Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Radiotherapy and Oncology 148 (2020) 201–202

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

COVID-19 Rapid Letter

COVID-19 and radiation induced pneumonitis: Overlapping clinical features of different diseases ☆

To the Editor

SARS-CoV-2 is a novel human coronavirus, first observed at the end of December 2019 in China. In March 2020, with the outbreak of the epidemic, the World Health Organization (WHO) declared the global public health emergency [1]. COVID-19 is the respiratory syndrome associated with SARS-CoV-2. The most serious clinical entity is characterized by severe interstitial pneumonia [2].

Cancer patients are more susceptible to infection due to their lower immunity and therefore might be at increased risk of COVID-19 infection. Furthermore, the prognosis of cancer patients dealing with COVID-19 disease is unpaired as they are usually older with multiple comorbidities. Chinese cancer patients with COVID-19 showed a higher risk of serious events compared with patients without cancer (39% vs 8%, p = 0.0003) [3]. Lung cancer patients may be further at risk as they have a reduced lung function and often suffer from recurrent pulmonary infections.

Radiotherapy is a cornerstone in both definitive or adjuvant treatment of lung malignancies. The clinical picture of radiation induced lung injury (RILI) is radiation pneumonitis (RP) that is relatively common, occurring in 15–40% of patients receiving concurrent chemoradiation (CCRT) for NSCLC [4].

In patients treated with thoracic radiotherapy, discerning RP from COVID-19 disease can be particularly challenging as RP characteristics can mimic SARS-CoV-2 interstitial pneumonia. The most common symptoms are dyspnoea and a dry non-productive cough. High fever (the most common initial symptom of COVID-19) frequently occurs in patients presenting severe lung RP. No laboratory test can definitively identify RP. However, most patients will have a high erythrocyte sedimentation rate (VES) or C-reactive protein and normal procalcitonin. Furthermore, high serum ferritin and D-Dimer are elevated in these patients due to cancer disease [5,6]. In addition, lymphopenia (the most common laboratory finding in patients diagnosed with COVID-19) can be relatively frequent in RP as lymphocytes are known to be more radiosensitive and lymphocyte count reduction has been reported by a median of 67% in NSCLC patients undergoing CCRT [7].

Chest CT is the preferred imaging technique to detect RP. The radiological characteristics of RP are ground-glass opacities (GGO) in the initial phase and patchy areas of consolidation in the peak phase. Furthermore, the thickened pulmonary interstitium and the crazy paving pattern is a common chest CT manifestation of severe RP and COVID-19 (Fig. 1). Linear scarring appearance is typical of later stages, as fibrosis has developed [8,9].

In order to discern between the two clinical entities, some considerations should be made. Firstly, acute symptomatic RP usually occurs within 3 months from the end of radiotherapy. In the Pacific trial in the placebo group, the median time to the onset of RP was 76.5 days [10]. Therefore, an interstitial pneumonia with high fever occurring several months after radiotherapy is unlikely to be radiation induced. Secondly, RP is usually unilateral and the distribution of chest CT abnormalities correspond to radiation treatment fields. It can, therefore, be helpful to correlate CT abnormalities with volumes of treatment and distribution of different doses to lungs. Thirdly, the onset of symptomatic RP is slower than COVID-19 disease, which can show an unfavourable clinical course with the onset of dyspnoea within 5 days and ARDS within 8 days [2].

In conclusion, even if there is still much more to learn about COVID-19 disease, in cancer patients with a history of thoracic radiotherapy treatment and a suspicion of COVID-19 disease, an extra effort should be made to differentiate COVID-19 interstitial disease from RP.

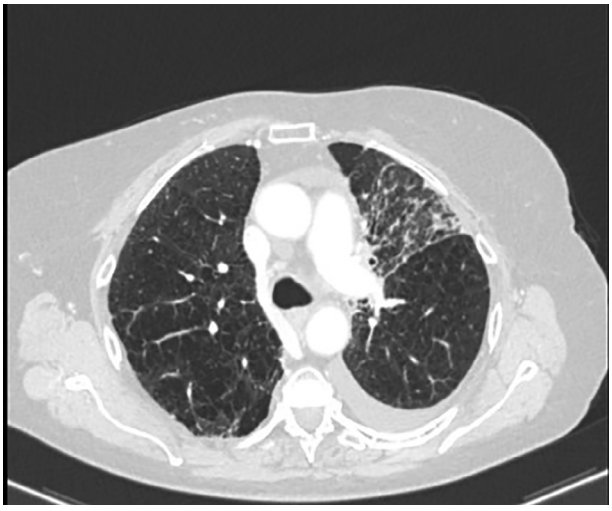

Fig. 1. Patient presenting severe radiation pneumonitis. CT scan shows reticular pattern on 20 Gy irradiated area.

☆ The Editors of the Journal, the Publisher and the European Society for Radiotherapy and Oncology (ESTRO) cannot take responsibility for the statements or opinions expressed by the authors of these articles. Practitioners and researchers must always rely on their own experience and knowledge in evaluating and using any information, methods, compounds or experiments described herein. Because of rapid advances in the medical sciences, in particular, independent verification of diagnoses and drug dosages should be made. For more information see the editorial "Radiotherapy & Oncology during the COVID-19 pandemic", Vol. 146, 2020.

https://doi.org/10.1016/j.radonc.2020.04.009

Conflict of interest statement

None.

Funding

None.

References

[1] World Health Organization. Coronavirus Disease 2019 (COVID 19). Situation Report-74, 3 April 2020. Available via: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200403-sitrep-74-covid-19-mp.pdf?sfvrsn=4e043d03_10.

[2] Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. China medical treatment expert group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020. https://doi.org/10.1056/NEJMoa2002032.

[3] Liang W, Guan W, Chen R, Wang W, Li J, Xu K, et al. Cancer patients in SARS-CoV-2 infection: a nationwide analysis in China. Lancet Oncol 2020;21:335–7. https://doi.org/10.1016/S1470-2045(20)30096-6. Epub 2020 Feb 14.

[4] Palma DA, Senan S, Tsujino K, Barriger RB, Rengan R, Moreno M, et al. Predicting radiation pneumonitis after chemoradiation therapy for lung cancer: an international individual patient data meta-analysis. Int J Radiat Oncol Biol Phys 2013;85:444–50. https://doi.org/10.1016/j.ijrobp.2012.04.043.

[5] Hanania AN, Mainwaring W, Ghebre YT, Hanania NA, Ludwig M. Radiation-induced lung injury: assessment and management. Chest 2019;156:150–62. https://doi.org/10.1016/j.chest.2019.03.033.

[6] Ramella S, Spoto S, Fiore M, Grasso G, Campanale RE, Ippolito E, et al. A clinical score, including biohumoral parameters, is a useful pretest index to discriminate pulmonary infections from radiation damage in chemoradiation-treated lung cancer patients. Cancer Invest 2014;32:110–4. https://doi.org/10.3109/07357907.2014.883525.

[7] Campian Jian L, Ye Xiaobu, Brock Malcolm, Grossman Stuart A. Treatment-related lymphopenia in patients with stage III non-small-cell lung cancer. Cancer Invest 2013;31:183–8.

[8] Choi YW, Munden RF, Erasmus JJ, Park KJ, Chung WK, Jeon SC, et al. Effects of radiation therapy on the lung: radiologic appearances and differential diagnosis. Radiographics 2004;24:985–97. discussion 998. Review.

[9] Ye Z, Zhang Y, Wang Y, Huang Z, Song B. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur Radiol 2020. https://doi.org/10.1007/s00330-020-06801-0.

[10] Antonia SJ, Villegas A, Daniel D, Vicente D, Murakami S, Hui R, et al. Durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. N Engl J Med 2017;377:1919–29. https://doi.org/10.1056/NEJMoa1709937.

Edy Ippolito [a]
Michele Fiore [a]
Carlo Greco [a,*]
Rolando Maria D'Angelillo [b]
Sara Ramella [a]
[a] *Radiation Oncology, Campus Bio-Medico University, Rome*
[b] *Radiation Oncology, "Tor Vergata" University, Rome, Italy*
* Corresponding author at: Carlo GRECO, Radiation Oncology, Campus Bio-Medico University, via Alvaro del Portillo 200, 00128 Rome, Italy.
E-mail address: c.greco@unicampus.it (C. Greco)

Received 8 April 2020
Accepted 9 April 2020

Available online 14 April 2020