Radiation Pneumonia

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23.1 Overview

Radiation pneumonia (RP) is an inflammatory reaction caused by the injury of normal lung tissue in the radiation range after radiotherapy for tumors (mainly lung cancer, breast cancer, esophageal cancer, lymphoma, and other malignant tumors in the chest), which is a common complication of chest radiotherapy [1].

The clinical manifestations of radiation pneumonia are different and mostly occur 2–3 weeks after radiotherapy. Mild cases may be asymptomatic. The main symptoms are irritating dry cough, accompanied by shortness of breath, palpitation, and chest pain, without fever or low fever, occasionally with high fever. With the progress of pulmonary fibrosis, shortness of breath is aggravated, often causing respiratory tract infection, thus further aggravating respiratory symptoms. Severe cases often show respiratory dysfunction and even death due to extensive pulmonary fibrosis. The occurrence and progress of radiation pneumonia are closely related to radiation methods, radiation dose, radiation area, frequency of X-ray examinations, individual tolerance, drug therapy, and basic lung diseases.

There have been several theories about the pathogenesis of radiation pneumonitis: the most common one is cytokine theory, including tumor necrosis factor-α (TNF-α), transforming growth factor-β (TGF-β), and interleukin-6 (IL-6). Among them, TNF-α is the initiator of cytokine regulation, which plays an important role in the occurrence and development of inflammatory changes and fibrosis of lung tissue [2]. TGF-β is the mediator most closely related to the occurrence and development of pulmonary fibrosis caused by radiation injury [3], which can predict the risk of radiation-induced lung injury [4], and the content of IL-6 in plasma can reflect the inflammatory state of lung tissue. Other theories include type II epithelial cell injury theory [5], vascular endothelial cell injury theory, free radical and radiation lung injury, and gene theory.

The treatment of radiation pneumonia mainly includes rest and oxygen inhalation when necessary, and adrenocortical hormone treatment. Because acute radiation pneumonitis is often complicated with lung infection, it must be treated with antibiotics at the same time and adrenocortical hormone should be gradually reduced until drug withdrawal. Radiation pneumonia patients can be accompanied by different degrees of pulmonary fibrosis more than 1 year after radiotherapy. At present, no special treatment is available for radiation pulmonary fibrosis, so prevention is important [6, 7].

23.2 Pathological Manifestations

Radiation pneumonia is closely related to the injury of type II alveolar epithelial cells and vascular endothelial cells. Endothelial cell injury leads to changes in blood perfusion, increased vascular permeability, and then pulmonary interstitial congestion and edema, as well as increased alveolar exudation. The disease can be complicated with microthrombosis and blockage of capillaries. Type II alveolar epithelial cell injury leads to the deterioration of alveolar surface stability, which causes alveolar to collapse, and then leads to hypoxia and dyspnea.

Pathological changes are mainly inflammatory exudative changes in the acute stage and extensive pulmonary fibrosis in the chronic stage. Early acute lung injury is manifested as fibrous exudation of serous fluid in alveolar cavity, formation of hyaline membrane, edema and thickening of alveolar wall, exfoliation of alveolar and bronchial epithelium, etc. Decreased alveolar surfactant may lead to lung collapse. Epithelial swelling of alveolar capillaries and pulmonary arterioles may lead to lumen stenosis and even embolism. After 6–12 months of radiation pneumonitis, the pulmonary

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lesions are gradually replaced by fibrous connective tissue and the histopathological manifestations in the chronic stage are nonspecific fibrosis.

23.3 Imaging Manifestations

1. X-ray: Radiograph may show no abnormal pulmonary manifestation in mild cases, and thickened and blurred lung markings in severe cases, which is limited to the irradiation field, and some of them may be accompanied by small patchy hyperdensities scattered among the thickened lung markings. With the progression of the lesions, radiographs show patchy hyperdensities consistent with the irradiation scope, mostly with clear edges of the lesions and the lung. In the later stage, the scope of lesions in the original irradiation field is further reduced, showing hyperdense stripe-like opacities mostly, which can be accompanied by pleural thickening, causing traction of adjacent structures, mediastinum shifting to the affected side. Thoracic collapse and deformation may occur in severe cases.
2. CT: The lesions are confined to the irradiation scope, usually not limited to a certain lung lobe, but distributed across lobes, with straight edges and clear demarcation from the unirradiated normal area of the lung. In the early stage, patchy hyperdensities can be found, with uneven density, and those lesions mainly distributed under the pleura can be complicated with fine reticular opacities. As the lesions progress, the fibrous stripe-like opacities gradually increase, with higher density and expanded scope, and the lesions gradually fuse into patchy opacities. After about 6 months, lesions similar to the radiation field occur, with smaller scope but higher density. Bronchial shadows can often be found inside and gradually progress into pulmonary fibrosis lesions, manifested as mass high-density opacities with straight and sharp edges, sometimes accompanied by bronchiectasis (Fig. 23.1), causing traction changes between adjacent pleura and mediastinal organs [8]. In addition, pleural thickening, pleural effusion, and other changes can be found.
3. PET/CT: Because of the systemic scan, PET/CT has important applications in tumor diagnosis, treatment, curative effect evaluation, and re-examination. Some patients who have undergone radiotherapy can show the existence of radiation pneumonia, which is mainly manifested as flaky, strip, or even lumpy hyperdensities in the lungs, with clear edges, slight increase of radioactive uptake, or indefinite abnormal increase of radioactivity uptake (Fig. 23.2). If residual tumor is found in the irradiation area, local radioactivity uptake may be increased. However, PET/CT has considerable advantages for patients with obstructive pneumonia, atelectasis, pleural invasion, and pleural effusion, for whom CT scan alone has difficulty in determining tumor boundary. PET/CT can better interpret the nature of lymph nodes and make the irradiation volume and dose more accurate, thus effectively reducing the irradiation volume of surrounding normal lung tissue and further reducing the incidence and severity of radiation pneumonia [9, 10].

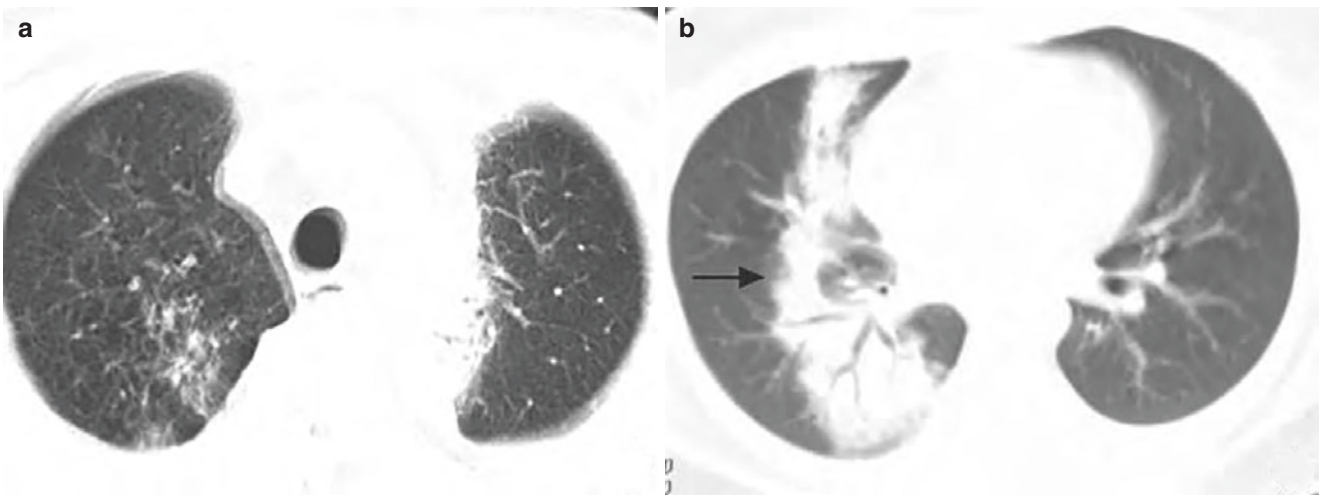

Fig. 23.1 Radiation pneumonia (I). (**a**) CT lung window showed patchy hyperdense opacities on both sides of spine, with blurred edges and (**b**) the right lung showed lateral-route stripe-like patchy hyperdensities (arrow), distributed across lobes, with straight edges and air bronchogram inside

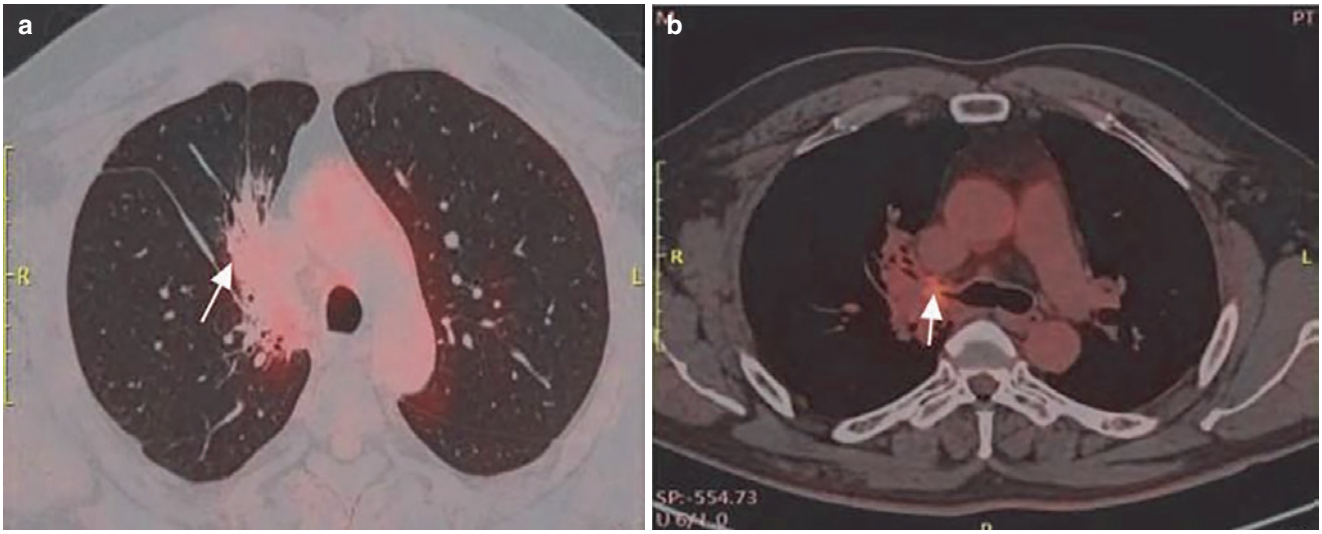

Fig. 23.2 Radiation pneumonia (II). The patient, a 58-year-old male, after radiotherapy of right lung cancer. (**a**) PET/CT lung window showed fusion image and patchy hyperdensities beside mediastinum of right lung, with clear edges and slightly increased FDG metabolism (arrow) and (**b**) PET/CT mediastinal window showed fusion image, local bronchial stenosis in the right lung, and increased FDG metabolism in the patchy opacities of the right hilum (arrow)

23.4 Diagnostic Key Points

1. Imaging manifestations include hyperdensities with clear edges, irregular shape, and consistent scope with the irradiation field, sometimes with traction of adjacent structures, and closed and twisted gas-filled bronchi.
2. Combined with medical history, the analysis must be made according to irradiation history and irradiation dose.
3. Combined with clinical manifestations and laboratory examinations, comprehensive analysis can be carried out to exclude lung diseases caused by other factors.

23.5 Differential Diagnosis

1. Pulmonary tuberculosis: It usually occurs in the posterior segment of the upper lobe and the dorsal segment of the lower lobe, which is manifested as stripe-like opacities, nodules, and irregular hyperdensities, showing cavities and calcification, mostly with satellite lesions. The diagnosis should be made by combining clinical and related laboratory examinations, and the anti-tuberculosis treatment is effective.
2. Acute and chronic pneumonia: It shows stripe-like opacities, patchy opacities, and irregular hyperdensities. Acute pneumonia mostly has unclear edges and may be accompanied by consolidation and acute course of disease. Anti-inflammatory treatment is effective, and the lesions are rarely distributed across lobes. Chronic pneumonia has clear edges and is rarely distributed across lobes.

By carefully inquiring the medical history of radiotherapy and comparing the original radiographs, it is not difficult to diagnose radiation pneumonia. After radiotherapy, it is sometimes necessary to identify whether there is residual tumor of central lung cancer. If it is difficult to distinguish radiation pneumonia from tumor on CT plain scan, CT enhanced scan or PET/CT should be performed to distinguish the two according to different degrees of enhancement of tumor and increased radioactivity uptake.

23.6 Research Status and Progress

Radiation pneumonitis is a common complication of thoracic radiotherapy, and there is no significantly effective treatment, which seriously limits the application of radiotherapy in tumor, so it is important to prevent radiation pneumonitis. The research on the influencing factors of radiation pneumonia is being further deepened. Some scholars use radiomics to establish a prediction model of radiation pneumonia by extracting the characteristics of imaging, clinical manifestations, and radiation dosimetry, thereby better predicting the occurrence of radiation pneumonia and guiding clinical practice [11, 12].

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