turn, improves overall survival in both early and locally advanced breast cancer patients who have undergone breast conservation surgery and mastectomy, respectively. The lung is one of the dose-limiting organs in thoracic radiation. The incidence of radiation pneumonitis is rare, ranging from 5% to 15%. The incidence has further decreased with newer techniques of radiation treatment delivery. Here, we present a case of right breast carcinoma with an atypical presentation of interstitial lung disease 5 years after treatment.

Keywords: Breast carcinoma, interstitial lung disease, radiation pneumonitis, radiotherapy

Introduction

The lung is one of the dose-limiting structures in radiotherapy for breast carcinoma. The toxicity is influenced by the dose received by the lungs, fractionation, radiation energy, and preexisting lung status. The incidence of radiation pneumonitis is rare at <15%,¹ which has reduced further with advanced radiation technology.

Interstitial lung diseases (ILDs) are a heterogeneous group of pulmonary fibrotic diseases including diffuse alveolar damage, bronchiolitis obliterans organizing pneumonia, nonspecific interstitial pneumonia, and eosinophilic pneumonia.¹ Herein, we present a patient with right breast carcinoma who was diagnosed with ILD 5 years after completing treatment and was successfully treated.

Case Report

A 71-year-old female with an Eastern Cooperative Oncology Group performance score of 2 and a history of chronic kidney disease (CKD) presented with a lump in her right breast for 1 week. She had been taking tablet betaloc 25 mg once daily and insulin for 8 years for hypertension and type II diabetes, respectively. She had undergone breast conservation surgery and axillary lymph node dissection within 1 week of presenting with a lump.

Address for correspondence: Dr. T. R. Arulponni, Department of Radiation Oncology, Ramaiah Medical College, Bengaluru, Karnataka, India. E-mail: arulponni@gmail.com

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respectively. Sonomammography, done at an outside hospital, showed a space-occupying lesion of 20 mm × 14 mm in her right breast at the 6 o’clock position. Fine-needle aspiration cytology of the lesion revealed low-grade invasive carcinoma. She was clinically staged as cT2N0M0. She opted for modified radical mastectomy (MRM) over breast conservation surgery, and right-sided MRM was performed on February 22, 2013. The postoperative period was uneventful. The final histopathology revealed grade I infiltrating ductal carcinoma, free margins with no extracapsular extension, and stage pT2N1M0. Immunohistochemistry showed estrogen receptors/progesterone receptor–positive, and Her-2/neu negative. In view of node positivity, she received adjuvant radiotherapy to the right chest wall and ipsilateral supraclavicular fossa as per our institutional policy. A radiation dose of 5000 cGy/25 fractions (fr), 5 fr/week, was delivered with appropriate electron energy (6 MeV) on LINAC from April 23, 2013, to May 25, 2013. She tolerated the treatment well and was then started on hormonal therapy, tablet letrozole 2.5 mg, once daily, and deferred chemotherapy in view of her CKD. She was regularly followed up. Five years later, on March 19, 2018, she presented with a cough with expectoration for 10 days and fever for 2 days. The cough was not associated with breathing difficulty or wheezing and on examination, she had bilateral basal crepitations. The chest X-ray was normal. A respiratory physician’s advice was sought and she was started on symptomatic therapy. As the symptoms did not resolve, high-resolution computerized tomography (HRCT) of the thorax was done and she was clinically diagnosed with bilateral ILD. Figure 1 shows an axial slice of the HRCT of the thorax. She refused a biopsy of the lung. She was started on formoflo 250 inhalation (fluticasone 250 mcg + formoterol 6 mcg) twice daily, tablet Wysolone 20 mg twice daily, and oxygen therapy at home whenever required. On telephonic inquiry, she was maintaining her daily routine with the above drugs and intermittent oxygen therapy. Although the symptoms were relieved, she refused a follow-up computed tomography scan of her thorax.

**DISCUSSION**

The differential diagnosis of radiation-induced ILD includes infection, lymphangitis carcinomatosis, radiation-induced neoplasms, and recurrent carcinoma. In a literature search, we found around 380 drugs that have been reported to cause ILDs with varying incidences ± radiation. The drugs reported to cause diffuse alveolar damage are bleomycin, busulfan, carbustine, cyclophosphamide, mitomycin, and melphalan. Amiodarone, methotrexate, carbustine, and chlorambucil have been reported to cause nonspecific interstitial pneumonitis. Eosinophilic pneumonia has been reported to be caused by penicillamine, sulfasalazine, nitrofurantoin, non-steroidal anti-inflammatory drugs (NSAIDs), and para-aminosalicylic acid. The anticoagulants amphotericin B and Ara-C have been reported to cause pulmonary hemorrhage. Tamoxifen and taxanes have been reported to increase the risk of ILDs, particularly when combined with adjuvant radiation therapy.[2] Radiation-induced pneumonitis occurs classically 4 to 12 weeks after completing radiotherapy. The symptoms include fever, dry cough, and dyspnea and on imaging, alveolar opacities confined to the treatment portal. However, Roberts et al.[3] reported that in most patients, lymphocytic alveoli develop in both lung fields 4 to 6 weeks after unilateral thoracic radiation, and this was more pronounced in patients who developed pneumonitis. Cases where limited irradiation...
produces generalized bilateral lung changes are rare. This rare bilateral presentation was seen in our patient.

Our patient was treated with adjuvant radiation and aromatase inhibitors. She deferred chemotherapy and was advised to avoid NSAIDs due to the presence of CKD. The diagnosis of therapy-induced ILD involves three elements: clinical suspicion, differentiation from other parenchymal lung diseases using HRCT and other clinical tests for alternative diseases, and a compatible histological pattern; however, our patient refused a biopsy.

Common toxicity criteria for adverse effects grading for radiation pneumonitis are described in Table 1. Our patient was Grade 3 according to the criteria for radiation-induced ILD. The management of interstitial pneumonitis is mainly cessation of the causative agent and administration of corticosteroids. A few trials have tried ACE inhibitors, amifostine (Vitamin E/pentoxifylline to prevent pneumonitis and these have shown significant results. However, there are currently no guidelines or protocols available in the literature.

Our patient developed ILD 5 years following completion of treatment. Keeping in mind the fact that she was not exposed to other causative agents such as NSAIDS, taxanes, tamoxifen, or other chemotherapeutic agents, the most likely causative factor is radiation. On the other hand, pneumonitis changes are seen in whole lungs bilaterally not confined to the field of radiation. On retrospectively analyzing the dosimetric data, the chest wall was irradiated using electrons (6MeV) and a planning target volume coverage of 84% was obtained. The volume of the lung receiving a 20% dose (V20) of the ipsilateral lung was 18% and V20 of the opposite lung was 0, well below the constraints given by QUANTEC. V5 of the ipsilateral lung was 40% and V5 of the opposite lung was 5%, whereas V10 of the ipsilateral lung was 20% and V10 of the opposite lung was 0. Figure 2 shows an isodose color wash in an axial slice, and Figure 3 shows the dose–volume coverage of V20 of the right lung.

A trial by Shi et al. stated that the chance of developing ILD depends on both the dose received by the lung and/or any of the drugs, and also on other factors such as performance status, preexisting chronic obstructive pulmonary disease, or other lung diseases and baseline forced expiratory volume 1 (lung function) levels.

**Conclusion**

The varied presentation of bilateral interstitial pneumonitis is not confined to the lung within the radiation portal and is one of the rarest presentations. Regular follow-up with timely detection and interventions plays a vital role in limiting morbidity and preventing mortality.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**


**Table 1: Radiotherapy-induced interstitial lung disease is graded as per the Common terminology criteria for adverse effects v5.0 criteria**

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
<th>Grade 5</th>
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<tr>
<td>Pneumonitis/ pulmonary infiltration</td>
<td>Asymptomatic, only radiological observation, intervention not indicated</td>
<td>Symptomatic, limiting instrumental ADL, medical intervention indicated</td>
<td>Severe symptoms, limiting self-care ADL, O₂ required</td>
<td>Life-threatening respiratory compromise, urgent intervention indicated (e.g., tracheostomy, intubation)</td>
<td>Death</td>
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