Clinical Case Reports

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CASE REPORT

Polymyositis and fatal interstitial pneumonia following pelvic irradiation that led to unexpectedly severe adverse effects: a case report

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Key Clinical Message

Interstitial pneumonia (IP) sometimes precedes collagen vascular disease (CVD) onset. A patient with bladder cancer and mild IP received pelvic irradiation and experienced unexpectedly severe urinary toxicity followed by polymyositis onset and fatal IP exacerbation. Careful observation for "alarm adverse effects" of radiotherapy in IP patients may help predicting CVD onset.

Keywords

Collagen vascular disease, interstitial pneumonia, radiation toxicity.

Introduction

Patients with collagen vascular disease (CVD) such as rheumatoid arthritis, systemic lupus erythematosus, scleroderma, polymyositis, and dermatomyositis, are known to be sensitive to ionizing radiation [1–9]. Thus, radiotherapy is considered a relative contraindication for the CVD patients. Irradiation to the lung in patients with interstitial pneumonia (IP) is also considered a relative contraindication because IP is a risk for severe radiation-induced pneumonitis [10]. Meanwhile, in general, irradiation of extrapulmonary sites in IP patients is not contraindicated. Here, we report a patient with bladder cancer and mild IP who received pelvic irradiation and showed unexpectedly severe adverse effects that followed by the onset of polymyositis and fatal exacerbation of IP.

Case Report

A 70-year-old Japanese man with bladder cancer (cT1N0M0) presented to the radiation oncology department in March 2014. He had IP, which had been controlled stable with prednisolone (10 mg/day) since 2010. A chest computed tomography (CT) revealed ground-glass opacity in the subpleural region (Figs. 1 and 2). Spirometry test results showed a restrictive pattern (vital capacity, 55%; forced expiratory volume 1.0, 76%). Although he was diagnosed as being tolerable for surgery under general anesthesia, he refused surgery and selected

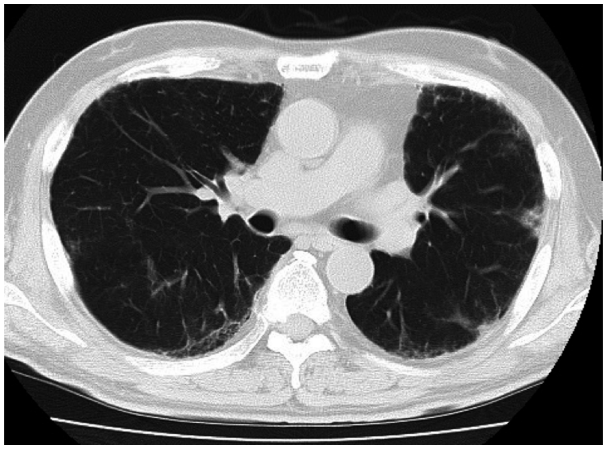

Figure 1. Chest computed tomography showing stable interstitial pneumonia (July 2010).

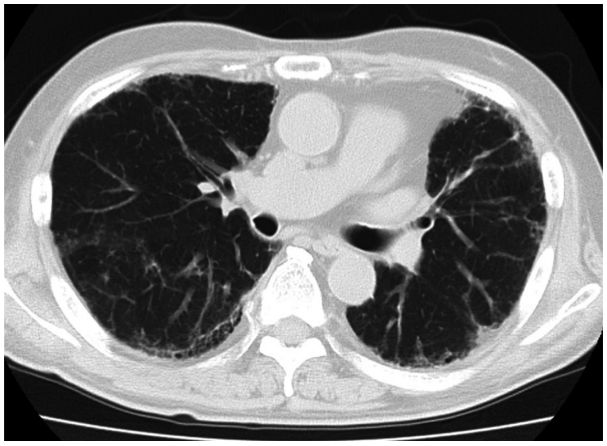

Figure 2. Chest computed tomography showing stable interstitial pneumonia (March 2014).

radiotherapy for his bladder cancer. He had a previous history of spinal canal stenosis and cataract in the left eye, however, he did not have a medical history indicative of a risk for severe radiation toxicity including diabetes mellitus. He had no physical symptoms. Radiotherapy targeting the bladder and pelvic lymph node regions was initiated, with a daily fraction of 2 Gy. However, he developed urinary tract pain and erythema in the radiation field much earlier than expected (i.e., within the first week). These symptoms worsened as the total delivered dose increased. Alpha-blockers, loxoprofen, intravesical infusion of lidocaine, and betamethasone valerate ointment were ineffective. In the third week, he showed Grade 3 urinary tract pain, Grade 3 radiation dermatitis (assessed using the Common Terminology Criteria for Adverse Events, Version 4.0), and needed to urinate every 5 to 10 min. Thus, radiotherapy was terminated at 34 Gy, much less than the target bladder dose of 60 Gy.

In June 2014, he was admitted to our hospital with proximal muscle weakness, which had worsened over the previous 2 weeks. Elevated serum creatine kinase (CK, 2657 IU/L) and C-reactive protein (3.66 mg/dL) levels, myogenic changes in the left deltoid and biceps brachii on electromyography, a high signal in the proximal muscles on magnetic resonance imaging (short-TI inversion recovery), and the presence of autoantibodies against aminoacyl-tRNA synthetase (anti-ARS antibodies) led to a diagnosis of polymyositis. Meanwhile, CT (chest through pelvis) showed no signs of infection or progression of cancer. An increased dose of prednisolone (60 mg/day) over 1 month improved the muscle weakness and CK levels (639 IU/L). However, in August he experienced a sudden and rapid deterioration of respiratory status. Chest CT showed extensive areas of ground-glass opacity and consolidation, suggesting an acute exacerbation of IP (Fig. 3). Despite maximum medical therapy, including prednisolone pulse (1 g/day) and cyclophosphamide, he died 1 week later.

Discussion

We conducted radiotherapy to this patient because he had not presented with any symptoms suggestive of CVD. Although we could not identify the specific reason of the severe adverse effects during radiotherapy, the following onset of polymyositis suggested that the patients had vulnerability to ionizing radiation. To the best of our knowledge, this is the first case reported in the literature of unexpectedly severe adverse reactions to radiotherapy followed by the onset of CVD. The current case suggests that unexpectedly severe adverse effects after radiotherapy

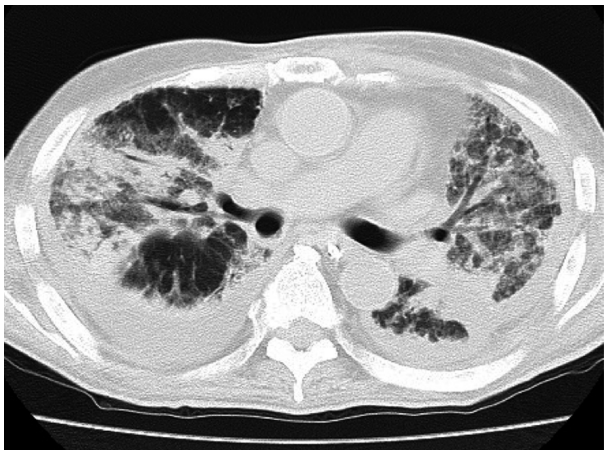

Figure 3. Chest computed tomography showing acute exacerbation of interstitial pneumonia (August 2014).

can be an alarm of CVD onset, which enables the prediction and early intervention of the CVD.

Collagen vascular disease is often accompanied by respiratory system involvement [11–13]. Overall, IP is reported in approximately 15% of CVD patients [11]. Notably, CVD-associated IP can precede the appearance of systemic CVD symptoms by many years; sometimes by more than 5 years [12, 13]. These findings are consistence with our case which had a 4-year history of IP before the onset of polymyositis. In such cases, it is impossible to distinguish CVD-associated IP from other types of IP (e.g., drug-induced IP or idiopathic IP) because the clinicopathological findings of CVD-associated IP show wide variation [11–13]. At the time of radiotherapy, the current patient showed manifestations of IP but not of myositis. Therefore, we were unaware of the underlying risk for severe radiation toxicity. Irradiation of extrapulmonary sites is not contraindicated in patients with IP. However, there may be a considerable number of patients with IP-preceding CVD who are at risk of unexpectedly severe toxicity after radiotherapy.

Anti-ARS antibodies are highly specific for polymyositis and dermatomyositis [14]. Anti-ARS antibody-positive polymyositis and dermatomyositis are strongly associated with IP [15]. Of note, 29–50% of anti-ARS antibody-positive IP-associated cases polymyositis and dermatomyositis are IP-preceding type [15]. Taken together, these findings suggest that measurement of anti-ARS antibody levels in IP patients prior to radiotherapy may help predict severe radiation toxicity associated with the late onset of polymyositis or dermatomyositis.

The following points can be raised as limitations of the present case. Pulmonary biopsy and pathological examination to determine the type of IP were not performed. CVD markers such as antinuclear antibody were not evaluated in the stable IP period.

In summary, extrapulmonary irradiation to patients with IP-preceding CVD may promote CVD onset. Careful observation for the "alarm" adverse effects of radiotherapy, especially in IP patients, may lead to the prediction and early intervention of the CVD.

Informed Consent

Written informed consent was obtained from the patient's next of kin for publication of this case report and accompanying images.

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Competing Interests

The authors declare that they have no competing interests.

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