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CASE REPORT

RADIATION INDUCED LUNG DISEASE: A RISK TO ASSUME

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Summary

Radiation induced lung disease (RILD) is an important complication of thoracic irradiation for different forms of intrathoracic malignancies. The incidence of RILD varies and it is influenced by the total dose administered, the degree of fractionation, the radiation field and prior chemotherapy. There are two phases of the disease: acute (radiation pneumonitis) and chronic (radiation fibrosis). We present the case of a 86 yo woman who was admitted for progressive dyspnea. She had a history of right breast cancer diagnosed in 2009, treated with chemo and radiotherapy, arterial hypertension, permanent atrial fibrillation and diabetes mellitus. The high-resolution computed tomography (HRCT) scan revealed pericardial fluid, bilateral pleural effusion (more important on the right) and a round, imprecisely delimited opacity in the right lung upper lobe. The opacity had similar characteristics when compared to previous chest X-rays. The patient was diagnosed with heart failure and RILD. Under treatment with beta blocker, calcium antagonist, diuretic, anticoagulant and oxigenotherapy the evolution was favorable, the patient being discharged 5 days later. In front of a suspicion of a RILD we should always keep in mind to differentiate it from recurrent malignancy or superimposed infection.
Key words: intrathoracic cancer, irradiation, pulmonary radiation fibrosis

Résumé

La maladie de la fibrose pulmonaire de rayonnement est une complication importante de la radiothérapie thoracique pour les différentes formes de tumeurs malignes intrathoraciques. L'incidence de la maladie varie et elle est influencée par la dose totale administrée, le degré de fractionnement, le champ de rayonnement et de chimiothérapie antérieure. Il y a deux phases de la maladie: aiguë (pneumopathie radique) et chroniques (fibrose de rayonnement). Nous présentons le cas d'une femme de 86 ans qui a été admise pour dyspnée progressive. Elle avait des antécédents de cancer du sein droit diagnostiqué en 2009, traité avec la chimiothérapie et la radiothérapie, l'hypertension artérielle, fibrillation auriculaire permanente et diabète sucré. La tomodensitométrie avec haute résolution a révélé du liquide péricardique, un épanchement pleural bilatéral (le plus important sur la droite) et une opacité ronde, imprécisément délimitée, dans le lobe supérieur du poumon droit. L'opacité avait des caractéristiques similaires par rapport aux examinations avec rayons X précédentes. La patiente a été diagnostiquée avec insuffisance cardiaque et maladie de la fibrose pulmonaire de rayonnement. Sous traitement par bêta-bloquant, un antagoniste du calcium, diurétique, anticoagulant et oxigenotherapy, l'évolution a été favorable, la patiente étant déchargée cinq jours plus tard. En face d'un soupçon d'une maladie pulmonaire de rayonnement nous devons toujours la différencier de la malignité récurrente ou de l'infection superposée.
Mots-clé: cancer intrathoracique, irradiation, fibrose pulmonaire de rayonnement

Introduction

Radiation induced lung disease (RILD) is an important complication of thoracic irradiation for intrathoracic malignancies, such as lung, breast or hematologic cancers. It was first described in 1898, but only in 1925 the distinction between radiation pneumonitis and radiation fibrosis has been made (1). The positive diagnosis of RILD is based on a high suspicion index; it is essential to be differentiated from an active malignancy in order to establish the right treatment strategy.

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Case report

We report the case of a 86 year-old woman who was admitted in our hospital for progressive dyspnea and fatigue. Her medical history included right breast cancer diagnosed in 2009, treated with chemo and radiotherapy, arterial hypertension, permanent atrial fibrillation and diabetes mellitus. The patient never smoked and she had no other respiratory risk factors.The physical exam has found moderate dyspnea with dullness in the right inferior thorax, SaO_2 90% while breathing ambient air, respiratory rate of 18/min, blood pressure 160/110 mmHg, heart rate 90/min, ankle edema; the rest of the examination was within normal limits. The laboratory tests showed a mild inflammatory syndrome, hyperglicemia (seric glucose 151 mg/dL), chronic kidney disease (creatinine 1.29 mg/dL, BUN 102.5 mg/dL) and mild hyponatremia of 134 mmol/L. The ECG showed atrial fibrilation without repolarization changes. The chest X-ray revealed right lung opacity, bilateral pleural effusion and cardiomegaly (Fig. 1). At this point the differential diagnosis included heart failure, pneumonia, primary or secondary lung tumor. A cardiac ultrasound was performed: preserved systolic ejection fraction (50%), severe pulmonary hypertension (systolic pulmonary artery pressure 74 mmHg), pericardial fluid 10 mm posterior of the left atrium in diastole. The thoracic HRCT scan revealed pericardial fluid, bilateral pleural effusion (more important on the right) and a round, imprecisely delimited opacity in the right lung upper lobe (Fig. 2). A thoracenthesis was performed, with pleural fluid analysis, which proved to be a transudate. The positive diagnosis was heart failure with preserved ejection fraction, pulmonary right upper lobe fibrosis post radiotherapy for breast cancer, pericardial effusion post-irradiation, diabetes mellitus, chronic kidney disease stage 3B (Cl_{Cr}42 ml/min/1.73 m^2). Treatment with beta blocker, calcium antagonist, diuretic, anticoagulant, anti-inflammatory drugs and oxigenotherapy was initiated, with amelioration of dyspnea. Ten days later, thoracic X-ray revealed an inhomogeneous opacity, imprecisely delimited, in the right lung upper lobe, suggestive of fibrosis (Fig. 3).

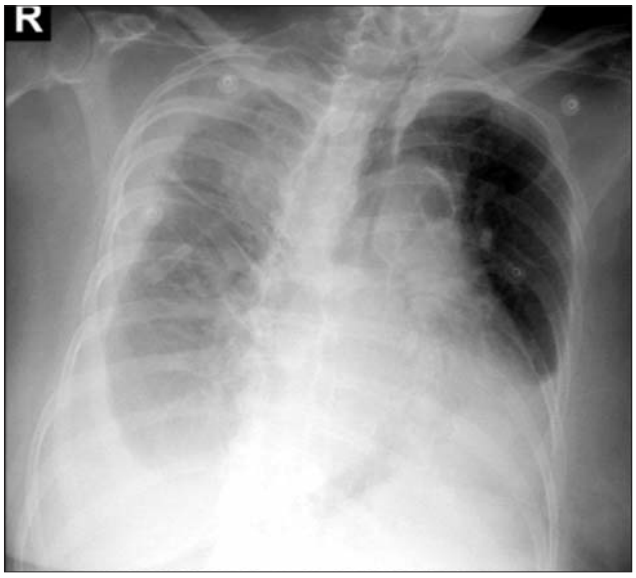

Figure 1 - Chest X-ray at admission: bilateral pleural effusion with opacity of the right lung, cardiomegaly

Discussion

Radiation induced lung disease (RILD) is a complication of radiotherapy of the chest. The risk of developing RILD is influenced by the by the total dose administered (usually over 40 Gy), the degree of fractionation, the radiation field and concurrent chemotherapy (bevacizumab, doxorubicin, bleomycin, cyclophosphamide, vincristine, gemcitabine increase the risk) (2). The incidence of RILD after thoracic irradiation for breast cancer is between 0-10% and 5-10% after thoracic irradiation for lung cancer (1). There have been described two phases of RILD: acute (radiation pneumonitis) and chronic (radiation fibrosis). The acute phase occurs

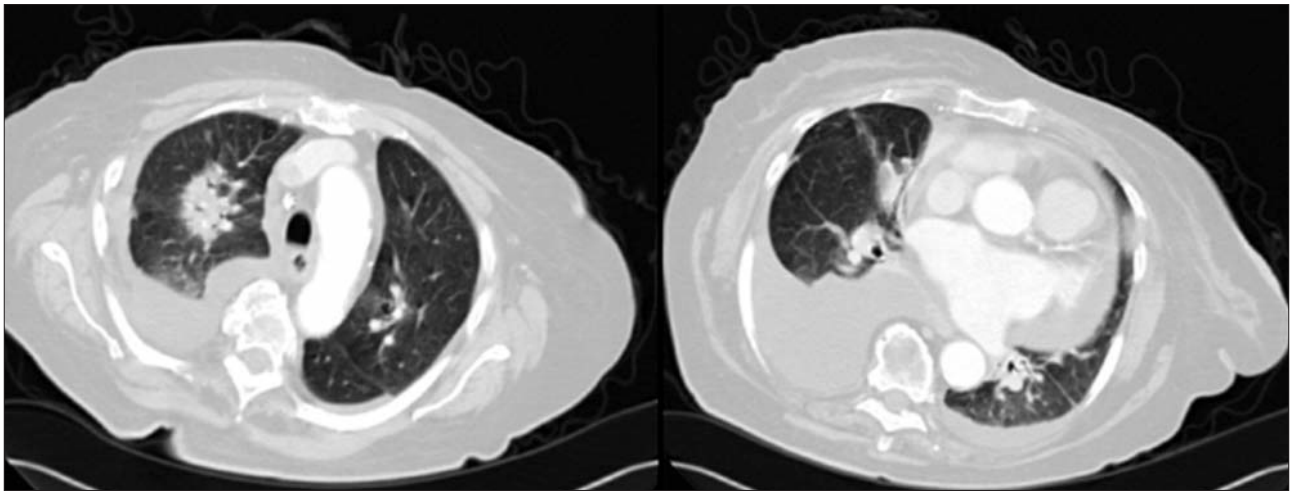

Figure 2 - Thoracic HRCT scan: bilateral pleural and pericardialeffusion, opacity in the right upper lobe.

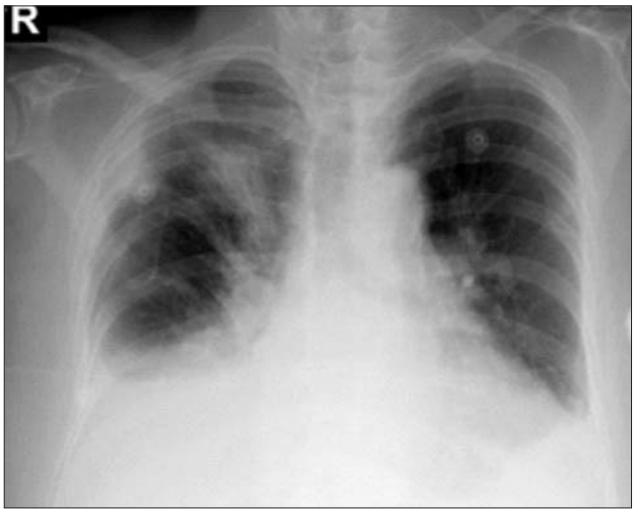

Figure 3 - Thoracic X-Ray at discharging:inhomogeneous opacity, imprecisely delimited, in the right lung upper lobe, suggestive of fibrosis, right pleural effusion

between 4-12 weeks after the end of treatment. The imaging appearance includes ground glass opacities, nodular or consolidation pattern, tree-in-bud sign, atelectasis (3). Sometimes, an ipsilateral pleural effusion has been reported. All these lesions of the radiation pneumonitis usually are self limited, but sometimes they may progress to fibrosis. The radiation fibrosis occurs within 6-12 months after radiotherapy and it can progress for up to 2 years (3). The thoracic high-resolution computed tomography (HRCT) appearance includes linear scarring, consolidation, traction bronchiectasis, ipsilateral pleural effusion, pleural thickening. Our patient presented on the HRCT bilateral pleural effusion with a round, imprecisely delimited opacity in the right lung upper lobe, which did not progress in comparison with the previous imaging evaluation.

Clinical presentation of RILD is variable. During the acute phase, cough, dyspnea, fever and pleuritic pain may appear. During the chronic phase, the patient may be asymptomatic or may present with dyspnea (4). Fever is most likely to appear in the acute phase. Furthermore, thoracic irradiation is associated with an increased risk of radiation-induced cardiac disease, which may manifest with dyspnea (5). Biomarkers of chronic heart failure (BNP, NT-proBNP) may be useful for the differential diagnosis between pulmonary and cardiac dyspnea.

The positive diagnosis of RILD is based on the correlation between the onset of symptoms and irradiation date. Because imaging aspects are not specific, it is necessary to exclude other possible differential diagnoses, especially an active malignancy. The differential diagnosis includes: bacterial or fungal infection, eosinophilic pneumonia, cryptogenic pneumonia, bronchiolitis-associated interstitial lung disease, sarcoidosis, pulmonary oedema, Wegener granulomatosis, recurrence of the underlying cancer, lymphangitic carcinomatosis, radiation-induced malignancies (3,6). A key role for diagnosis is played by previous chest X-rays or CT scans. When RILD can not be differentiated from an active cancer, PET-CT scan may be helpful in differentiating radiation fibrosis. The PET-CT scan should be performed at least 3 months after the irradiation, in order to avoid the false positive results (7). Sometimes, despite an extensive imaging study, the definitive diagnosis is obtained only by invasive procedures (bronchoscopy, lung biopsy, percutaneous biopsy) (1). In our patient, an invasive confirmation was not necessary because the imaging aspect of the opacity was stable over the last years.

Although the efficiency of different treatments in RILD has not been established, systemic steroids have been used in symptomatic patients in order to reduce the severity of acute radiation pneumonitis (1). Immuno-supressive agents, such as azathioprine and cyclosporine, have been used in patients with glucocorticoids intolerance or refractory to corticoid treatment (8). Experimental agents (pentoxifyline, inhibitors of collagen synthesis, amifostine) have been succesfully used in single case reports (9,10). Up to date, there are no proven effective therapies for pulmonary radiation fibrosis (4).

In conclusion, RILD develops after radiotherapy for thoracic cancers. The clinical manifestations and the radiological aspects vary in a timely manner. The knowledge of this temporal pattern and the understanding of various presentation forms are necessary to differentiate RILD from recurrent malignancy or superimposed infection.

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REFERENCES

1. Merrill WW. Radiation-induced lung injury. www.uptodate.com (accessed January 2016).
2. Rancati T, Ceresoli GL, Gagliardi G, et al. Factors predicting radiation pneumonitis in lung cancer patients: a retrospective study. Radiother Oncol 2003; 67:275.
3. Choi YW, Munden RF, Erasmus JJ, et al. Effects of Radiation Therapy on the Lung: Radiologic Appearances and Differential Diagnosis. RadioGraphics 2004; 24:985–998.
4. Abratt RP, Morgan GW, Silvestri G, Willcox P. Pulmonary complications of radiation therapy. Clin Chest Med 2004; 25:167.
5. Darby SC, Ewertz M, McGale P, et al. Risk of ischemic heart disease in women after radiotherapy for breast cancer. N Engl J Med 2013; 368:987.
6. Goe A, Gaillard Fet al. Radiation induced lung disease. www.Radiopedia.org. (accessed January 2016).
7. Robbins ME, BrunsoBechtold JK, Peiffer AM, et al. Imaging radiation-inducednormal tissue injury. Radiat Res 2012; 177:449.
8. Muraoka T, Bandoh S, Fujita J, et al. Corticosteroid refractory radiation pneumonitis that remarkably responded to cyclosporin A. Intern Med 2002; 41:730.
9. Vujaskovic Z, Feng QF, Rabbani ZN, et al. Assessment of the protective effect of amifostine on radiation-induced pulmonary toxicity. Exp Lung Res 2002; 28:577.
10. Seidensticker M, Seidensticker R, Damm R, et al. Prospective randomized trial of enoxaparin, pentoxifylline and ursodeoxycholic acid for prevention of radiation-induced liver toxicity. PLoS One 2014; 9:e112731.