Radiation pneumonitis and chemotherapy in a patient with multiple myeloma

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A 66-year-old man attended our hospital with increasing shortness of breath, asthenia, and fever.

He had a history of multiple myeloma, which, 9 weeks earlier, necessitated him having a vertebral arthrodesis for a painful fracture of the fourth thoracic vertebra; after the operation, he had stereotactic radiotherapy on the surgical site. 7 weeks after the radiotherapy, the patient received a single dose of a proteasome inhibitor—2·2 mg of bortezomib—and 4 days of an immunomodulatory drug—25 mg per day of lenalidomide.

On examination we found the patient had a dry cough, and was hypoxic with a peripheral blood oxygen saturation of 86% breathing room air; his temperature was 39·2°C and heart rate 120 beats per min.

A week later, the patient's respiratory state rapidly deteriorated: he required invasive mechanical ventilation and fulfilled the criteria for severe acute respiratory distress syndrome.

A chest x-ray showed an acute pneumonia (figure) and a CT showed central alveolar condensations with ground glass opacities and reticulations sparing the subpleural area and lower lobes (figure).

Cardiac and infectious causes of the patient's difficulties were investigated and excluded, and we diagnosed Radiation Therapy Oncology Group grade 4 radiation-induced lung injury because the opacities were located around the site of the vertebral osteosynthesis (figure). We started corticosteroid treatment, which improved the patient's condition and allowed him to be weaned off mechanical ventilation 11 days after they had been started. The patient left hospital for a rehabilitation centre 40 days after the corticosteroids had been started; he went home after rehabilitation.

The correlation between the distribution of the lung opacities and the calculated radiation fields supported the diagnosis of radiation pneumonitis. However, we estimated that the predictable risk of developing high grade radiation pneumonitis with our protocol of radiotherapy was very low because of the method—stereotactic radiotherapy—limiting the dose of undesired lung radiation to a mean lung dose of 11·2 Gy on a small lung volume. Essentially, the dose of stereotactic radiation given to our patient, we believe, was unlikely to have caused such a severe pneumonitis alone. Furthermore, it is noteworthy that the patient's symptoms developed soon after he received the chemotherapy.

We therefore postulate that there may have been a synergistic effect of the radiation and the chemotherapy—which were given in very low doses—in causing our patient's severe lung disease.

Radiation pneumonitis usually occurs within 4–12 weeks of the radiotherapy and is related to pneumocyte and endothelial cell damage from the radiation and an inflammatory response mediated by cytokines and reactive oxygen species. The alveolar barrier is thus impaired with interstitial oedema and exudate in the alveoli. We speculate that the inflammatory reaction could have been enhanced by bortezomib, which inhibits the ubiquitin–proteasome pathway, and the immunomodulatory effect of lenalidomide, which reinforces T-cell and natural killer cell immunity (video).

See **Online** for video

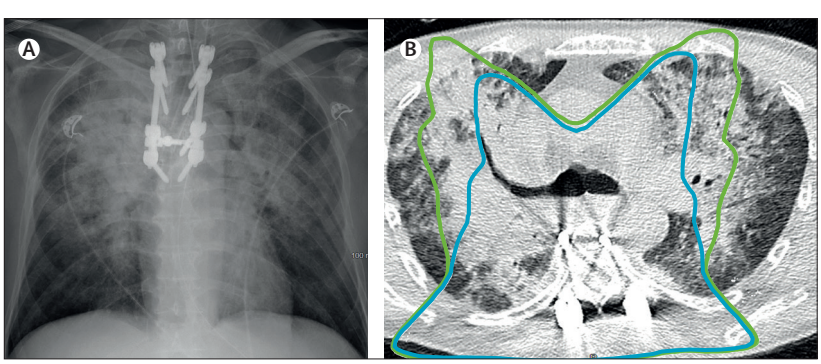

Figure: **Radiation pneumonitis and chemotherapy in a patient with multiple myeloma**
(A) Chest x-ray shows acute pneumonia and previous vertebral arthrodesis. (B) CT scan shows the lung opacities and the calculated radiation fields (green line shows lung volume receiving irradiation of 25% of total dose of 44 Gy and blue line shows lung volume receiving 30% of total dose of 44 Gy).

Contributors
We were both involved in the management, diagnosis, and treatment of the patient. We both contributed equally to writing and editing the final manuscript. Written consent for publication was obtained from the patient.

Declaration of interests
We declare no competing interests.