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Correlation between imaging features of Pneumocystis jiroveci pneumonitis (PCP), CD4+ T lymphocyte counts, and plasma HIV viral load: a study in 50 consecutive

来源：本站原创 时间：2010年08月14日 关注： 【字体：大 中 小】

Correlation between imaging features of *Pneumocystis jiroveci* pneumonitis (PCP), CD_4^+ T lymphocyte counts, and plasma HIV viral load: a study in 50 consecutive AIDS patients

LU Pu-xuan,DENG Ying-ying,LIU Shui-teng,LIU Yan,LIU Ying-xia,WANG Yi-xiang,ZHU Wen-ke,LE Xiao-hua,YU Wei-ye and ZHOU Bo-ping

Department of radiology,Shenzhen Third People's Hospital, Guangdong Medical College,Shenzhen 518020, China(Lu PX,Deng YY,Liu ST,Liu Y,Liu YX,Wang YX,Zhu WK,Le XH,Yu WY and Zhou BP)

Correspondence to:Dr. LU Pu-xuan, Department of radiology, Shenzhen Third People's Hospital, Guangdong Medical College, Shenzhen 518020, China (Tel: 0755-25509800-8113.Email:lupuxuan@126.com)

This study was supported by a grant from Science and Technology Funding projects of Shenzhen Health Bureau (NO.200607)

Abstract

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Purpose: To investigate imaging manifestations of AIDS with *Pneumocystis jiroveci* pneumonitis(PCP), the correlation between among imaging features, CD_4+ lymphocyte count, and plasma HIV viral load.

Material and Methods: A total of 50 patients AIDS with PCP were review retrospectively. Chest CT manifestations, CD_4+ lymphocyte count, and plasma HIV viral load were analyzed to investigate their correlation. Results: 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 type (3/50,6%), and mixed lesions in 3 cases (3/50,6%). CD_4 + lymphocyte counts ranged from 2～373 cells/μl. Plasma HIV viral load ranged from 500～5.28×10^7 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 PCP patients ($p<0.05$). Conclusion: The typical chest imaging features of AIDS with PCP were lung ground-glass opacities and lung cysts. The chest imaging features were correlated with CD_4^+ T lymphocyte count and plasma HIV viral load.

Keywords: Acquired Immunodeficiency Syndrome(AIDS); Pneumocystis Jiroveci; Pneumonitis; Tomography, x-ray computed;CD_4 + lymphocyte counts; Viral load

【摘要】 目的：探讨艾滋病合并肺孢子菌肺炎(PCP)的影像学表现特征以及影像表现与病毒载量、CD_4^+T 淋巴细胞计数的相关性。 **方法：**回顾性分析50例艾滋病合并肺孢子菌肺炎的胸部CT影像学表现，并检测患者HIV病毒载量和CD_4^+T淋巴细胞计数的变化。 **结果：**50例艾滋病合并 PCP患者中，表现磨玻璃密度影28例（28/50,56%），肺气囊10例（10/50, 20%），实变表现6例(6/50,12%), 间质性损伤3例(3/50,6%), 混合性损伤3例(3/50,6%)。检测50份标本，CD_4^+T淋巴细胞计数为2～373个/μl，血浆病毒载量界于<10^2至5.28×10^7拷贝数/mL之间。磨玻璃组CD_4^+T细胞数高于肺气囊组CD_4^+T细胞数，差异有统计学意义（p值<0.05）；肺气囊组病毒载量高于实变组病毒载量，差异有统计学意义（p值<0.05）。**结论：**AIDS合并PCP的特征性影像学表现是肺部磨玻璃密度影及肺气囊，该影像表现与HIV病毒载量及CD_4^+T淋巴细胞水平有良好的相关性。

Correlation between imaging features of *pneumocystis jiroveci* pneumonitis (PCP), CD_4^+ T lymphocyte count, and plasma HIV viral load: a study in 50 consecutive AIDS patients

LU Pu-xuan,DENG Ying-ying,LIU Shui-teng,LIU Yan,WANG Yi-xiang,ZHU Wen-ke,LE Xiao-hua,YU Wei-ye,ZHOU Bo-ping

Acquired immunodeficiency syndrome (AIDS) patients have low immune function, with CD4+ lymphocyte counts progressively decreased as disease progress. When the CD4+ counts falls below 200 cells/μl, AIDS patients gradually presented with clinical symptoms (1,2). Plasma HIV virus load and CD4+ lymphocyte counts are important biomarkers for assessing clinical course of HIV-infected patients, predicting clinical progress and evaluating therapy of anti-HIV drugs (3). CD4+ lymphocyte counts provide 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 infection that threaten lives in AIDS patients (4). Vigilance for PCP, early diagnosis and early treatment are crucial to reduce the resulting mortality. In this study, CT lung manifestations of 50 AIDS patients complicated with PCP were retrospectively analyzed. The chest imaging manifestation and the correlation between imaging features, CD4+ lymphocyte counts, and plasma virus load was investigated.

Materials and Methods

Study population

Between March 2007 and July 2009, 50 consecutive AIDS patients complicated with PCP, who were all treated at our 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. Among these patients 3 cases had lung biopsy and the diagnosis were confirmed by Gomori methenamine silver staining. Risk behaviors for HIV infection of these patients were as follow: sex contact 35, intravenous drug abuse 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 diagnosis of PCP was made according to the following: 1). sputum, bronchoscopic biopsy or bronchoalveolar lavage tested Pneumocystis jirovecii positive; 2). consistent with diagnosis standards of AIDS or other severe immunosuppression; 3). CD4+ ≤200/μl; 4). dry cough, dyspnea ,fever, chest pain or body weight loss, but without obvious chest sign; 5). typical chest X ray characteristics; 6). responsive to anti-PCP therapy; 7). 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. All these patients had various degrees of body weight loss. 34 patients had fever (range 37.2 ^{0}C～39.5^{0}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.

Chest CT examination and observation

All the patients underwent chest CT Scan coverage was from the pulmonary apices to the diaphragm. Scan parameters included 120 kV, 200 mA, 10mm 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.

CD4+ T lymphocyte count and HIV virus load RNA Quantification

The percentage of CD_4^+ 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 CD_4^+ 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)

Statistics Analysis

All the data was analyzed by the SPSS 11.13 statistics package. The logarithmic value of HIV virus load, mean and standard deviation (SD) of the CD_4^+ T lymphocyte count were evaluated. 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: (1) 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 perihilar regions of the lungs.Bronchovascular bundles were 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. (2) lung cysts dominated (figure 2, 10/50,20%), lung cysts varied in appearance, the size ranged from1.2mm to 26 mm. Cysts tended to have thin wall, inner and outer walls were sharply defined. Around the lung cysts existed various extents of ground-glass opacities and patchy infiltrations. All these 10 cases had multiple lobes distribution, 7 cases involved the upper lung lobes, 3 cases involved all lobes of the lungs. (3) 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 consolidation. These consolidations occurred at pulmonary segments and subsegments 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%). (4) Interstitial lesions dominated (3/50,6%), 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 changes and another case had diffuse interstitial fibrosis. (5) mixed lesions pattern (figure 4, 3/50,6%), presented with four kinds 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 side in 2/50).

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

CD4+ lymphocyte counts ranged from 2 cells/μl to 373 cells/μl. In 40 cases(80%) CD4+ lymphocyte counts were less than 50 cells/μl, in 4 cases (8%) CD4+ lymphocyte counts ranged from 50～100

cells/μl, in 3 cases (6%) CD4+ lymphocyte counts ranged from 100～200 cells/μl, in 3 cases(6%) CD4+ lymphocytes count were more than 200 cells/μl. Plasma HIV viral load ranged from 500～5.28×10^7 copies/ml(highest measurable value), 3 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 10^6copies/ml, 2 cases (4%) were 10^7 copies/ml. CD4+ lymphocyte counts and plasma HIV virus load of patients with different lung imaging manifestations are shown in table 1. CD4+ lymphocyte counts in ground-glass opacities dominated patients was higher than that of lung cysts dominated patients ($p<0.05$). Plasma virus load of lung cysts dominated PCP patients was higher than that of consolidation PCP patients ($p<0.05$).

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 counts. Further investigation on PCP, particularly its imaging feature, and understand the relation between PCP lung manifestations, CD4+ lymphocyte counts and HIV plasma viral load can be important. This relationship will be valuable in the early diagnosis, differential diagnosis and therapeutic response evaluation of PCP.

In our series of 50 cases of AIDS complicated with PCP, the chest CT manifestations in 28 patients (56%) were ground-glass opacities, presented with patchy and diffuse distribution in lobes and segments of lungs, which corresponded to early stage of pulmonary alveolus infiltration of Pneumocystis jiroveci 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 an intraparenchymal location. Rupture of subpleural cysts may cause spontaneous pneumothorax. Our data suggest that 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 counts below 200 cells/μl (10, 11). As CD4 + lymphocyte counts drop further, disseminated fungus and virus infections can occur. CD4 + lymphocyte counts<100 cells/μl is an important sign of disease further progression or deterioration. WHO recommended CD4+ lymphocyte counts as an indicator of AIDS disease

deterioration. In the meantime, plasma virus load is also directly related to decreased immune function and progress of AIDS complications. In our series, 43 cases (43/50, 86%) had CD4+ lymphocyte counts<100 /μl and were determined to be at advanced stage of AIDS diseases. The relation between imaging findings of PCP and CD4+ lymphocyte counts and plasma virus load had the following characteristics: (1) CD4+ lymphocyte cells count in ground-glass opacities pattern was higher than that of lung cysts pattern, with difference reached statistical significance (P<0.05). The level of CD4+ lymphocyte counts was relatively higher in ground-glass opacities dominated PCP patients, which suggested that it was 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 counts in lung cysts dominated PCP patients and mixed lung patients were generally lower, suggesting severe compromise the immune function of these patients, these patients might have a longer disease course and poorer prognosis. (2) 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 lymphocytes is more likely to fluctuate, and some authors suggested that HIV virus load may more accurately reflect clinical condition (12, 13).

In conclusion, this current study suggested that ground-glass opacities and lung cysts are chest CT characteristic features of PCP in AIDS patients, and may suggest PCP diagnosis. There was correlation between the imaging features of PCP in AIDS and CD4+ T lymphocyte counts, plasma virus load. The knowledge of the relation between PCP imaging manifestations, CD4+ lymphocyte counts and plasma virus load will be valuable for the prevention, early diagnosis, and effective treatment and control of PCP in AIDS patients.

References:

Table 1. CD4+ lymphocyte counts and plasma virus load in 50 AIDS patients with PCP

Imaging classification	CD4+ 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

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

Figure 2. Chest CT of a lung cysts dominated AIDS complicated PCP 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 AIDS complicated PCP patient. One patchy shadow is shown in the upper lobe of right lung (arrow). This consolidation has inhomogeneous density and ill defined edge.

Figure 4. Chest CT of a mixed lesion AIDS complicated PCP patient. Fig 4A 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. Fig 4B shows ground-glass opacities in the lower lobe of both lungs with disturbed lung markings (arrow).

上一篇：Analysis on the imaging features of AIDS with pulmonary fungal infection
下一篇：CT image demonstrations of HIV-seropositive tuberculosis and their relationship with CD4+ T-lymphocyte count

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