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RADIATION-INDUCED UNILATERAL DIAPHRAGMATIC PARALYSIS FOLLOWING BREAST AND NODAL RADIOTHERAPY

Sathish Kumar Krishnan[1], Vijaya Sivalingam Ramalingam[2], Venu Pararath Gopalakrishnan[3], Jennifer Heisick[1]

[1] Division of Pulmonary and Critical Care, Community Health Network, Indianapolis, USA
[2] Division of Pulmonary and Critical Care, Northeast Georgia Medical Center, Gainesville, USA
[3] Division of Hospital Medicine, University of Massachusetts Chan Medical School, Worcester, USA

Corresponding author's e-mail: dr.skkrish@gmail.com

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ABSTRACT

Unilateral diaphragmatic paralysis is a rare but important complication of thoracic radiotherapy, typically resulting from unintended injury to the phrenic nerve when it lies within or adjacent to the radiation field. While radiation-induced pulmonary toxicities such as pneumonitis and fibrosis are well documented, neurological complications like phrenic neuropathy remain underrecognized and likely underreported, despite their potential to cause significant respiratory dysfunction. We present the case of a 52-year-old woman with triple-negative breast cancer who developed progressive dyspnoea and orthopnoea 2 months after completing adjuvant breast and nodal radiotherapy. Imaging revealed new elevation of the right hemidiaphragm, and pulmonary function tests showed a restrictive ventilatory pattern. A fluoroscopic sniff test confirmed paradoxical motion of the right hemidiaphragm, consistent with unilateral diaphragmatic paralysis. The patient's symptoms improved with nocturnal non-invasive ventilation.

KEYWORDS

Diaphragmatic paralysis, phrenic nerve injury, radiotherapy complications, hemidiaphragm elevation, non-invasive ventilation

LEARNING POINTS

- Clinicians should be aware that thoracic radiotherapy, particularly for breast cancer involving regional nodal irradiation can inadvertently damage the phrenic nerve due to its anatomical proximity to the treatment field.
- New-onset dyspnoea or orthopnoea following radiation therapy should prompt evaluation with chest imaging, pulmonary function testing, and a fluoroscopic sniff test to assess diaphragmatic dysfunction.
- Although management of diaphragmatic paralysis is primarily supportive, interventions such as non-invasive ventilation can alleviate symptoms. Timely diagnosis is crucial, as prolonged dysfunction may lead to persistent morbidity.

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INTRODUCTION/BACKGROUND

Unilateral diaphragmatic paralysis is an uncommon clinical entity that may arise from various aetiologies, including surgical trauma, malignancy, neuromuscular disease, and less frequently, radiation-induced phrenic nerve injury[1]. Although radiation therapy is a cornerstone in the management of breast and thoracic malignancies, its potential to cause collateral damage to nearby neural structures such as the phrenic nerve is often underrecognized[2,3].

The phrenic nerve traverses the thoracic cavity in close proximity to structures frequently targeted in regional nodal irradiation. As a result, it may receive significant unintended radiation exposure, particularly when the clinical target volume abuts the nerve's anatomical path[2]. Radiation-induced phrenic nerve palsy can present acutely or in a delayed fashion, with clinical manifestations ranging from incidental imaging findings to exertional dyspnoea and orthopnoea due to diaphragmatic dysfunction[4].

Given its rarity and nonspecific presentation, phrenic nerve injury following radiotherapy is likely underdiagnosed, necessitating timely recognition through imaging, pulmonary function testing, and dynamic fluoroscopy to prevent prolonged morbidity. We present the case of a 52-year-old woman who developed symptomatic unilateral diaphragmatic paralysis shortly after completing adjuvant radiotherapy for triple-negative breast cancer, highlighting a rare but clinically significant complication that underscores the need for vigilance in patients presenting with unexplained respiratory symptoms after treatment.

CASE DESCRIPTION

A 52-year-old female with a history of triple-negative right breast cancer (cT2N1M0) presented to the pulmonary clinic with a 6-week history of progressive exertional dyspnoea and orthopnoea. Her oncologic treatment had included neoadjuvant weekly carboplatin and paclitaxel followed by dose-dense doxorubicin and cyclophosphamide, culminating in right breast lumpectomy. Immunotherapy with pembrolizumab was initiated but subsequently discontinued due to immune-mediated colitis.

Two months prior to symptom onset, the patient completed adjuvant radiotherapy targeting the right breast and regional lymph nodes, receiving a total dose of 6000 cGy over 30 fractions.

A chest computed tomography (CT) scan performed 4 weeks after radiotherapy revealed an elevated right hemidiaphragm, a new finding compared to a CT scan performed 2 weeks prior to radiotherapy initiation, which demonstrated a normal right diaphragm *(Fig. 1 and 2)*.

Pulmonary function tests revealed a moderately severe restrictive ventilatory defect with a forced vital capacity of 49% predicted and a total lung capacity of 57% predicted. The diffusing capacity corrected for haemoglobin was also reduced at 58% predicted *(Table 1)*.

To further evaluate diaphragmatic function, a fluoroscopic sniff test was performed, demonstrating paradoxical elevation of the right hemidiaphragm during inspiration, consistent with unilateral diaphragmatic paralysis. The patient was started on nocturnal non-invasive ventilation, which resulted in improvement of her orthopnoea and overall respiratory symptoms.

DISCUSSION

Unilateral diaphragmatic paralysis is a rare but clinically significant consequence of thoracic radiotherapy, particularly when the phrenic nerve is exposed to high doses or lies in proximity to the radiation field. While pneumonitis and pulmonary fibrosis are well-recognized complications of

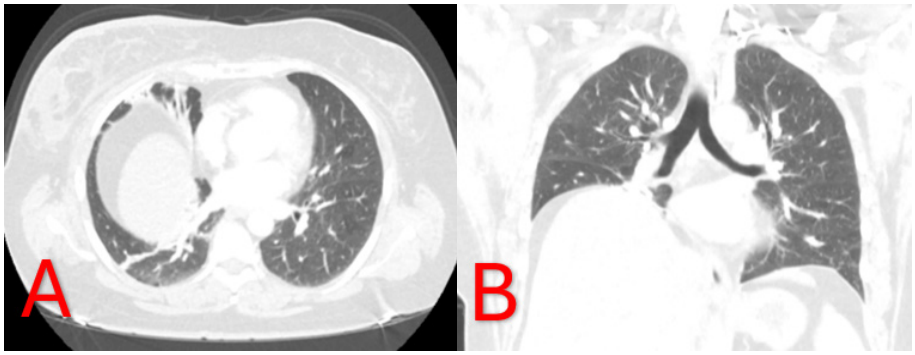


Figure 1. Chest computed tomography scan, 4 weeks post radiotherapy: A) axial and B) coronal views showing elevation of the right hemidiaphragm.

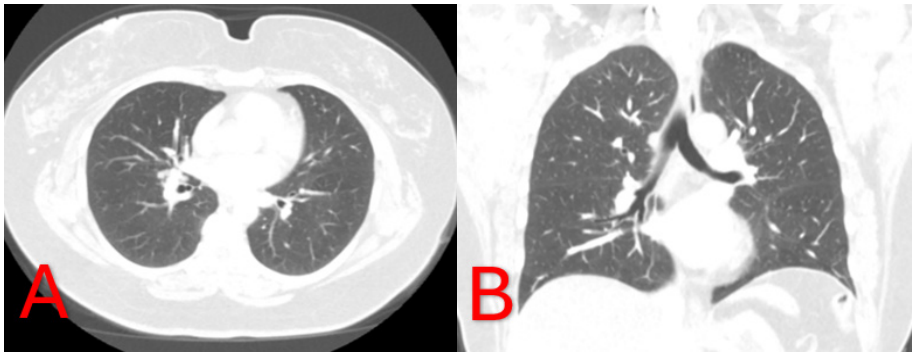


Figure 2. Chest computed tomography scan obtained 2 weeks prior to radiotherapy: A) axial and B) coronal views showing a normal right hemidiaphragm.

Variables	Actual (% predicted)	Reference (%)
FEV_1	50	>80
FVC	49	>80
FEV_1/FVC ratio	0.79	>0.7
TLC	57	>80
cDLCO	58	>80

Abbreviations: FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; TLC, total lung capacity; cDLCO, diffusing capacity of the lung for carbon monoxide corrected for hemoglobin.

Table 1. Pulmonary function test results.

breast cancer radiation therapy, phrenic nerve injury leading to diaphragmatic paralysis is less frequently reported in the literature[1].

The phrenic nerve descends through the mediastinum and can be incidentally encompassed in radiation fields for breast cancer, especially during regional nodal irradiation[2]. The risk is further accentuated when the tumour or planning target volume abuts the nerve's course, as reported in stereotactic ablative radiotherapy series for both breast and lung cancers[3]. Damage to the phrenic nerve can be either immediate or delayed, manifesting as neuropathy and resulting in diaphragmatic dysfunction, which may be unilateral or, less frequently, bilateral[4,5].

Latency to symptom onset can vary from several weeks to many years post-treatment[1,4,5]. In our case, the patient developed symptomatic unilateral diaphragmatic paralysis within weeks of completing adjuvant radiotherapy, consistent with the timeline described in earlier reports[1,4].

The pathogenesis of radiation-induced neuropathy is multifactorial, involving direct axonal injury, microvascular compromise, and progressive fibrosis along the nerve sheath[6,7]. Neural tolerance thresholds can be exceeded by cumulative doses in conventional fractionation, increasing the risk of injury. The association between radiation dose and the development of phrenic nerve palsy is not well established due to uncommon nature and limited available evidence. Although modern techniques such as intensity-modulated radiation therapy may reduce incidental exposure, they do not eliminate this complication[2,8].

Differential diagnoses include malignancy-related invasion, infectious neuritis, idiopathic neuropathies, and iatrogenic causes such as surgical trauma or immunotherapy-related inflammation[9,10]. A careful oncological and treatment history, complemented by imaging and functional assessment, is essential for diagnosis. A paradoxical elevation of the hemidiaphragm on fluoroscopic sniff testing, supported by CT scan, is highly suggestive of phrenic nerve dysfunction[1,9].

Management remains primarily supportive. Nocturnal non-invasive ventilation can alleviate orthopnoea and improve respiratory symptoms, as observed in our patient[9]. For patients with persistent symptoms causing functional limitations, surgical interventions such as diaphragmatic plication may be warranted[9]. While some degree of nerve function recovery is possible, many patients experience lasting impairment—emphasizing the importance of early recognition and intervention[5,7].

Ultimately, radiation-induced neuropathies remain an inherent risk of effective oncologic therapy. Nonetheless, meticulous treatment planning, judicious avoidance of high-dose exposure to critical neurovascular structures and sustained post-treatment surveillance are essential to mitigate long-term morbidity[7,8]. This case adds to the evolving literature on radiation-induced phrenic neuropathy and reinforces the need for heightened clinical awareness to enable timely diagnosis and tailored management of this uncommon yet consequential complication.

CONCLUSION

Radiation-induced unilateral diaphragmatic paralysis is an uncommon but clinically significant complication of breast cancer radiotherapy. High clinical suspicion, timely imaging, and functional testing are essential for diagnosis. Supportive measures can significantly alleviate symptoms, and thoughtful radiation planning remains crucial to reduce neurotoxic risks.

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