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Acute Post-Radiation Pneumonitis: A Case Report

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Abstract **Case Report**

Acute radiation pneumonitis is a rare cause of pneumonitis. The diagnosis is considered in the presence of respiratory symptoms that appear with recent thoracic exposure. We report the case of a 67-year-old patient followed for mediastinal lymphoma who presented an acute pneumonitis when she started her radiotherapy sessions. Two diagnostics were suspected: radiotherapy toxicity or metastatic origin. Acute post-radiation pneumonitis can be very serious if the diagnostic is delayed. The diagnosis of acute post-radiation pneumonitis constitutes a diagnosis of elimination of any pneumonitis with an unfavorable evolution under antibiotic therapy, in the context of semi-recent thoracic radiotherapy.

Keywords: Acute post-radiation pneumonitis, radiotherapy.

INTRODUCTION

Acute radiation pneumonitis is a rare cause of pneumonitis. The diagnosis should be considered if there are respiratory symptoms in the context of recent or semi-recent thoracic radiotherapy and radiological lung lesions in the irradiation field. It can be serious if the diagnosis is delayed.

We report the case of a 67-year-old patient followed for mediastinal lymphoma who presented an acute pneumonitis when she starts her radiotherapy sessions. However, the label of post-radiation pneumonitis was not easy to establish, because the metastatic track was also plausible.

CASE REPORT

This is a 67-year-old female patient with no toxic habits, no particular medical or surgical history. The history of his disease dates back to 2019, with the appearance of right cervical lymphadenopathy in a context of weight loss, and a lymph node biopsy returned in favor of a Malignant Non-Hodgkin's B large cell lymphoma.

An initial extension scan was done in the month of October 2019 (figure A), the Cerebro-thoraco-abdomino-pelvic scan had objectified at the thoracic level:

- Two Non-specific nodules, one at the right scissural level (9 mm) and the other at the right upper lobe (5.5 mm), but no other parenchymal abnormalities
- Upper mediastinal adenopathies, from the pre-carinal, barety box, bilateral hilar, measuring for the highest grade 11 mm from the pre-carinal short axis.

A PET-Scan supplement was carried out, and chemotherapy cures were started on 22/11/2019 and stopped on 10/03/2020 = six cures of R-CHOP (Rituximab, Cyclophosphamide, Hydroxyadriamycine, Oncovin, Prednisone + 4 therapeutic lumbar puncture.

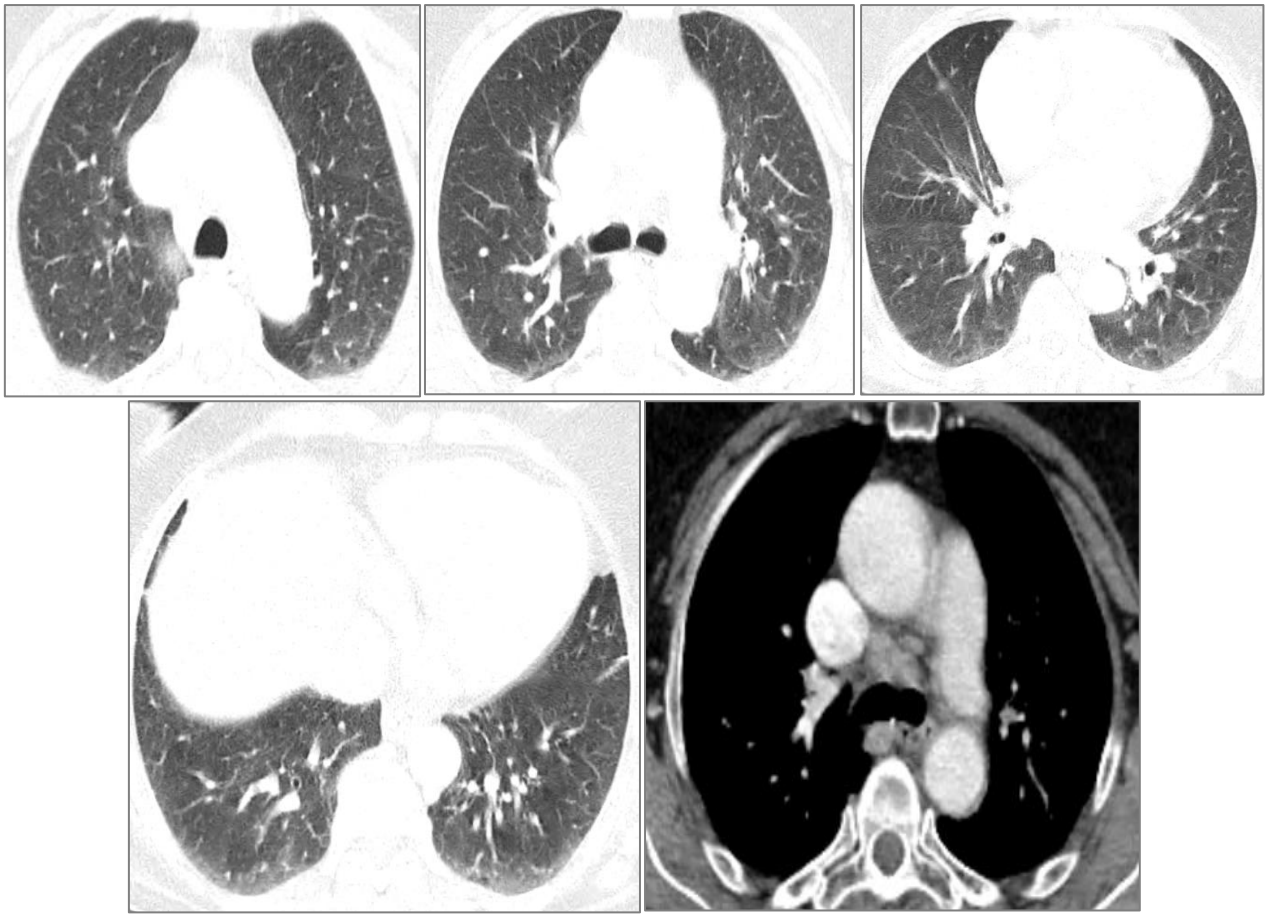
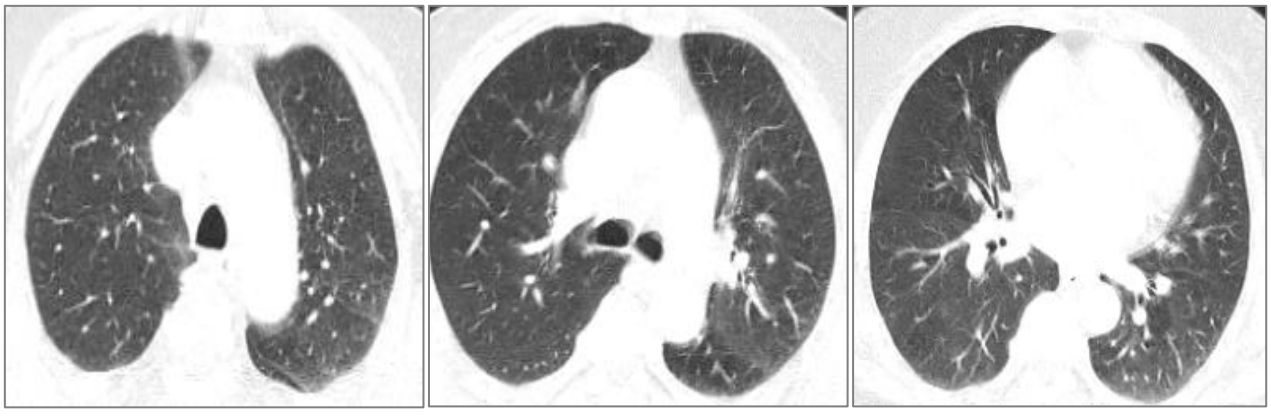


Figure A: Extension CTAP scan (October-2019)

Then a control with a Cerebro-thoraco-abdomino-pelvic scan was performed after the end of the treatment (figure B), objectifying a complete response of the cervico-facial lesions, but a stability of the mediastinum-pulmonary lesions. Two other cures of R-CHOP were added from 04-jan-2020 to 22-april-2020, with a second control scan performed in the month of May-2020 (figure C) which did not show any regression of the mediastinum-pulmonary lesions.



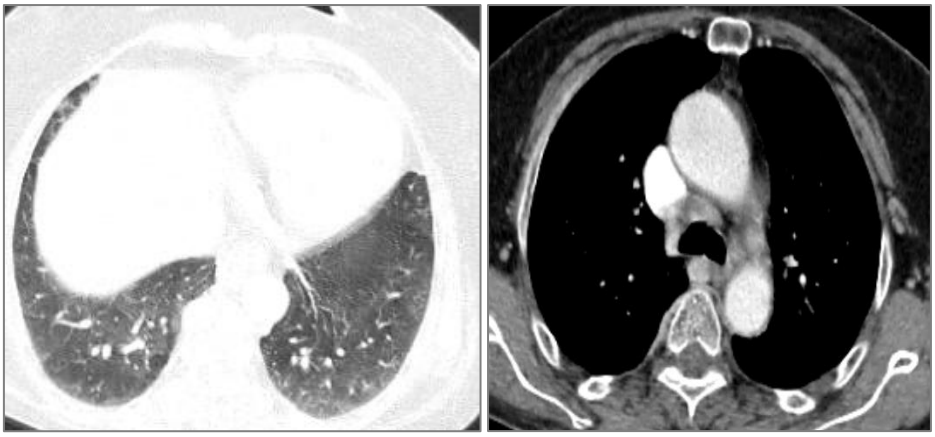


Figure B: CTAP control scan (07-Feb-2020)

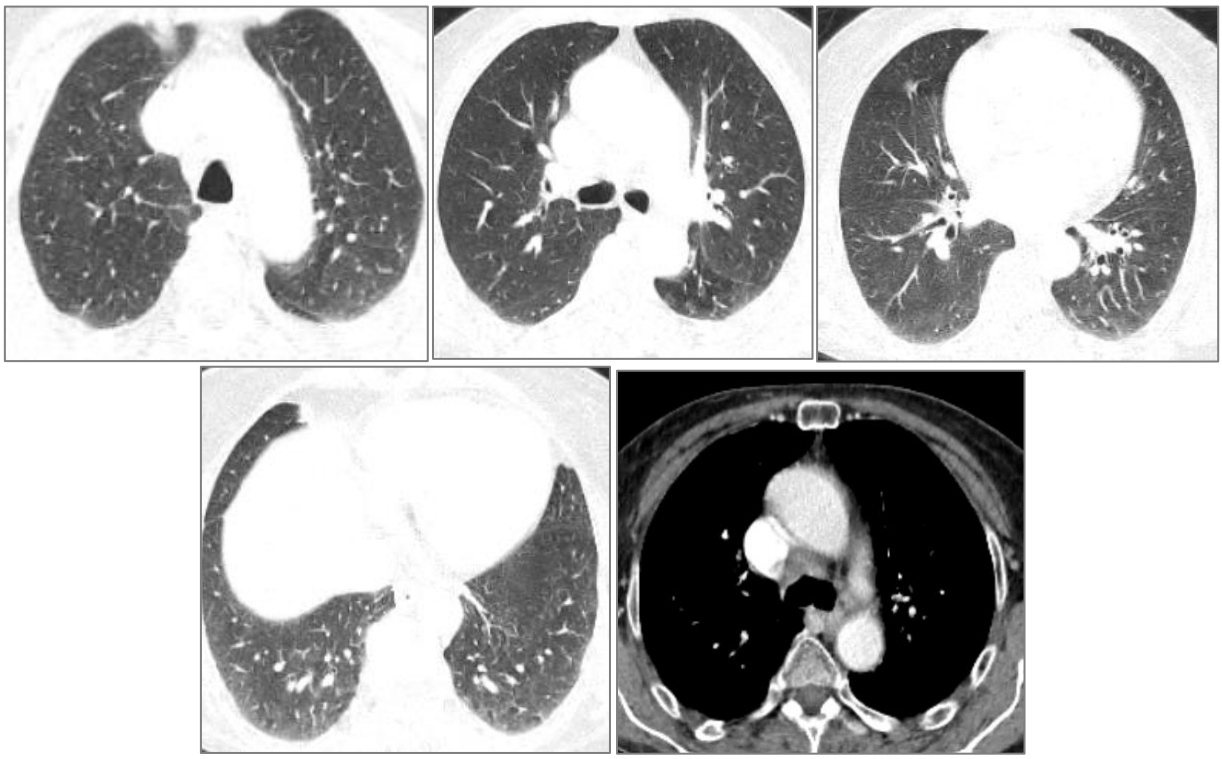
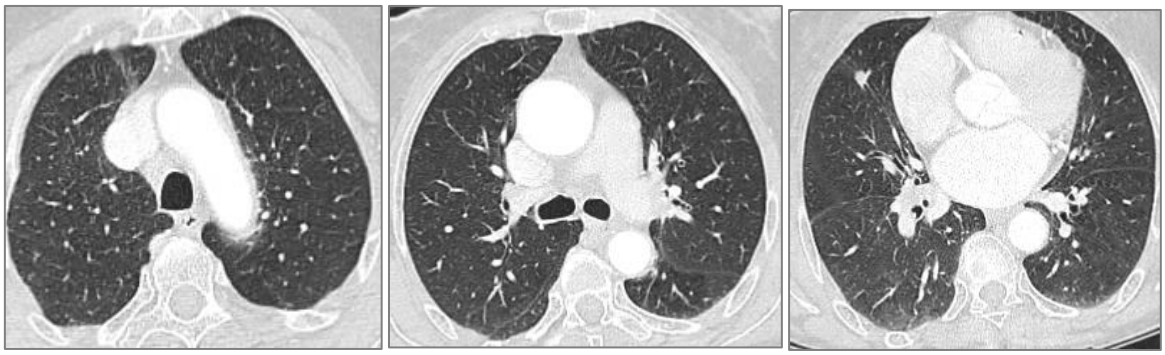


Figure C: CTAP control scan CTAP le 14-May-2020

Scans of control as well as a pet scan revealed the progression of the mediastinal disease. Then a second chemotherapy protocol was attempted, and a control scan after four cures showed the persistence of the same mediastinal lesions (Figures D, E).



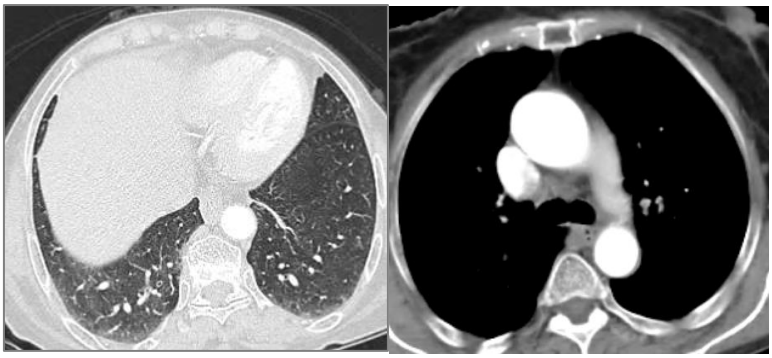


Figure D: CTAP scan before the second chemotherapy cure

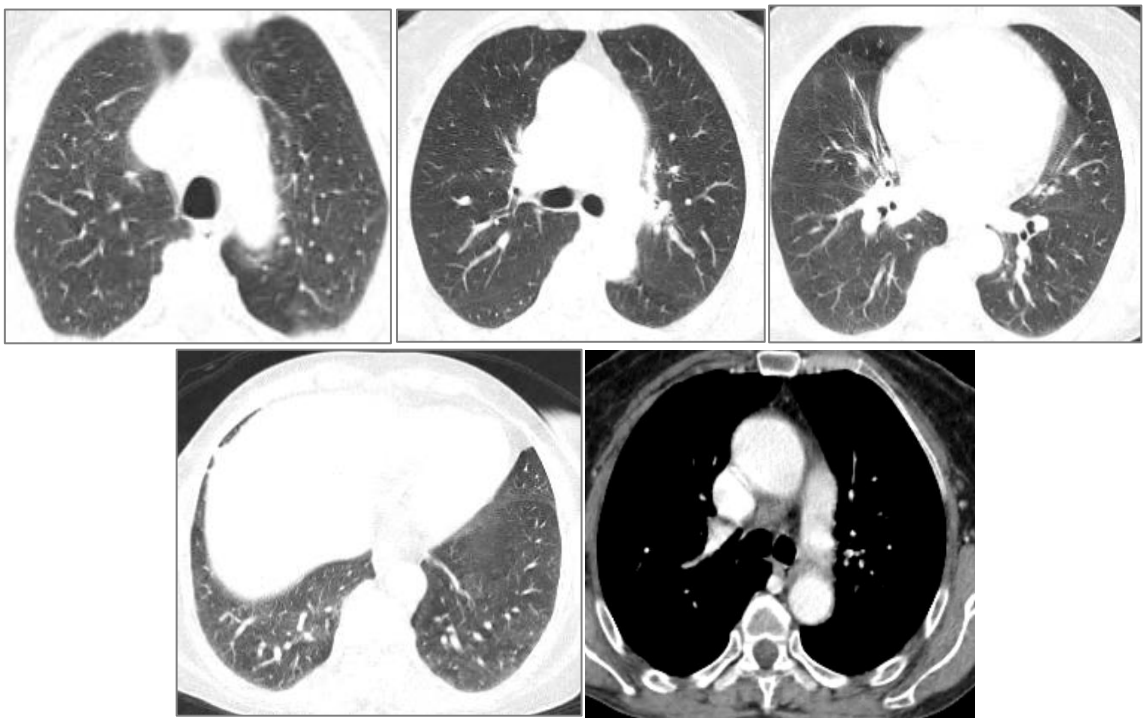


Figure E: CTAP scan after the second chemotherapy cure

A PET-Scan of control after 8 cures of R-CHOP and 4 cures of R-DHAOX done on 27-May-2021 revealed that the mediastinal lesions are still the same, the decision was to add a 5th cure of R-DHAOX on 17-june-2021 and to start radiotherapy sessions.

It should be noted that throughout this follow-up period, the patient showed no respiratory complaint. At the various consultations, she showed correct saturation, was eupneic and without any respiratory symptoms.

The first radiotherapy session was performed on 08-june-2021. Just after the session, the patient complains of atypical chest pain radiating to the back with a burning sensation and intra-thoracic heat, and a dry cough. The symptoms persisted until his consultation a week later. A Covid infection was suspected but a PCR came back negative and radiotherapy was continued.

The evolution was marked by the installation of progressively worsening dyspnea becoming on effort with an increase dry cough and chest pain.

Standard chest X-ray was performed on 09-July-2021 (figure F), which objectified scattered opacities of medium density, with blurred contours, more localized on the bilateral hilo-axillary lines.

Radiotherapy was continued despite the respiratory symptoms and the radiological signs were attributed to a pulmonary infection. It ended on 10-Sept-2021, the patient received 40Gy with a Fractionation of 2Gy/fr, 1Fr/D, 5D/7.

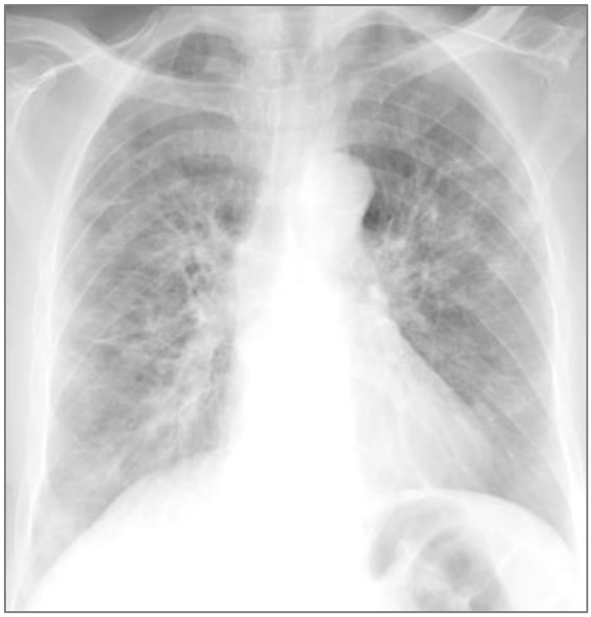


Figure F: Chest X-Ray

Presence of scattered opacities of medium density, with blurred contours, more localized on the bilateral hilo-axillary lines

A Chest CT scan was done on 03-Oct-2021 (figure G) in front of the worsening of the respiratory symptoms, objectifying areas of alveolar condensation and bilateral pulmonary ground glass opacification, involving the different lobes in a bilateral and symmetrical way but with hilar predominance.

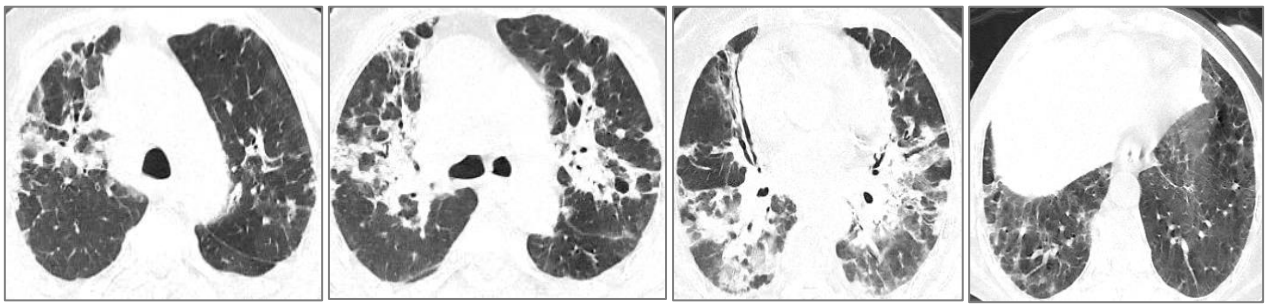


Figure G: Chest CT scan of the 03-Oct-2021:

The patient was referred, then, for consultation for advice and evaluation. On admission, we find a patient who desaturated to 85% in AMBIENT AIR, and who presented bilateral crackles on pulmonary auscultation. A cerebro- thoraco-abdomino-pelvic scan at the end of treatment was done 3 weeks after the chest CT scan (figure H): we find bilateral proximal condensations with an air bronchogram; the bronchi are distorted there, testifying the evolution towards fibrosis: the same lesions with a more condensed character.

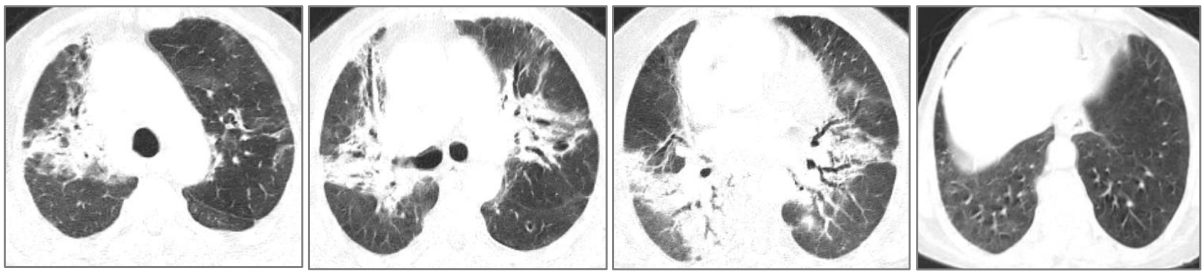


Figure H: Control chest CT scan after 3 weeks

The pulmonology team staffed the patient; the decision was to hospitalize the patient, in order to perform a bronchial endoscopy. A post-radiation interstitial pneumonitis was the most highly probable diagnosis (the chronology of the appearance of the radiological lesions with radiotherapy, the brutality of the lesions and its rapid installation severity, the

aggravation of the radiological lesions in a short time). The patient died before further explorations.

DISCUSSION

Described for the first time in 1922 [1], pulmonary lesions linked to ionizing radiation can take two forms: acute pneumopathy, occurring less than a year after irradiation, and later post-radiation pulmonary fibrosis [2]. They concern between 5 and 15% of patients who have undergone chest irradiation [3].

One of the feared complications of radiotherapy is pulmonary toxicity, especially when symptomatic. Although considered an acute side effect, radiation pneumonitis can also evolve into a late complication, with pulmonary fibrosis generally developing between 6 and 24 months and generally stabilizing after 2 years [4, 5].

The pathophysiological mechanism results from the radio sensitivity of the functional subunit of the lung, the alveolar-capillary complex, within which gas exchange takes place [3, 9]. The alveolar membrane is made up of type I pneumocyte cells, which are fine epithelial cells, and type II pneumocyte cells, responsible for surfactant secretion.

Lung involvement evolves in three phases [4, 6]:

- The exudative phase (acute, from 0 to 2 months) results from the loss of type I pneumocytes, the alteration of type II pneumocytes (with secretion of surfactant) and endothelial cells (increased vascular permeability responsible for edema of the interalveolar septa and microthromboses).
- The organizational (or proliferative) phase, from 2 to 9 months, is characterized by both proliferation and destruction of pneumocytes II (filling of the alveolar lumen with the surfactant thus released), and colonization by macrophages and fibroblasts (responsible for collagen secretion).

During the chronic phase, beyond 9 months, an excessive deposition of collagen is responsible for a fibrous thickening of the alveolar walls and a collapse of the air spaces, in parallel with an obliteration of the capillaries by fibrosis.

It is common to see changes in the contralateral lung, which could be explained by a lymphocyte-mediated immune reaction [7–9].

Radiologically, the changes are visible earlier on a chest CT scan than on a standard chest X-ray (6 weeks versus 8 weeks) [4, 6]. Parenchymal condensations and ground glass hyperdensities may appear, or more rarely pleural effusion or atelectasis [8-10]. Kimura *et al.*, described them on the scan:

- Diffuse condensation;
- Localized condensation and frosted glass opacities;
- Diffuse frosted glass opacities;
- Localized frosted glass opacities;
- No increase in density [11].

After conventional three-dimensional radiotherapy, the changes observed are most often confined to the paths of the irradiation beams, which is no longer the case with the techniques of conformal radiotherapy with intensity modulation (IMRT) or radiotherapy under stereotactic conditions [12]. Indeed, in IMRT, high doses are concentrated around the tumor while low doses are wider [13]. Moreover, the radiological aspects appear later after radiotherapy in stereotaxic conditions (often after 3 months) than after conventional three-dimensional radiotherapy (from the first week) [13–15].

The classic picture of acute post-radiation pneumonitis usually occurs within one to three months after exposure and associates non-specific respiratory symptoms such as dry cough, dyspnea, chest pain and radiological abnormalities in the field of radiation. Antibiotic therapy proves ineffective [16, 17].

In the specific context of thoracic irradiation, the diagnoses of post-radiation bronchiolitis obliterans with organized pneumopathy (BOOP), resurgence of radiation lesions by so-called recall effect and also the responsibility of the tumor in the pneumopathy should be mentioned [18, 19].

Post-radiation BOOP can be ruled out here because it is characterized by lung damage not limited to the irradiation field, is generally of later onset compared to irradiation. A so-called recall effect corresponds to the resurgence of an inflammatory reaction of a previously irradiated tissue following the administration of a drug [20]. In our observation, this diagnosis cannot be retained in the absence of introduction of a new drug before the first symptoms. Finally, the responsibility of the tumor, whether carcinomatous lymphangitis or endobronchial localization, must be eliminated as in our observation by CT imaging and bronchial fibroscopy with BAL [21].

The predictive factors are mainly: female gender, large tumor volume (projected target volume greater than or equal to 37.7 mL) and a history of interstitial lung disease. With regard to the dosimetric parameters, the following recommendations should be applied for the homolateral lung: Dmean < 10 Gy, V10Gy < 35%, V30Gy < 15%. For the contralateral lung: V5Gy< 26%. For both lungs: Dmean < 6 Gy, V5Gy < 30%, V20Gy < 12%. When subtracted from

macroscopic tumor volume, mean dose should be less than 4 Gy, V20Gy < 4%, V25Gy < 3.4% and when subtracted from predicted target volume, V20Gy should be less than 5 .8% and the V25Gy < 4.2%. The routine use of these parameters is difficult to apply [22].

As for the treatment of symptomatic radiation pneumonitis, it is done by corticosteroid therapy at a dose of 1 mg/kg/day for 2 to 4 weeks, then progressive reduction over 3 to 12 weeks. Preventive treatment is also started for pneumocystosis and osteoporosis. In addition, there is no indication for antibiotic therapy apart from superinfection. Antioxidants, vitamin E, pentoxyphilin have not shown any efficacy against established pneumopathy [23].

CONCLUSION

Acute post-radiation pneumonitis are rare and can mimic a serious infectious picture. In the elderly, the picture is more severe and the presence of misleading extra pulmonary signs can delay the diagnosis. The diagnosis of acute post-radiation pneumonitis constitutes a diagnosis of elimination to be carried out in the face of a pneumopathy with an unfavorable evolution under antibiotic therapy, in a context of semi-recent thoracic radiotherapy.

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