

Correlation between imaging features of Pneumocystis Jiroveci Pneumonitis (PCP), CD₄⁺ T lymphocyte count, and plasma HIV viral load: A study in 50 consecutive AIDS patients

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Purpose: To investigate the imaging manifestations of Pneumocystis Jiroveci Pneumonitis (PCP) in AIDS patients, and the correlation between imaging features, CD₄⁺ lymphocyte count, and plasma HIV viral load.

Materials and methods: A total of consecutive 50 AIDS patients with PCP were reviewed retrospectively. Chest CT manifestations, CD₄⁺ lymphocyte count, and plasma HIV viral load were analyzed to investigate their correlation.

Results: PCP chest CT manifestations included ground-glass opacities dominated in 28 cases (28/50, 56%), lung cysts dominated in 10 cases (10/50, 20%), consolidation dominated in 6 cases (6/50, 12%), interstitial lesion dominated in 3 cases (3/50, 6%), and mixed lesions in 3 cases (3/50, 6%). In these 50 patients, CD₄⁺ lymphocyte count ranged from 2 to 373 cells/ μ L. Plasma HIV viral load ranged from 500 to 5.28×10^7 copies/mL. CD₄⁺ lymphocyte count in ground-glass opacities dominated patients was higher than that of lung cyst dominated patients ($P < 0.05$). Plasma virus load of lung cysts dominated PCP patients was higher than that of consolidation dominated patients ($P < 0.05$).

Conclusions: The typical chest imaging features of PCP in AIDS patients included lung ground-glass opacities and lung cysts. The chest imaging features were correlated with CD₄⁺ T lymphocyte count and plasma HIV viral load.

Key Words: Acquired Immunodeficiency Syndrome (AIDS); Pneumocystis Jiroveci Pneumonitis; Tomography; X-ray computed; CD₄⁺ lymphocyte counts; Virus load



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Acquired immunodeficiency syndrome (AIDS) patients have low immune function, with CD₄⁺ lymphocyte count progressively decreases as disease progresses. When the CD₄⁺ count falls below 200 cells/ μ L, AIDS patients gradually present with clinical symptoms (1,2). Plasma HIV virus load and CD₄⁺ lymphocyte count are two important biomarkers for assessing clinical course of HIV-infected patients, predicting clinical progress and evaluating therapy of anti-HIV drugs (3). CD₄⁺ lymphocyte count provides information of the status of the compromised immune

system of HIV-infected patients. Because of severe cellular immune disfunction, AIDS patients can have a variety of fateful opportunistic infections. Pneumocystis Jiroveci Pneumonia (PCP) is one of the most common opportunistic lung infections that threaten the life of AIDS patients (4). Vigilance for PCP, early diagnosis and early treatment are crucial to reduce the resulting mortality. In this study, the CT lung manifestations of 50 consecutive AIDS patients complicated with PCP were retrospectively analyzed. The chest imaging manifestation, and the correlation between

imaging features, CD₄⁺ lymphocyte count, and plasma virus load were investigated.

Materials and methods

Study subjects

Between March 2007 and July 2009, 50 consecutive AIDS patients complicated with PCP, who were all treated at the Shenzhen Third People's Hospital, were retrospectively analyzed. There were 33 males and 17 females. The mean age was 34 years (age range, 19~57 years). All these patients were confirmed HIV positive by western blotting technique, and were classified as AIDS stage IV. Risk behaviors for HIV infection of these patients were as follow: sex contact 35, i.v. drug usage 7, blood transfusion 2, illegal blood sampling 1, unknown reason 5. The AIDS diagnosis was according to the Centers for Disease Control and Prevention of USA (5) and the Guidelines for diagnosis and treatment of HIV/AIDS in China (2005) (6). The criteria for the diagnosis of PCP include: (I) sputum, bronchoscopic biopsy or bronchoalveolar lavage tested *Pneumocystis jirovecii* positive; (II) consistent with diagnosis standards of AIDS or other severe immunosuppression; (III) CD₄⁺ ≤200 /μL; (IV) dry cough, dyspnea, fever, chest pain or body weight loss, but without obvious chest sign; (V) typical chest X-ray characteristics; (VI) responsive to anti-PCP therapy; (VII) Serum lactate dehydrogenase (LDH) increase continuously by three consecutive testings. The diagnosis of AIDS complicated with PCP was made when a patient had the first item and any 4 items of the rest 6 items. Among these patients 3 cases had lung biopsy and the diagnosis was confirmed by Gomori methenamine silver staining. All these patients had various degrees of body weight loss. 34 patients had fever (range 37.2~39.5 °C); 31 had dry cough; 3 had cough with sputum. 31 patients had short breath and progressive dyspnea. With auscultation, 29 cases had coarse breath sounds, 5 had interspersed fine moist crackles, and 1 had dry crackles in both upper lungs.

CD₄⁺ T lymphocyte count and HIV virus load RNA Quantification

The percentage of CD₄⁺ T lymphocytes in the peripheral blood was tested using Coulter Epics XL flow cytometry (FLM, Beckman Coulter Co. USA.) and triad-color fluorescence labeled monoclonal antibody kit (Immunotech Co. France). All the CD₄⁺ T lymphocytes tests were

carried out before or within one month after initial clinical diagnosis. HIV virus load was quantified in plasma by RT-PCR according to the manufacturer's instruction (Amplicor HIV-1 Monitor test, Roche Diagnostic Systems, Madrid, Spain).

Chest CT examination and observation

All the patients underwent chest CT. The interval between the CD₄⁺ T lymphocyte count and HIV virus load RNA quantification and CT examination was within 48 hours. Scan coverage was from the pulmonary apices to the diaphragm. Scan parameters included 120 kV, 200 mA, 10 mm collimation and 1.2 pitch. Lung parenchyma, as well as hilum and pleural space were inspected by two experienced radiologists, and consensus was reached in all cases.

Statistics analysis

All the data was analysed by the SPSS 11.13 statistics package. The logarithmic value of HIV virus load, mean and standard deviation (SD) of the CD₄⁺ T lymphocyte count were evaluated. A P value less than 0.05 was considered statistically significant.

Results

Chest CT manifestations of PCP in AIDS patients

The imaging findings in our series of 50 cases included: (I) Ground-glass opacities dominated (*Figure 1*, 28/50, 56%), these patients often had extensive distribution in bilateral lungs (27 cases), with a predilection for the central and peihilar regions of the lungs. Aerial bronchogram was seen in some cases. In one case ground-glass opacities was limited to left lower lung. 13 cases had well defined crescent-shaped clear areas in subpleural region. (II) Lung cysts dominated (*Figure 2*, 10/50, 20%), lung cysts varied in appearance, with size ranging from 1.2 to 26 mm. Cysts tended to have thin wall, with inner and outer walls sharply defined. Around the lung cysts existed various extents of ground-glass opacities and patchy infiltrations. All these 10 cases had multiple lobes distribution, with 7 cases involved the upper lung lobes, and the remaining 3 cases involved all lobes of the lungs. (III) Consolidation dominated (*Figure 3*, 6/50, 12%), patchy consolidation presented with opacification of the parenchyma with obscuration of the underlying vessels. Aerial bronchogram was seen within



Figure 1 Chest CT of ground-glass opacities dominated PCP in an AIDS patient. There is extensive distribution of ground-glass opacities in upper lobe of both lungs



Figure 2 Chest CT of lung cysts dominated PCP in an AIDS patient. Numerous thin walled lung cysts in upper lobe of both lungs. The cysts have various shapes and sizes. In some cysts there are interior separations (arrow). Infiltration lesions are seen around some of the cysts



Figure 3 Chest CT of a consolidation dominated PCP in an AIDS patient. Patchy shadows are shown in the upper lobe of right lung

consolidation. These consolidations occurred at pulmonary segments and subsegment level, with inhomogeneous density, and in bilateral lungs (5/50, 10%). In one case one solitary patchy shadow was observed on the upper lobe of right lung (1/50, 2%). (IV) Interstitial lesions dominated (3/50, 6%), lesions presented with coarsened pulmonary markings, reticular opacities and linear opacities in both lung fields, and thickened septal and subpleural lines. These lesions mostly had lower lobe distribution. There was one case had honeycombing pattern change and another case had diffuse interstitial fibrosis. (V) Mixed lesions pattern (Figure 4, 3/50, 6%), lesions presented with four types of above mentioned imaging findings. Overall, ground-glass opacities (28/50, 56%) and lung cysts (10/50, 20%) were

the main image manifestations of PCP in AIDS patients.

Other imaging signs included mediastinal and hilar lymph node enlargement (17/50), which located predominantly in aortic-pulmonary window and behind the superior vena cava and upper carina, and minimal pleural effusion (bilateral in 4/50 and right sided in 2/50).

The correlation between chest CT features, CD₄⁺ lymphocyte count, and Plasma HIV viral load

In the patients CD₄⁺ lymphocyte count ranged from 2 cells/ μ L to 373 cells/ μ L. In 40 cases (80%) CD₄⁺ lymphocyte count was less than 50 cells/ μ L; in 4 cases (8%) CD₄⁺ lymphocyte count ranged from 50~100 cells/ μ L; in 3 cases (6%) CD₄⁺ lymphocyte count ranged from 100~200 cells/ μ L; and in 3 cases (6%) CD₄⁺ lymphocytes count was more than 200 cells/ μ L. Plasma HIV viral load ranged from 500~5.28 $\times 10^7$ copies/mL (highest measureable value). Three cases (6%) were less than 10^3 copies/mL; 3 cases (6%) were 10^3 copies/mL; 8 cases (16%) were 10^4 copies/mL; 25 cases (50%) were 10^5 copies/mL; 9 cases (18%) were 10^6 copies/mL; and 2 cases (4%) were 10^7 copies/mL. CD₄⁺ lymphocyte count and plasma HIV virus load of patients with different lung imaging manifestations are shown in Table 1. CD₄⁺ lymphocyte count in ground-glass opacities dominated patients was higher than that of lung cyst dominated patients ($P < 0.05$). Plasma virus load of lung cysts dominated PCP patients was higher than that of consolidation PCP patients ($P < 0.05$).

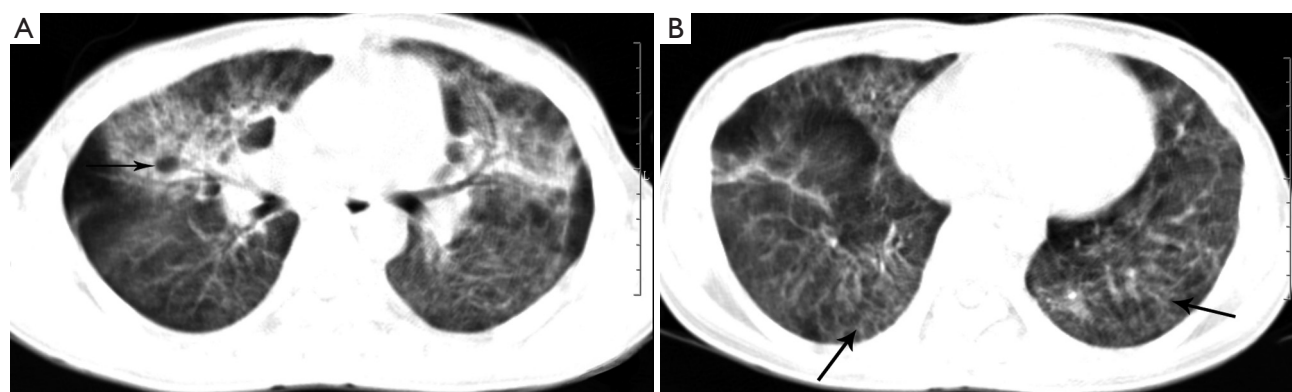


Figure 4 Chest CT of mixed lesion PCP in an AIDS complicated patient. A: Shows a lung cyst (arrow) in the middle zone of right lung with patchy shadows around it. A few irregular patchy shadows are also shown in the middle zone of left lung; B: Shows ground-glass opacities in the lower lobe of both lungs with disturbed lung markings (arrow)

Table 1 CD₄⁺ lymphocytes count and plasma virus load in 50 AIDS patients with PCP

Imaging classification	CD ₄ ⁺ lymphocyte count		Log HIV		Number of patients
	Mean±SD	Median(range)	Mean±SD	Median(range)	
ground-glass opacities dominated	58±85	25(2-373)	5.17±1.06	5.55(2.70-6.52)	28
lung cysts dominated	12±12	6(2-36)	6.01±0.90	5.76(5.04-7.72)	10
Consolidation dominated	76±107	19(3-266)	4.50±1.26	5.17(2.70-5.81)	6
interstitial lesion dominated	15±11	15(4-25)	5.66±0.24	5.91(5.42-5.91)	3
mixed lesions	22±30	5(5-57)	5.54±0.41	5.32(5.28-6.01)	3
total	45±76	15(2-373)	5.31±1.07	5.49(2.70-7.72)	50

Discussion

The CD₄⁺ T lymphocyte count is an explicit biomarker that provides assessment of immune system status of HIV-infected patients, while plasma HIV virus load reflects activity of HIV virus (7). PCP remains the most common and important complication of AIDS. Its occurrence and progress, and treatment response are closely related to the level of CD₄⁺ lymphocyte count. Further investigation on PCP, particularly its imaging feature, and understanding the relation between PCP lung manifestations, CD₄⁺ lymphocyte counts and HIV plasma viral load can be important.

In our series of 50 cases of PCP in AIDS patients, the chest CT manifestations in 28 (56%) were ground-glass opacities, presented with patchy and diffuse distribution in lobes and segments of lungs, and corresponded to early stage of pulmonary alveolus infiltration of *Pneumocystis jirovecii* induced inflammation. Lung cysts of PCP in AIDS

patients were once considered uncommon, however, with the increased detection sensitivity using modern imaging techniques such as helical high resolution CT, incidence rate of lung cyst in PCP was reported to be 10~34% (8,9), therefore now considered a typical manifestation of this infection. Our data showed the incidence rate of lung cyst was 20% (10/50), which agrees with literature data. In our study, lung cysts were of thin wall, inner and outer walls were sharply defined and there was no fluid in the cyst cavity. Cysts could be solitary, multiple or honeycomb appearance. Although an upper lobe predominance was seen, cysts could involve any portion of the lungs. They could also be found in either a subpleural or intraparenchymal location. Rupture of subpleural cysts may cause spontaneous pneumothorax. Identification of ground-glass opacities, lung cysts and spontaneous pneumothorax in AIDS patient are highly suggestive of PCP.

It is known that 90% of AIDS complicated PCP patients have CD₄⁺ lymphocyte count below 200 cells/μL (10,11).

As CD₄⁺ lymphocyte count drops further, disseminated fungus and virus infections can occur. CD₄⁺ lymphocyte counts <100 cells/ μ L is an important sign of disease further progression or deterioration. WHO recommended CD₄⁺ lymphocyte count drop as an indicator of AIDS disease deterioration. In the meantime, plasma virus load is also directly related to decreased immune function and AIDS complications. In our series, 43 cases (43/50, 86%) had CD₄⁺ lymphocyte count <100 / μ L and were determined to be at advanced stage of AIDS disease. CD₄⁺ lymphocyte cells count in ground-glass opacities pattern was higher than that of lung cysts pattern, with the difference reached statistical significance ($P < 0.05$). The level of CD₄⁺ lymphocyte count was relatively higher in ground-glass opacities dominated PCP patients, which suggested that they were in the relative early stage of the disease. Together with experimental biomarkers and clinical status, with ground-glass opacities dominated PCP patients, effective treatment may be installed. While CD₄⁺ lymphocyte count in lung cysts dominated PCP patients and mixed lung patients were generally lower, suggesting severe compromised immune function of these patients, and these patients might have a longer disease course and poorer prognosis. Plasma virus load of lung cysts dominated PCP patients was generally higher, and that of consolidation PCP patients were relatively lower. Plasma virus load in lung cysts dominated patients and consolidation dominated patients groups had significant difference ($P < 0.05$). CD₄⁺ lymphocytes can be influenced by many factors including infection, complicated hepatic cirrhosis, and other diseases that may affect autoimmune system of the body. Therefore CD₄⁺ T lymphocyte count is more likely to fluctuate, and some authors suggested that HIV virus load may be more accurate in reflecting clinical condition (12,13).

In conclusion, this current study suggested that ground-glass opacities and lung cysts are the main chest CT features of PCP in AIDS patients. CD₄⁺ lymphocyte count in ground-glass opacities dominated patients is higher than that of lung cyst dominated patients. Plasma virus load of lung cysts dominated PCP patients is higher than that of consolidation PCP patients.

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