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Preliminary Study of Fourteen AIDS-Associated Lung Complications from Imaging, Pathology and Microbiology

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Abstract

HIV-related pulmonary complication is a serious problem in the worldwide. In order to understand features of AIDS-associated pulmonary complications in clinical. Imaging features, microbe characterization and pathology of 14 AIDS-associated pulmonary disease patients derived from Nanyang Medical College hospitals were measured by corresponding techniques. 14 patients infected by different virus, fungus and bacteria showed special features of image and pathology, respectively. Regarding of various clinical characterizations derived from AIDS-associated pulmonary complications, combination different strategy is contributing to elucidate characterizations of AIDS-associated pulmonary complications.

Keywords: AIDS; AIDS-associated pulmonary complications; Imaging; Pathology; Microbiology

Introduction

Respiratory diseases are the most common manifestation of human immunodeficiency virus/acquired immune-deficiency syndrome (HIV/AIDS). Among AIDS patients, accounting for more than 50% of HIV-associated mortality in children is associated with respiratory diseases [1-4]. Diagnosis and treatment of major HIV-related pulmonary complications is affecting health of infants, children and adult in resource-poor countries, especially those in sub-Saharan Africa, the most heavily afflicted region of the world. Introduction of combination antiretroviral treatment (cART) has been followed by a dramatic decrease in the morbidity and mortality associated with HIV-related pulmonary complications [1]. Notably, at the same time, the incidence of various non-HIV-related pulmonary complications seems to have risen with infection of pathogens. Increased life expectancy and the reduction of competing causes of death are both driving the increased incidence of non-HIV-related pulmonary complications in the HIV-infected population. On another hand, the greater prevalence of co-infection with lung microorganism and different environmental factors such as tobacco and alcohol use that is also affect the AIDS patients [3]. Therefore, HIV-related pulmonary complication is a serious problem in the worldwide.

It has demonstrated that occurrence of HIV-related pulmonary complications is close related with infection of numbers of pathogenic microorganism, such as parasites, fungus, viruses and mycobacteria [5-8]. Characterizations of HIV-related pulmonary complications become more and more diverse in the clinical. Therefore, elucidation of characterizations of them play an important role in diagnose and treatment. In order to further understand clinical characterizations of HIV-related pulmonary complications, in the current study, 14 cases of HIV-related pulmonary complications were analyzed from imaging, pathology and microbiology.

Materials and Methods

Patient selection

The study was approved by Ethical Review Committee of Pingdingshan Medical University. Available participants were approached and informed of the study objectives, procedure and confidentiality issues by study coordinator. Patients who decided to participate in this study and provided written informed consent were asked to complete a survey to assess presence of HIV/AIDS-related symptoms.

Methods

Quantity of $CD^{4+}T$ cell was measured using flow cytometry instrument (BD, USA) according to kit instructions. Histological analysis was performed by different staining. Morphological determination of pathogens was fulfilled by microbe culture. Results of X-ray and computed tomography (CT) were used in imaging analysis, respectively.

Results

HIV-associated pulmonary complication of tuberculosis infection

Case 1: A male, 48-year-old, was definitely diagnosed as AID by CDC, and showed ache of chest, dyspnea, fever, night sweats and fatigue. Quantity of $CD^{4+}T$ cell was 45/μl. A half-moon-shaped mass bulged to the right lung hilum, enlarged and fuzzed stripes around mass, thickened chest pleural were observed by X-ray digital radiography (Figure 1a). Narrowed right chest, thickened lateral thoracic pleural with fluid, heterogeneous density mass located in right lung hilum, narrowed left bronchial vessels caused by pressure were detected by CT (Figure 1b). Patient was belongs to one of HIV-associated pulmonary lymph nodes of tuberculosis infection patients.

Case 2: A female, 39-years-old was definitely diagnosed as AID by CDC, and showed fever, night sweats and fatigue. Quantity of $CD^{4+}T$ cell was 73/μl. Diffused shadow characterized by millet grain shape, uniformed size and bilateral symmetry of left and right lung was fund by

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X-ray (Figure 1c). CT scan showed diffused shadows with millet grains shape were distributed both lungs and exhibited uniform of size and distribution, symmetry of left and right lung (Figure 1d). AIDS patient was belongs to one of HIV-associated pulmonary miliary tuberculosis patients.

Case 3: A male, 36-years-old showed fever and fatigue and was definitely diagnosed as AID by CDC. Quantity of $CD^{4+}T$ cell was 168/μl. Left lung was irregularly presented with granulation tissue and caseous necrosis that was fund by pathological analysis (Figure 1e). Substantial shadows of the left lung and gland bubble shaped nodules around shadows were observed by CT (Figure 1f). AIDS patient was belongs to one of HIV-associated pulmonary infiltrating tuberculosis patients.

Case 4: A female, 34-year-old, was definitely diagnosed as AID by CDC and showed fever and chest pain. Quantity of $CD^{4+}T$ cell was 261/μl. Anti-acid bacilli were observed by pleural fluid culture. Enhanced high-density shadows with spindle shape and wall of right chest were fund by X-ray (Figure 2a). Encapsulated liquid density shadow of pleura was detected by CT (Figures 2b and 2c). AIDS patient was belongs to one of HIV-associated pulmonary tuberculous pleurisy patients.

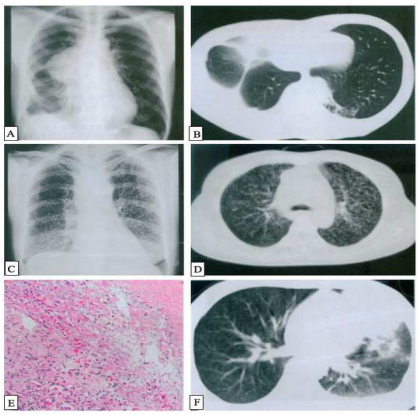

Figure 1: HIV-associated pulmonary lymph node tuberculosis, miliary tuberculosis and infiltrative tuberculosis. A is result of X-ray of HIV-associated pulmonary lymph node tuberculosis. B is result of CT of HIV-associated pulmonary lymph node tuberculosis. C is result of X-ray of HIV-associated pulmonary miliary tuberculosis. D is result of CT of HIV-associated pulmonary miliary tuberculosis; E is histological result of HIV-associated pulmonary infiltrating tuberculosis. F is result of CT of HIV-associated pulmonary infiltrating tuberculosis.

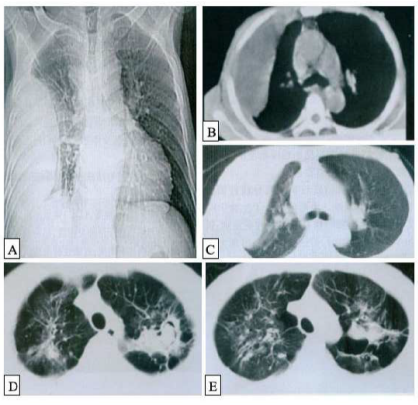

Figure 2: HIV-associated pulmonary tuberculous pleurisy and chronic fibrous cavitary tuberculosis. A is result of X-ray of HIV-associated pulmonary tuberculous pleurisy. B and C are results of CT of HIV-associated pulmonary tuberculous pleurisy; D and E are results of CT of HIV-associated pulmonary chronic fibrous cavitary tuberculosis.

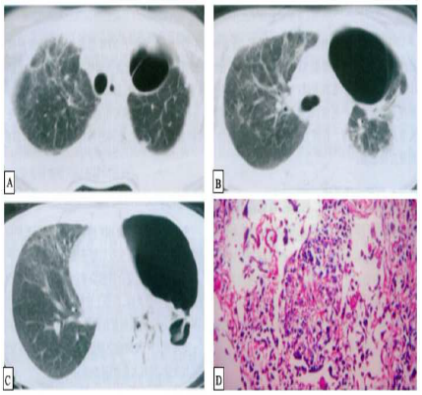

Figure 3: HIV-associated pulmonary non-tuberculosis infection tuberculous. A, B and C are results of CT of HIV-associated pulmonary non-tuberculosis infection tuberculous. D is histological result of HIV-associated pulmonary histological result.

Case 5: A male, 43-year-old, was definitely diagnosed as AID by CDC, and showed ever and cough. Quantity of $CD^{4+}T$ cell was 257/μl. Anti-acid bacilli showed a positive dye by sputum culture. Flaky high-density shadow in upper regions of right and left lung, strip shape shadow caused by stretching of pleura around lung, empty holes located in shadows, satellites shaped lesions and nodules around shadow were observed by CT (Figures 2d and 2e). AIDS patient was belonging to one of HIV-associated pulmonary chronic fibrous cavitary tuberculosis patients.

HIV-associated pulmonary complication of no-tuberculosis infection

Case 6: A female, 26-year-old, was definitely diagnosed as AID by CDC and showed fever at 39°C. Quantity of $CD^{4+}T$ cell was 54/μl. Multiple cavities of left lung, numbers of round nodules and extensive branch linear shadows of both lungs were detected by CT (Figures 3a-3c). Mycobacterium avium-intracellulare complex infection and atypical nodular change were fund by histological analysis (Figure 3d). AIDS patient was belonging to one of HIV-associated pulmonary non-tuberculosis infected patients.

HIV-associated pulmonary complication of *Rhodococcus equi* infection

Case 6: A male, 39-year-old, was definitely diagnosed as AID by CDC and showed suppression of chest and recurrent cough. Quantity of $CD^{4+}T$ cell was 45/μl. Patchy high-dense shadow and ventilated shadow were observed in lower segment of left lung by CT (Figure 4a). A large of bleeding areas, widely appearance of erythrocytes with intact cell wall and numbers of basophilic particles of leukocyte were fund by histological analysis (Figures 4b and 4c). A number of orange colonies were detected by sputum fluid culture (Figure 4d). AIDS patient was belonging to HIV-associated pulmonary complication of *R. equi* infected patients.

HIV-associated pulmonary complication of aspergillus infection

Case 7: A male, 35-year-old, was definitely diagnosed as AID by CDC and showed high fever at a temperature of 40°C and lips cyanosis. Quantity of $CD^{4+}T$ cell was 45/μl. Scattered shadows with

different appearances including ground glass, patchy, flaky-blur and stripe, clear edge, heterogeneous density were observed in right and left lungs by CT. In addition, different sizes of nodules, more lesions occurred in upper lobe of both lungs and middle lobe of right lung, substantial shadows sited in tips of upper lobe of right lung, enlarged lymph nodules located right hilum were also fund (Figure 5a). Dark green colonies were observed in medium by sputum culture (Figure 5b). Short columnar shaped conidiophores with smooth wall, balloon-shaped top vesicle, small terrier single layer of small-conidiophores was found under microscope (Figures 5c and 5d). AIDS patient was belonging to HIV-associated pulmonary aspergillus infected patients.

HIV-associated pulmonary complication of cryptococcal infection

Case 8: A female, 54-year-old, was definitely diagnosed as AID by CDC and showed high fever at a temperature of 39°C. Quantity of $CD^{4+}T$ cell was 153/μl. Blur shadows of fore-breast, nodular density shadow in the back of lower region of right lung with smooth sharp edges were measured by X-rays (Figure 6a). Nodules and circular holes were fund in right and left lungs by CT (Figure 6b). HE staining showed double coating cryptococcus cells were detected (Figures 6c and 6d). AIDS patient was belonging to HIV-associated pulmonary cryptococcal infected patients.

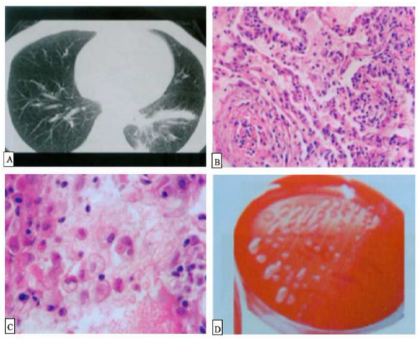

Figure 4: HIV-associated pulmonary complication of *Rhodococcus equi* infection. A is result of CT of HIV-associated pulmonary complication of *Rhodococcus equi* infection. B and C are results of HE staining of HIV-associated pulmonary complication of *Rhodococcus equi* infection. D is result of microbial culture.

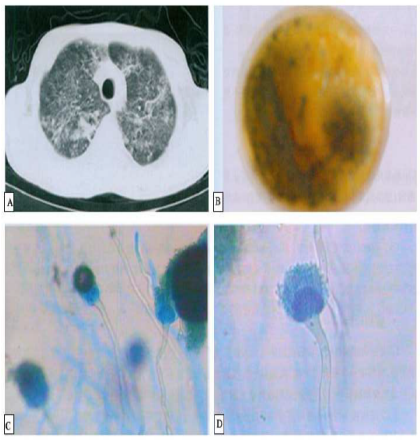

Figure 5: HIV-associated pulmonary aspergillus infection. A is result of CT of HIV-associated 497 pulmonary aspergillus infection. B, C and D are results of microbial culture.

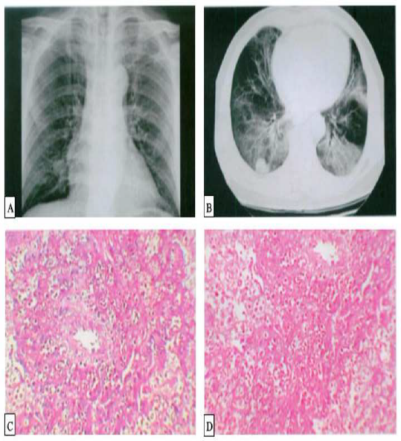

Figure 6: HIV-associated pulmonary cryptococcal infection. A is result of X-ray of HIV-associated pulmonary cryptococcal infection. B is result of CT of HIV-associated pulmonary cryptococcal infection. C and D are results of HE staining.

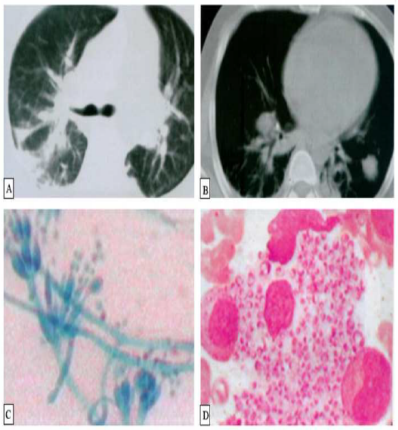

Figure 7: HIV-associated pulmonary *Penicilliosis marneffei* infection. A and B are results of CT of HIV-associated pulmonary *Penicilliosis marneffei* infection. C is result of microbial culture; D is result of bone marrow smear.

HIV-associated pulmonary complication of *Penicilliosis marneffei* infection

Case 10: A male, 35-year-old, was definitely diagnosed as AID by CDC and showed cough, dizziness and fatigue. Quantity of $CD^{4+}T$ cell was 40/μl. Large patch density shadow of right and left lung with irregular shape, enlarged left hilum and increased diameter of vessels with cords were fund by CT (Figures 7a and 7b). Mycelium composed by beaded small spores with typical broom-shape was fund in microbial culture (Figure 7c). Macrophages with round and oval shapes, and myceliums of *P. marneffei* with a curve of end located around of macrophages were detected in bone marrow smear (Figure 7d). AIDS patient was belongs to HIV-associated *P. marneffei* pulmonary infected patients.

HIV-associated pulmonary complication of cytomegalovirus infection

Case 11: A male, 6-month-old, and was definitely diagnosed as AID by and are infected HVIS by mother to child vertical transmit. Texture with disorders of lungs and blur shadow with nodular shape were fund by X-ray (Figure 8a). Diffused shadows with small nodules

were detected in textures of right and left lungs (Figures 8b and 8c). Inclusion bodies of cytomegalovirus were fund by HE staining (Figure 8d). AIDS patient was belonging to HIV-associated pulmonary cytomegalovirus infected patients.

HIV-associated pulmonary complication of herpes virus infection

Case 12: A male, 28-year-old, was diagnosed as HIV-1 antibody positive by CDC. $CD^{4+}T$ cell count was 35/μl. An enhanced signal of stripe with disorder distribution, blur shadows with node shape and cloudy shadows were observed in right and left lungs by X-rays (Figure 9a). Eosinophilic inclusion bodies were detected by periodic acid Schiff staining (Figure 9b). Results of methenamine silver staining showed that inclusion bodies were belong to herpes virus (Figure 9c). AIDS patient was belonging to HIV-associated pulmonary herpes virus infected patients.

HIV-associated pulmonary kaposi's sarcoma

Case 13: A male, 27-year-old, was diagnosed as AID by CDC and showed cough. Quantity of $CD^{4+}T$ cell was 49/μl. High-density shadows with shapes of cloud, flake and nodules, heterogeneous density, blur edge were fund in both lungs by CT. In addition, fused part lesions and multiple consolidated lesions were detected in right and left lungs (Figures 10a and 10b). A large number of deformed spindle cells with a big nucleus and deep dye were observed by HE staining (Figures 10c and 10d). Immuno-histochemical results showed that complements of C^3/C^4 showed a positive expression (Figures 10e and 10f). Patient belonged to the HIV-associated Kaposi's sarcoma patients.

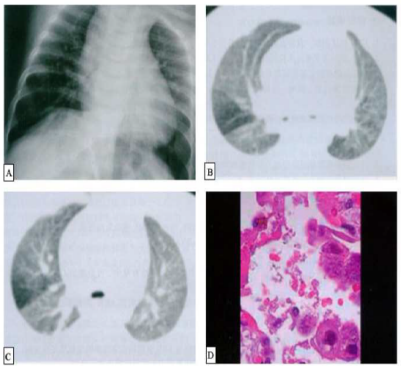

Figure 8: HIV-associated pulmonary cytomegalovirus infection. A is result of X-ray of HIV-associated pulmonary cytomegalovirus infection. B and C are results of CT of HIV-associated pulmonary cytomegalovirus infection. D is result of HE staining.

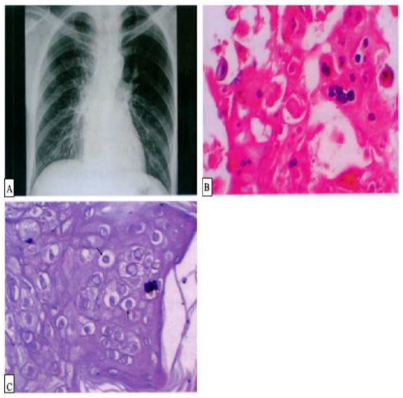

Figure 9: HIV-associated pulmonary herpes virus infection. A is result of X-ray of HIV-associated pulmonary herpes virus infection. B is result of periodic acid-schiff staining. C is result of hexamine silver staining.

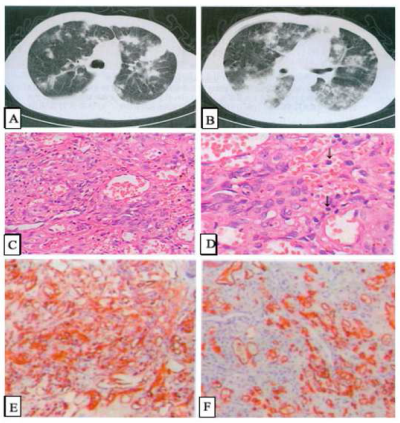

Figure 10: HIV-associated pulmonary Kaposi's sarcoma. A and B are results of CT of HIV-associated pulmonary kaposi's sarcoma C and D are results of HE staining. E and F are results of immunohistochemical analysis.®

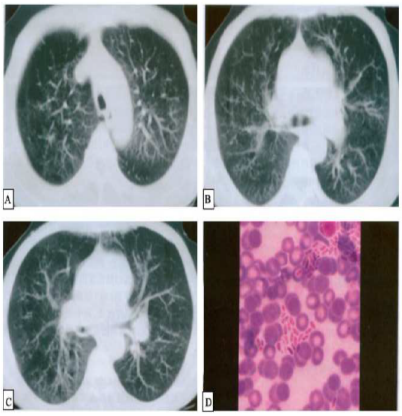

Figure 11: HIV-associated pulmonary toxoplasma infection. A, B and C are results of CT of HIV-associated pulmonary toxoplasma infection. D: is result of HE staining.

HIV-associated pulmonary complication of toxoplasma infection

Case 14: A male, 39-year-old, was diagnosed as AID by CDC and showed cough and fever. Quantity of $CD^{4+}T$ cell was 29/μl. Increased diameter of stripes were stretched to middle and outside regions of right and left lungs that was observed by CT (Figures 11a-11c). Clumps of gathered spores and toxoplasma gondii were detected by biopsy (Figure 11d). AIDS patient was belonging to HIV-associated pulmonary toxoplasma infected patients.

Discussion

AIDS patients can be infected by *M. tuberculosis* at any stage. Clinical symptoms of HIV-associated *M. tuberculosis* infection are consistent with that of non-HIV-infected patients characterized by with fever, chills, night sweats, fatigue, poor appetite and loss of weight [9]. Symptoms of respiratory system are cough, sputum, hemoptysis, chest pain and dyspnea [10]. As to characterizations of imaging, there

is no significant difference between non-HIV infected patients and HIV-associated *M. tuberculosis* infected patients [10]. Noteworthy, a tremendous damage derived from infections of pathogens are rapidly emerged in patients of HIV-associated *M. tuberculosis* infection. Symptoms of cavity, fibrosis, thickened pleura, calcification of lung are fund in advanced with respect of that of non-HIV infected patients [11]. In addition, as to the patients of HIV-associated pulmonary tuberculosis, millet and exudation of lesions are key features of acute case, cavity, fibrosis and calcification are characterizations of chronic ones which are rarely occurred in the clinical [12]. After *M. tuberculosis* infection, different HIV-associated pulmonary complications should also be detected. Therefore, it is great challenge to distinguish features in the clinical in order to give an exact diagnose of them.

As to AIDS patients, except of *M. tuberculosis* and *M. leprosy*, infection of other bacillus can also cause HIV-associated non-tuberculous pulmonary complications in which infections of these pathogens show a lower toxicity compared with that of *M. tuberculosis* and *M. leprosy* [10]. So, imaging features of lung in HIV-associated non-tuberculous infected patients are similar to that of bacterial infection of lung disease that brings about a challenge for diagnosis as well a delay of treatment in the clinical [12]. Compared with that of HIV-associated pulmonary tuberculosis, multiple focuses, cavity, longer course of illness and scarce lesions of lung lower lobe are observed in HIV-associated non-tuberculous pulmonary complications. Generally, anti-tuberculous drugs work as a poor sensitivity to patients of HIV-associated non-tuberculous pulmonary complication [9,13].

In AIDS patients, pulmonary complication of *R. equi* infection often cause an acute onset, high fever, chills, chest pain, dyspnea, cough and purulent sputum [14]. A few of special characterizations are observed HIV-associated *R. equi* pulmonary infection, but different features of imaging observed in different stages are helpful to diagnose. A flaky soft shadow with blurred edge is observed around hilum of one lung at early stage. Ball shaped mass of lung hilum with an aggravating shadow, a high consolidation, a clear edge are fund at middle stage [15]. Cavity, pneumothorax and pleurisy are all observed in the latter stage. It is worth note that great efforts are required to distinguish HIV-associated *R. equi* pulmonary infection from lung neoplasms. Infection of *R. equi* can also cause chronic suppurative bronchopneumonia and extensive lung abscesses [16].

As to AIDS patients, aspergillus is an opportunistic pathogen. In the early stage, its infection can cause exudative and necrotic lesions in bronchial wall and lung tissue after inhaling. Next, suppurative pneumonia and lung abscess in which discharge of pus and necrosis are observed that in turn cause formation of cavity [17]. Patients manifested a serious of symptoms such as chills, fever, asthma, cough, mucus sputum, hemoptysis and chest pain in the clinical. Type of allergy can cause breathing difficulties and asthma [18]. Results of X-ray examination showed infiltration of lung, lesions of cavity, round shadow with clear border which can drift with movement of body position. Infected vessels of lung can cause formation of thrombosis and hemorrhagic infarction. Therefore, ground-glass-like changes, nodules and cavity with inserted nodules are widely fund, but cavity without inserted nodule is seldom observed in clinical [18,19].

Meningitis is generally regard as maker of cryptococcal infection, so cryptococcal infection of lung is often accompanied with meningitis or lonely occurred. Clinical manifestations of patients are fever, cough and shortness of breath [20]. Cryptococcal infection may be appeared in any site of lung. Multiple lesions are mainly occurred in the bottom of bilateral lungs. Increase of stripes, lonely mass and various nodules fused mass are fund in imaging. Ground glass shadow is fund in right and left lungs by CT [21]. A lot of cryptococcal spores and growing mycelium are detected in the lesion tissue. Meanwhile, exudation and granulomatous are mainly characterizations of diseased tissue in which infiltration derived from macrophages, lymphocytes, and multi-nuclear macrophages infiltration are also widely detected, but purulent lesions are rarely fund [22].

Patients of *P. marneffei* infection are manifested by a long time fever, progressive weight loss, cough, expectoration, rash, anemia and enlarged lymph nodes [23]. Multiple nodules with a high density are fund in the lungs by CT view. In addition, various sizes holes sited in lower part of right lung with heterogeneous wall thickness and smooth inner wall are also observed [13,24]. Branched mycelum and clusters of small spores with typical broom-shaped sticks are detected under microscope view. In the AIDS patients, quantity of $CD^{4+}T$ cell is significantly decreased compared with that of normal ones. HIV-associated *P. marneffei* lung infection can result in an obvious destroy of phagocytosis of macrophage. Therefore, infiltration of macrophage is seldom fund, but proliferation is widely observed by Monte et al. [25]. In this condition, it only causes necrosis of inflammation and formation of cavity.

Flu virus and cytomegalovirus are main ones of virus and can cased lung infection. Among of them, cytomegalovirus is common pathogen of pulmonary infection in AIDS patients [26]. Patients of HIV-associated cytomegalovirus infection have no distinctive symptoms, and mainly characterized by fever, aches of joints and muscle, paroxysmal cough, shortness of aerosols and breathing barrier in the clinical [27]. Bacteria, fungus, Jeremiah's pneumocystis and combination of fungus and bacteria can cause secondary infection in the lung that can result in an obstacle for clinical remedy. Cytomegalovirus can spread into every tissues of body that can cause an injury on host cell. In addition, its infection can also produce side impact on immunity [28]. Scenario of ground glass, consolidation of lung, grid-like formation, thickened bronchial wall is fund by CT. Among of them, bronchiectasis, nodule and mass are important manifestations of CT. In addition, ground-glass in the early stage and opacity change in the late mass are key markers [29]. Symptoms of lung are usually diffused interstitial infiltration, alveolar infiltration, ground-glass density shadows accompanying with multiple small nodules which are pathological basis of hemorrhage and necrosis [1].

Patients of HIV-associated herpes virus infection have distinctive features in the clinical, such as a number of skin lesions, bullae of lungs, blood blisters, systemic symptoms, long course of ill, high incidence of pneumonia and encephalitis and other serious complications [30,31]. A high-incidence of herpes infection is observed in the AIDS patients, 26.4% occurred in the stage of HIV infection, 73.6% of them in the AIDS stage [32]. Noteworthy, culture of microbe is a key measure to identify infection of herpes virus.

Like multiple vascular sarcoma and multiple pigmented sarcoma, Kaposi's sarcoma is a malignant tumor and a major complication of HIV infection [33]. Lung is an important target of Kaposi's sarcoma emerged. Inflation of lung lymph node, peripheral nodular infiltration, bilateral interstitial change and thoracic effusion are typical characterizations of X-ray. Capillary dense clumps including hemosiderin cells and tight arranged of endothelial cells are the fund in the early stage that is similar with that of general hemangioma [34]. Active proliferation of endothelial cells and fibroblasts, increase of cell fission and distortion, and scattered lymph cells and tissue cells in blood vessels are detected in the middle stage. Therefore, occlusion and

necrosis of vessel lumen are fund [34,35]. Tumors can be detected in irregular lumen and crack of newborn capillaries filled of blood.

Toxoplasma gondii, a transcellular parasite, its infection may cause toxoplasma pneumonia characterized by cough, sputum, dyspnea and cyanosis [36]. Toxoplasma pneumonia can be grouped into bronchial pneumonia scattered patchy blur shadow in bronchopneumonia, interstitial pneumonia formed reticular and nodular shadows, but pleurisy is rarely observed by imaging. In respect of absence of distinctive features of imaging, combination with etiology and imaging is an important way to define toxoplasma pneumonia. Bleeding and edema of alveolar walls and bronchial walls, small amount of serous fibrin infiltration in macrophages and lymphocytes can be observed in pathology. Toxoplasma cysts can be observed in lung interstitium, macrophages, epithelium of alveolar [37].

Conclusion

In summary, AIDS patient can be infected by various pathogens in respect of unbalance of homeostasis that cause multiple tissue or organ complications including lung, liver, kidney, spleen, brain. Among of HIV-associated pulmonary complications, each of them has complex characterizations of imaging and pathology. Strategy of combination of various diagnostic methods is contributes to further understand and elucidate symptoms of AIDS pulmonary complications.

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