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Imaging features of IRIS caused by AIDS and complicated by tuberculosis

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Abstract: Immune reconstitution inflammatory syndrome (IRIS), a common complication of AIDS, is further complicated by tuberculosis. Its clinical symptoms lack specificity but can be evaluated using diagnostic imaging. High-resolution computed tomography (HRCT) is useful in evaluating the morphology and internal microstructure of lesions associated with the syndrome, as well as the relationship of the internal microstructure with the surrounding tissues. This paper summarizes the present state and progress of imaging research on IRIS caused by AIDS and complicated by tuberculosis.

Keywords: immune reconstitution inflammatory syndrome, AIDS, tuberculosis, imaging

1 Introduction

Tuberculosis is one of the most common opportunistic infections and an important cause of death among patients with AIDS [1]. According to a report by the World Health Organization, 13% of newly diagnosed tuberculosis patients exhibit complications associated with HIV infection, and 30% of dead tuberculosis patients are HIV positive [2]. Highly active antiretroviral therapy (HAART) is currently the only effective anti-HIV treatment. HAART can significantly inhibit HIV replication, improve immunity, and improve the prognosis of AIDS patients with tuberculosis complications. This treatment method, however, also introduces the risk of immune reconstitution inflammatory syndrome (IRIS). IRIS is the recurrence of original opportunistic infections during the immune reconstitution of AIDS patients undergoing HAART and causes the health of patients to deteriorate [3]. IRIS is a common complication of AIDS complicated by tuberculosis. Imaging examination, particularly high-resolution computed tomography (HRCT), provides a reliable basis for the diagnosis of IRIS. Therefore, the investigation of imaging features has important clinical value in the treatment and management of IRIS. This paper provides a review of the recent progress in the imaging examination of IRIS caused by AIDS and complicated with tuberculosis.

2 Prevalence of IRIS

Studies have shown that tuberculosis complications constitute one of the most common clinical types of IRIS in HAART [4]. At present, large epidemiological surveys on the incidence of IRIS in patients with AIDS and complicated by tuberculosis following HAART are lacking. Zhao et al [5], Lu X et al [6], and Lu Y et al [7] reported IRIS incidences of 6.7%, 48.8%, and 7.9%, respectively. These percentages are considerably higher than those in foreign countries. The incidence of IRIS 6 months after the initiation of HAART ranges from 10% to 15% in developed countries and from 20% to 25% in developing countries. The vast majority of IRIS cases occur during the first 3 months of treatment [8,9].

3 Pathogenesis of IRIS

The pathogenesis of IRIS is unclear. Most studies suggest that HAART, immune reconstruction, and enhanced pathological inflammatory response after antituberculosis treatment are the main reasons for IRIS [10,11]. In recent years, studies have shown that AIDS and tuberculosis affect each other and interact as both cause and effect [12]. The invasion of the human body by the HIV virus causes the destruction of CD4+ T-cells, in turn decreasing immunity and facilitating infection by *Mycobacterium tuberculosis*. The replication of numerous *M. tuberculosis* cells causes IRIS. Moreover, *M. tuberculosis* and its metabolites can promote HIV replication, thus accelerating the course of HIV infection [13,14]. HAART can effectively decrease HIV replication, improve the number and function of T-lymphocytes, and control HIV infection. Abnormal immune response and clinical symptoms occur during the early stages of HAART with the rapid increase in the number of CD4+ T-cells and the decrease in active HIV viral load [15]. These abnormal responses and symptoms manifest as aggravated symptoms of tuberculosis, common fever, cough, respiratory distress, increased lung lesion infiltration, lymph node enlargement, and increased inflammation of other organs; these symptoms can cause respiratory failure and threaten life [16]. Images of the chest present widely distributed inflammatory infiltrates, mediastinal lymph node enlargement, and thoracic and pericardial effusions.

4 Imaging Features of IRIS

4.1 Dissemination of Lesions

Chest X-ray images show lung lesions or enlarged existing lesions that indicate secondary or hematogenous pulmonary tuberculosis. Lesions associated with secondary pulmonary tuberculosis have no particular predilection sites and hence are distributed in multiple lobes and segments. In 35.0%–93.0% of IRIS patients, the lesions are distributed in three lobes or more. CT imaging reveals patchy infiltration that coexists with various forms and qualities of lesions, as well as lung segment and subsegment consolidations mixed with various lesions, such as miliary and alveolar nodule dissemination. Air bronchogram signs are present in the consolidations. Fibrosis, calcification, and voids are rare [6,7,17,18]. HRCT shows lobular central nodules; tree-in-bud structures; or fuzzy, patchy, or shadowy consolidations. The tiny holes inside the shadow of consolidations or pneumatic expanded bronchioles are typical signs of active lesions [19]. Hematogenous pulmonary tuberculosis has a high incidence and is identified as the hematogenous dissemination of pulmonary tuberculosis, which spreads rapidly. Acute hematogenous pulmonary tuberculosis is common; however, subacute and chronic forms of hematogenous disseminated tuberculosis are rare. The detection rate from X-ray imaging is low. In X-ray images, lesions present as a thickened and disordered texture of the lung. Miliary nodules in lungs present on CT images as diffusely distributed shadows. These nodules are 1–3 mm in diameter and are mainly localized in the middle lower lung. As the disease progresses, some lesions assume flake-like forms. These signs are different from those of simple hematogenous pulmonary tuberculosis. Yuan et al [19] reported that chest CT images of IRIS patients show that lesions usually appear during the first to the fifth week after HAART. The lesions then improve from the second to the third week after HAART and then gradually disappear. Nodes and tree-in-bud signs are generally replaced by fibrosis.

4.2 Lymph Node Enlargement

The incidence of lymph node enlargement in patients with IRIS caused by AIDS and complicated by tuberculosis is 37.8%–100.0%. Most chest images from IRIS patients exhibit numerous enlarged and widely distributed lymph nodes (mediastinum, hilus, neck, and axilla). In IRIS, the calcification rate of the enlarged lymph node is significantly lower than that in simple pulmonary tuberculosis, or the original narrowed lymph nodes rapidly enlarge and show lump-like fusions [6,7,17,18, 20]. In X-ray images, lymph node enlargement presents as a widened mediastinum and an enlarged bilateral hilus of the lung that protrudes into

the lung pulmonary field like a wave. A plain CT scan shows uniform or uneven low-density, partially fused, and defined or diffuse borders. Magnetic resonance imaging (MRI) examination can be used to distinguish whether the mediastinal mass is cystic or solid based on the signal strength. The enhanced scan can be used to analyze the status of the enlarged lymph nodes. Plain MRI scan mostly shows uneven and low T1-weighted image (T1WI) and T2WI signals. Lymph node enlargement is characterized by central liquefaction necrosis. CT and MRI enhanced scans reveal a mild ring strengthening of the edge [18].

4.3 Pleural and Pericardial Effusions

IRIS caused by AIDS and complicated by tuberculosis is followed by bilateral or unilateral pleural effusion in the thoracic cavity. A small amount of effusion might also be associated with a small amount of pericardial effusion. Rapose et al [20] believe that continuous antituberculosis and HAART treatments are conducive to the absorption of effusion. Lu et al [7] proposed that the occurrence of pericardial effusion in HAART is a characteristic of IRIS caused by AIDS and complicated by tuberculosis.

5 Imaging Features

5.1 Plain Film X-Ray Examination

Plain film X-ray is the most common and basic imaging examination method. It is widely used, convenient, inexpensive, and less radioactive. Chest X-ray imaging can be used to visualize and evaluate lung lesions but is inapplicable to tiny lesions in the lungs, minor changes in lesions, and morphological characteristics. Moreover, chest X-ray imaging is insensitive to the enlargement of mediastinal lymph nodes and to small amounts of pleural and pericardial effusions.

5.2 CT Examination

With the rapid development of spiral CT, multilayer HRCT has improved the spatial resolution of CT images and improved the detection rate of lesions. CT examination is thus valuable for the timely diagnosis of IRIS chest lesions.

HRCT can be used to find small nodules and assess the relationships among lesion boundaries, fine internal structure, bronchial or small blood vessels, and pleura. It can also be used to identify lung consolidation or small cavities in glass-like density shadow and it clearly shows tree-in-bud structures, lobular nodules, and other bronchial symptoms. Approximately 80% of active tuberculosis cases were diagnosed based on HRCT images [21]. Studies on the chest CT imaging features of IRIS caused by AIDS and complicated by tuberculosis have been rarely conducted. To improve the value of CT imaging diagnosis for IRIS, the following aspects should be studied: (1) predilection site and morphology of lesions associated with IRIS caused by AIDS and complicated by tuberculosis; (2) the presentation of bronchial stenosis, bronchial wall, and peripheral soft tissues or lymph nodes on CT and HRCT; (3) analysis of the mass shadow in tubercular tissue or mediastinal lymph node based on enhanced CT scan images; (4) CT examination of thoracic and pericardial effusions, and measurement of their thicknesses for comparison before and after observation.

5.3 Ultrasonic Examination

Ultrasonic examination is simple, quick, noninvasive, and radiation free. This examination method is highly valuable in the diagnosis of pleural and pericardial effusions associated with IRIS. Given the influence of gas-containing lung tissue, ultrasonic examination is not used for the diagnostic examination of lung diseases.

Moreover, although it has a certain value in the diagnosis of superficial diseases in the chest cavity, its definition and tissue resolution are lower than those of CT and MRI. Therefore, independent qualitative diagnosis using ultrasound images remains difficult. Nevertheless, integrated ultrasonography can guide tissue biopsy and the cytological examination of pleural effusion, lung lumps, and enlarged lymph nodes associated with IRIS caused by AIDS and complicated by tuberculosis.

5.4 MRI Examination

MRI examination provides direct and multidirectional imaging without radiation damage. The inflatable lung parenchymal signal, however, is weak. Moreover, MRI is insensitive to calcification within lesions. Although the new respiratory gating technology can be effectively applied to improve MRI, respiratory movement continues to affect the quality of MR images of the chest. Therefore, the clinical value of MRI in lung examination remains limited. MRI is commonly used to diagnose lesions in the mediastinum and hilus of the lung. It is sensitive to mediastinal lymph nodes and can clearly show enlarged lymph nodes in the mediastinum and hilus of the lung without the need for a contrast agent.

In summary, with the increasing incidence of AIDS and the widespread application of HAART, the incidence of IRIS caused by AIDS and complicated by tuberculosis has also gradually increased. Image-based examination has an important role in the diagnosis and treatment of IRIS given its atypical clinical manifestation. Researchers should improve image-based examination and conduct additional studies on the imaging characteristics of IRIS to provide a reliable basis for the clinical diagnosis and treatment of this syndrome.

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