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Acute Respiratory Distress Syndrome Secondary to Radiotherapy for Breast Cancer: A Case Report

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Patient: Female , 69-year-old
Final Diagnosis: ARDS secondary to radiotherapy for breast cancer
Symptoms: Acute respiratory distress • dyspnea • hypotension • hypoxemia
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine

Objective: Unusual or unexpected effect of treatment

Background: Radiotherapy is often used as an adjuvant therapy in breast cancer following surgical resection of the primary malignant tumor. It has multiple respiratory side effects, but acute respiratory distress syndrome (ARDS) is a rare complication. We describe here the case of a woman with breast cancer who developed ARDS 1 week after her final radiotherapy session.

Case Report: A 69-year-old female with breast cancer presented 1 week after her final session of radiotherapy. She had developed a sudden onset of hypotension unresponsive to fluids, oxygen desaturation unresponsive to high flow oxygen, and new bilateral infiltrates had appeared on chest x-ray (CXR) predominant in the left upper lobe, which was interestingly the main area affected by the radiotherapy beams. A diagnosis of atypical ARDS secondary to radiotherapy was established. She was intubated and a low tidal volume/high positive end-expiratory pressure (PEEP) strategy was utilized to manage her condition. After 48 hours, the infiltrates diminished remarkably, and she was extubated the following day. On discharge, she had a completely normal CXR; a computed tomography (CT) chest performed 1 month later showed complete resolution of the alveolar opacities.

Conclusions: ARDS remains an extremely rare complication of thoracic radiotherapy. However, physicians must be wary of its development in order to diagnose it quickly and treat accordingly.

MeSH Keywords: Breast Neoplasms • Radiotherapy, Adjuvant • Severe Acute Respiratory Syndrome

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/919477

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Background

Breast cancer is the most common cancer in women worldwide. Radiotherapy is often used as an adjuvant treatment modality following surgical resection of the primary tumor [1]. Albeit radiotherapy (RT) has multiple respiratory side effects [2], acute respiratory distress syndrome (ARDS) is a rare complication. We present here a case of a woman with breast cancer who developed ARDS post-radiotherapy with atypical imaging findings that was promptly diagnosed and successfully treated.

Case Report

Our patient was a 69 years old female recently diagnosed with grade III, estrogen-negative, progesterone negative, Her2 positive invasive ductal carcinoma of her left breast. She received 6 sessions of neo-adjuvant chemotherapy consisting of Decadron, docetaxel, and Herceptin. She then underwent a partial mastectomy of her left breast with axillary lymph nodes dissection, in March 2018. The pathology report revealed negative tumor margins but positivity in 5 of the 14 harvested lymph nodes (stage IIIA breast cancer). In June 2018, she started her adjuvant radiotherapy. The protocol consisted of a whole breast irradiation with inclusion of the lower axilla over 16 sessions. During each session, 42.5 Gy were delivered to the irradiated breast; the organs at risk were the ipsilateral lung and heart. The volume of lung receiving at least 20 Gy was estimated to be less than 25% of the total volume. Her last session was 1 week prior to her presentation. Upon her admission on August 7, 2018, she was scheduled to receive her first chemotherapy session post-mastectomy. However, the patient had a sudden onset of severe lower back pain, associated with a drop in her blood pressure to 80 mmHg systolic and a fall in her pulse oxygen saturation (SpO_2) to 85%. She was afebrile and her physical examination was only significant for end-inspiratory bi-basilar crackles. Her electrocardiogram showed normal sinus rhythm with no ST segment changes. Her chest x-ray (CXR) revealed bilateral infiltrates with a left upper lobe predominance (Figure 1). She remained hypotensive despite 3 L of normal saline, administered in 3 divided boluses. She was therefore started on 0.2 µg/kg/min of intravenous (IV) norepinephrine. Her oxygen saturation did not improve on 15 L O_2 via a face mask. She was transferred to our intensive care unit (ICU), where she was electively intubated and sedated with midazolam (5 mg/hour, IV) and fentanyl (100 µg/hour, IV). The patient was ventilated via a volume-controlled mode with a tidal volume of 400 mL/min, a respiratory rate of 15 breath/min, a fraction of inspired oxygen (FiO_2) of 100%, and a positive end-expiratory pressure (PEEP) of 10 cmH_20. Although her $Sp0_2$ stabilized around 90% to 92%, her arterial partial oxygen pressure ($Pa0_2$) was 66 mmHg with a PaO_2/FiO_2 ratio of 66. In order to rule out any pulmonary embolism or aortic dissection, an urgent thoracic-abdominal-pelvic angio computed tomography (CT) scan was performed and revealed the presence of bilateral pulmonary alveolar infiltrates, with a predominance in the left upper lobe and no pulmonary embolism or aortic dissection (Figure 2). This particular location matched that of the main area affected by her radiotherapy beams. A trans-thoracic cardiac echocardiography was conducted to assess for any myocardial dysfunction as a side effect of her Herceptin therapy. However, the patient had a normal ejection fraction (56%) with no major signs of any systolic or diastolic dysfunction. Her systolic pulmonary artery pressure was estimated at 30 mmHg. A diagnosis of atypical severe form of ARDS secondary to radiotherapy was established based on the Berlin definition. Given the patient's elevated C-reactive protein (CRP) of 69 mg/dL, her borderline

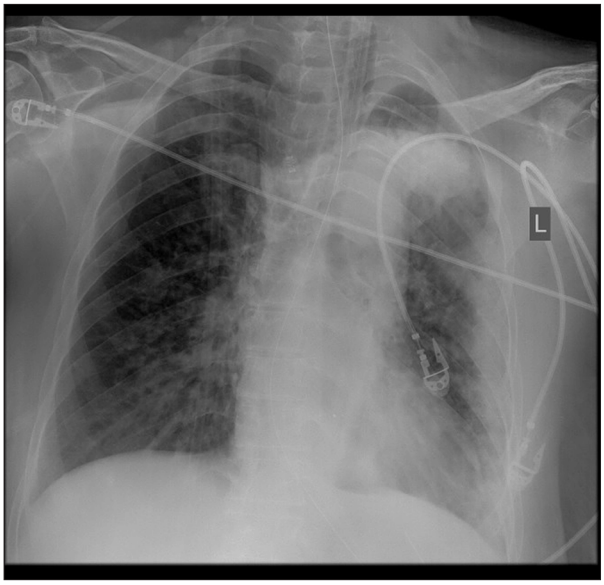

Figure 1. Chest x-ray on admission. Diffuse bilateral pulmonary infiltrates with a predominance to the left upper lobe.

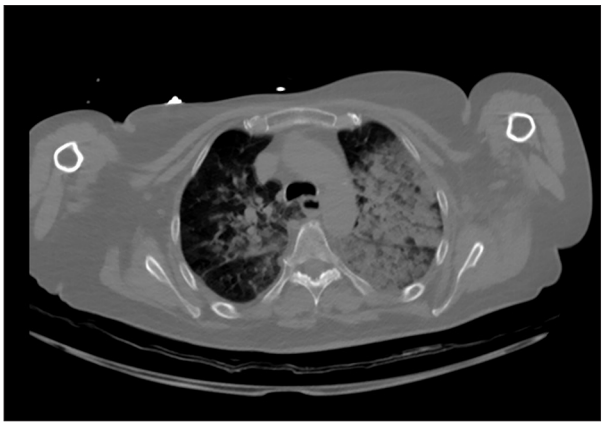

Figure 2. Computed tomography scan on admission. Diffuse patchy alveolar infiltrates with a predominance to the left upper lobe.

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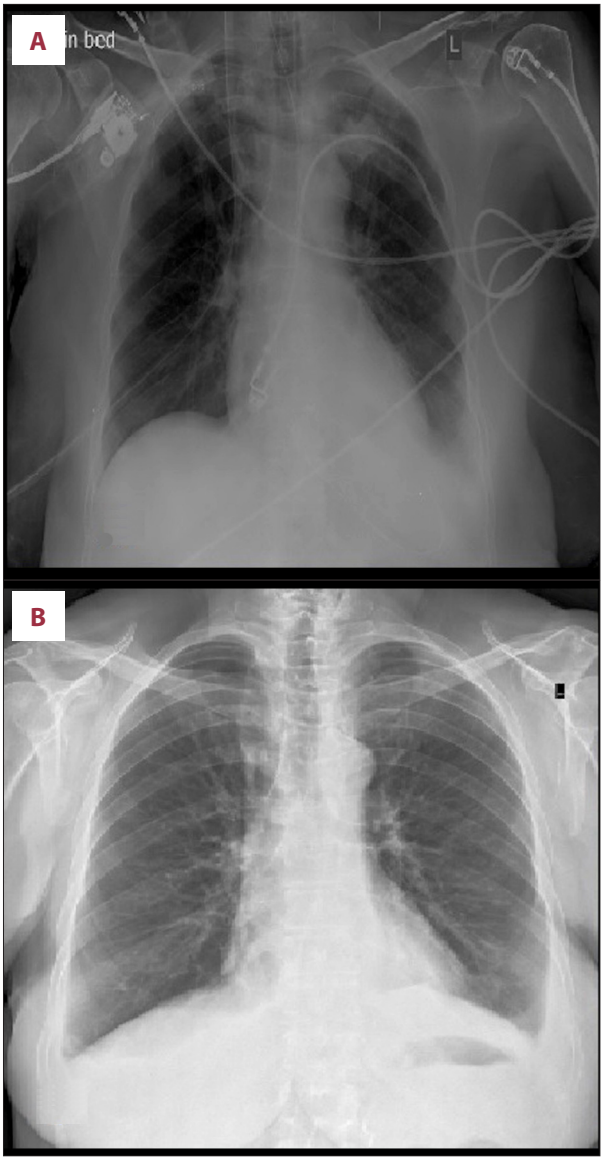

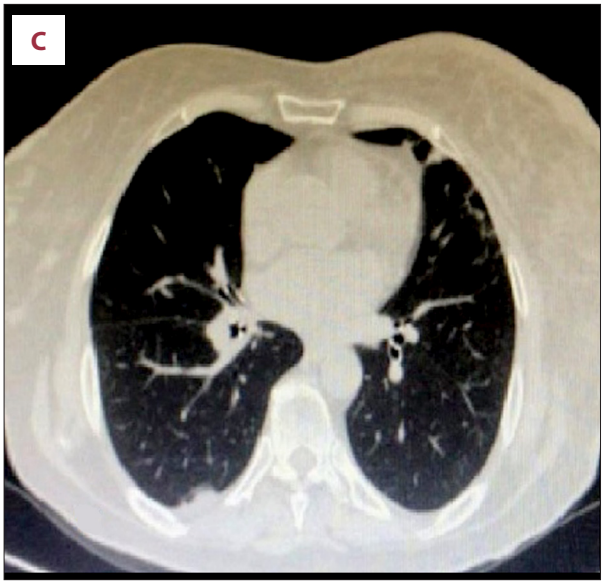

Figure 3. Follow up chest x-ray (CXR) and computed tomography (CT) scan. Marked reduction in the alveolar infiltrates on the CXR 48 hours post-intubation (**A**) with almost complete disappearance on the discharge day (**B**) and on a CT scan performed 1 month after (**C**).

procalcitonin (0.214 ng/mL) and elevated white blood cells (14 000 cell/mm^3 with 88% segmented neutrophils), she was empirically treated for healthcare-associated pneumonia with IV piperacillin-tazobactam 2.25 g every 8 hours. The dose was adjusted to her creatinine of 1.4 mg/dL, as the patient was most probably in an acute kidney injury state secondary to renal hypoperfusion. IV linezolid 600 mg every 12 hours was also added, taken into consideration her immunocompromised state, her hemodynamic instability, and the prevalence of methicillin resistant *Staphylococcus aureus* in our Lebanese hospitals. A bronchoscopy was performed to eliminate any endobronchial lesion and a broncho-alveolar lavage (BAL) from her left upper lobe was sent for culture. The patient was thereafter ventilated using the same low tidal volume/high PEEP strategy. The following day her PaO_2 increased to 81 mmHg with a decrease in the FiO_2 to 40% and a $Pa0_2/FiO_2$ ratio of 202.5. IV hydrocortisone 50 mg every 6 hours was also initiated. On August 9, 2018, the left upper lobe infiltrates markedly diminished (Figure 3A), and the oxygen requirement decreased to as little as 30% of FiO_2 and 5 cm of H_2O. Midazolam and fentanyl were stopped, and the patient was started on low dose dexmedetomidine with a Richmond Agitation-Sedation Scale of 0. Norepinephrine was progressively tapered off and the antibio-therapy was discontinued after a negative BAL culture result and normalization of the patient's CRP, creatinine, and white blood cells. The next morning, the patient was successfully extubated and transferred to the regular ward in the evening. The patient was also switched from hydrocortisone to IV methylprednisolone 40 mg twice daily. On her discharge day on August 16, 2018, her CXR was completely normal (Figure 3B) and a comparison to a thoracic CT performed on her following hospitalization in September 2018 for an infected mammillary epidermal cyst revealed a marked reduction in the alveolar opacities (Figure 3C).

Discussion

Breast cancer is the most frequent non-cutaneous cancer in women accounting for a quarter of female cancers. In Lebanon, the age-standardized rate was estimated to be around 78.7 per 100 000 women in 2012 [1]. Multiples treatment strategies have been established, including primary surgical resection, chemotherapy with taxane-based agents, and hormonotherapy [3]. Radiotherapy is often used following surgical resection [2].

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The former is known to cause frequent mild/moderate pulmonary toxicity, the probability and severity of which depends on the total dose of radiation, the fraction per dose, and the incidentally irradiated lung volume [4]. In a study conducted by Rancati et al. concerning early respiratory complication induced by RT, 28% of patients developed acute pneumonitis in one of the following 3 categories: x-ray pneumonitis, CT pneumonitis and/or clinical+x-ray pneumonitis [5]. On the other hand, long-term complications are mainly characterized by pulmonary fibrosis, occurring 6 to 24 months following radiation [6]. Neugut et al. noted an increase in the risk of secondary lung cancer in smokers who underwent RT for breast cancer [7].

According to the most recent Berlin definition, ARDS is an acute onset hypoxemia with bilateral pulmonary infiltrates on chest imaging within 1 week of a known clinical insult. ARDS is further sub-divided into mild forms when the PaO_2/FiO_2 ratio is between 200 mmHg and 300 mmHg with a PEEP ≥5 cmH_2O, and severe forms when the same ratio is below 100 mmHg. In addition, the pulmonary edema should not be fully explained by an underlying cardiac failure or volume overload [8]. Although acute radiation pneumonitis is not an uncommon complication, it usually manifests 6 to 12 weeks after the last radiation session with a non-productive cough, mild to moderate dyspnea, low grade fever, and a subtle change in the patient general status [9]. Thoracic irradiation can exceptionally cause ARDS with extremely few cases reported in the literature. These patients were mainly receiving thoracic irradiation for lung cancer and to a lesser extent Hodgkin lymphoma [10,11]. It is difficult to determine an accurate survival rate for patients with malignancies who develop ARDS, since these patients are generally excluded from the majority of observational studies and interventional trials [12]. Nonetheless, in one study, Azoulay et al. concluded that patients with solid tumors, including breast cancer, who developed ARDS had a lower mortality rate compared to patients with hematological malignancies [13]. Similar results were reported by Azevedo et al. who concluded that patients with good performance status and non-progressive disease (especially locoregional solid tumors, with no direct involvement of the respiratory tract by tumor) have a hospital survival rate of 53%, the highest amongst patients with malignancy [14].

Our patient represents an interesting clinical case for multiple reasons. The patient lacks any predisposing respiratory comorbidities that might explain the occurrence of ARDS. In addition, this is, to the best of our knowledge, the first reported case of ARDS secondary to RT for breast cancer. The 1-week interval between the last RT session and the onset of ARDS is relatively shorter than the normal radiation pneumonitis latency. The irradiated lung volume is much smaller in breast cancer RT than in lung cancer. In addition, the predominance of the lesions in the left upper lobe interestingly delignated the irradiated lung field. The rapid clinical and radiological improvement after 48 hours was remarkable and the complete resolution of the infiltrates 1 month after the event makes the diagnosis of simple acute pneumonitis less likely.

However, the possibility of an acute radiation pneumonitis component, in addition to ARDS, that responded to the steroids therapy cannot be eliminated.

Conclusions

ARDS remains an extremely rare complication of thoracic radiotherapy. However, physicians must keep a high clinical suspicion for its development in order to establish a fast diagnosis and treat accordingly

Department and Institution where work was done

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Conflict of Interest

None.

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