PULMONARY NOCARDIOSIS: RADIOGRAPHIC FINDINGS IN HIV INFECTION AND OTHER COMPROMISED STATUSES.

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ABSTRACT

After the wide spread of HIV infection, in addition to the widely use of corticosteroid and other immunosuppressive therapy in many diseases as well as post organ transplantation, the incidence of pulmonary nocardiosis is significantly rising. Pulmonary manifestations in 11 cases of proved pulmonary nocardiosis and 7 cases of presumptive diagnosis of pulmonary nocardiosis are presented. The most pertinent radiographic abnormality is inhomogenous consolidation with multiple cavitary changes in both groups. Other radiographic abnormalities include pulmonary nodules, masses and reticulonodular infiltration. Pleural effusion and hilar lymphadenopathy are rarely seen. Pulmonary nocardiosis should be in the differential diagnosis if the above radiographic findings are observed in compromised patients and if sputum smear reveals weakly acid fast branching filamentous organisms, the diagnosis even be in highly suggestive. Prompt diagnosis and treatment may yield good clinical result even for these type of patients.

INTRODUCTION

In the past, pulmonary nocardiosis was considered to be an uncommon infection and usually encountered in patients who were on immunosuppressive therapy for their underlying diseases. Its occurence has significantly increasing especially after the beginning of HIV infection epidemic[1,2,3] and involution of organ transplantation.[4-8] Many studies in immunological aspect have pointed out that cell mediated immunity play an important role against nocardial infection.[4, 9-12] This can explain the marked out numbers of nocardial infections in immunocompromised patients. Descriptions of various pulmonary radiographic abnormalities caused by nocardial infection are presented with some speculations of findings to include for the differential diagnosis.

MATERIALS AND METHODS

From January 1991 to August 1993, there were 11 cases of culture proved pulmonary nocardiosis available for the study. Presumptive diagnosis of pulmonary nocardiosis in 7 cases based on the positive acid fast branching filamentous organisms on sputum smear with significant clinical and radiologic response to specific antibiotic for nocardia were also included. All medical records, bacteriologic reports and chest radiographs were retrospectively reviewed. Patients with extrapulmonary nocardiosis without pulmonary involvement were excluded.

RESULTS

The patients ranging in ages from 26 to 52 years, with the mean of 43 years. All patients were immunocompromised. Fourteen cases were men and all had positive HIV antibody. The remaining four cases were women who were in corticosteroid therapy for a long duration to control their underlying diseases, these included systemic lupus erythematosus for two, over – lapped syndrome and polymyositis for one case each.

Definite diagnosis of pulmonary nocardiosis was made in eleven cases, eight with HIV infection and the

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remaining three with systemic lupus erythematosus, overlapped syndrome and polymyositis. All had positive culture, nine from sputum, one from bronchial biopsy and the other from pleural fluid. The remaining seven cases had positive acid fast branching filamentous organisms on sputum smear but negative on sputum culture. All 18 patients were treated with trimethoprim-sulfamethoxazole and significant clinical improvement with much regression of lesions, on the one month interval follow up chest film, were recognized. Eight cases had positive sputum smear and positive sputum culture. There were two cases of positive culture for nocardia from liver abscess, one had positive sputum culture and the other had positive sputum smear.

The most common clinical manifestations were fever and minimal productive cough. The other respiratory symptoms were mild dyspnea and less commonly, pleuritic chest pain. Duration of symptoms ranged from 3 days to 3 months, median duration was 3 weeks. In the HIV infected group, deterioration of general health (fatigue, anorexia and weight loss) was noted in seven cases, chronic intermittent diarrhea in two cases, oral thrush in two cases and skin lesion from Penicillium marneffei infection in one case. Concurrent right upper quadrant pain and tender due to nocardial liver abscesses were also noted in two cases of HIV infected patients.

The initial chest radiographic abnormalities were summarized in table 1.

The spectrum of radiographic abnormalities includes consolidation, nodule or mass with multiple cavitary changes in most of the patients in both groups, 64% and 86% respectively. (Fig. 1,2,3) The reticulonodular infiltration was seen but not as a sole manifestation. Frank abscess formation was presented in one case. (Fig. 4) Hilar lymphadenopathy and pleural effusion are seen in only one and two cases respectively. In case 10, progression of noncavitating nodule to cavitating mass and consolidations on the serial follow up films is noted. (Fig. 5) Later development of cavitations on follow up film was also observed in case 3. If both initial and follow up films were evaluated, the incidence of cavitary change is higher (82% and 86%). The most commonly radiographic pattern was inhomogenous consolidation in both groups (63% and 71%). More than one radiographic features were noted in four and three cases in both groups, respectively. Spontaneous pneumothorax on initial radiograph was observed in one case.

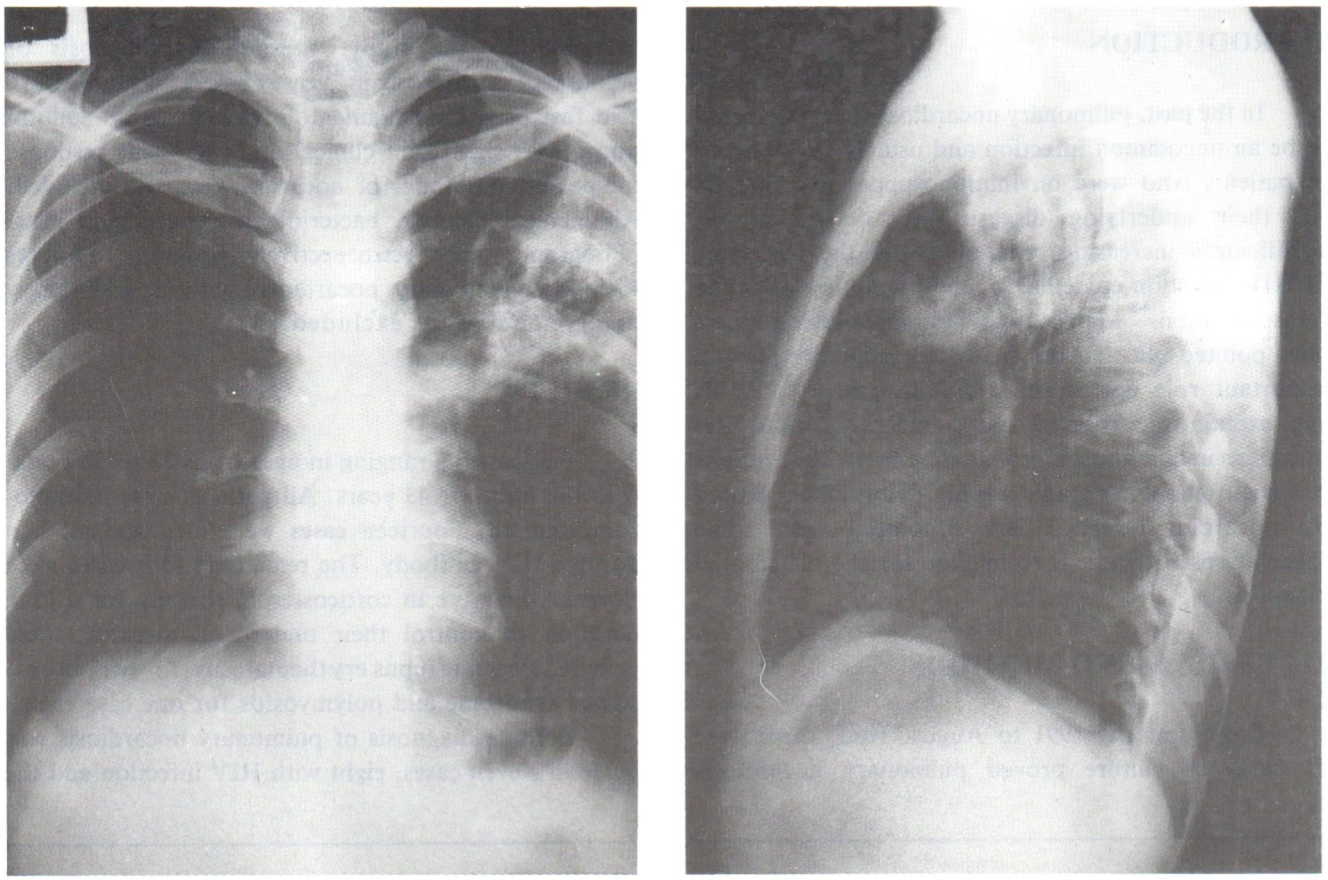

Fig. 1 Single inhomogenous consolidation at the anterior segment of LUL was noted. No lymphadenopathy nor pleural effusion.

DISCUSSION

In general, nocardial infection of the lung is not usually considered in patients presenting with clinical lower respiratory tract infection since its relatively low incidence as compared to pneumonias caused by other causative organisms. Although pulmonary nocardiosis can affected patients without concurrent disease or therapy,[13,16] most cases of pulmonary nocardiosis are encountered in patients who were treated for a long period with corticosteroid or other immunosuppressive drugs for their underlying diseases such as collagen vascular disease (particularly, systemic lupus erythematosus), chronic obstructive pulmonary disease, asthma, bronchiectasis, primary alveolar proteinosis, etc.[8,14,16-20] and antineoplastic agents for various malignant neoplasms.[11,16]

Recently, a significant number of nocardial infections is being diagnosed in a couple of patient groups. First, patients present with specific organ failure from other causes and was undergoing organ transplantation.[4-8] These patients must be on immunosuppressive therapy to prevent organ rejection and in turn increased susceptibility to opportunistic infections. Nocardial infection in cases post renal transplantation,[5,6,14,18] cardiac transplantation,[4] and hepatic transplantation[7] have been reported. The other group is that,the HIV infected patients.[1,2,3] It is known that HIV infection causes a gradual but irreversible depletion in number and functional destruction of T-helper lymphocytes. Postulated mechanisms include direct virus mediated lysis of infected cells and the induction of toxic substances that suppress or destroy T-helper lymphocytes. Progressive loss of T-helper lymphocytic function and number leads to opportunistic infections and certain types of neoplasms (Kaposi' sarcoma and B-cell lymphoma). The organisms that take advantage of T-lymphocytes defect are presented in Table 2, and common causes of pulmonary infection in AIDS patients are presented in Table 3.

Nocardia is a genus of aerobic actinomycetes and considered to be true bacteria rather than fungus.[10,14,16] Nocardia is native to soil.[14,16] The modes of infection are direct inoculation of the pathogen into skin during trauma or by inhalation into lungs.[16] Spectrum of disease is wide and nearly all organs can be affected by this pathogen.[10,19] Lung is the most frequently affected initial site of involvement.[6,12,19,22] N. asteroides is the most common pathogen for the majority of cases of pulmonary nocardiosis.[13,14,16] The clinical manifestation of pulmonary infection are included in fever, cough with or without mucoid or mucopurulent sputum, mild dyspnea and rarely pleuritic chest pain. These can be presented in either acute, subacute or chronic course.[14,15] Sometimes the patients may have no any symptoms at all.[12] Various extrapulmonary clinical manifestations of nocardiosis may also be presented

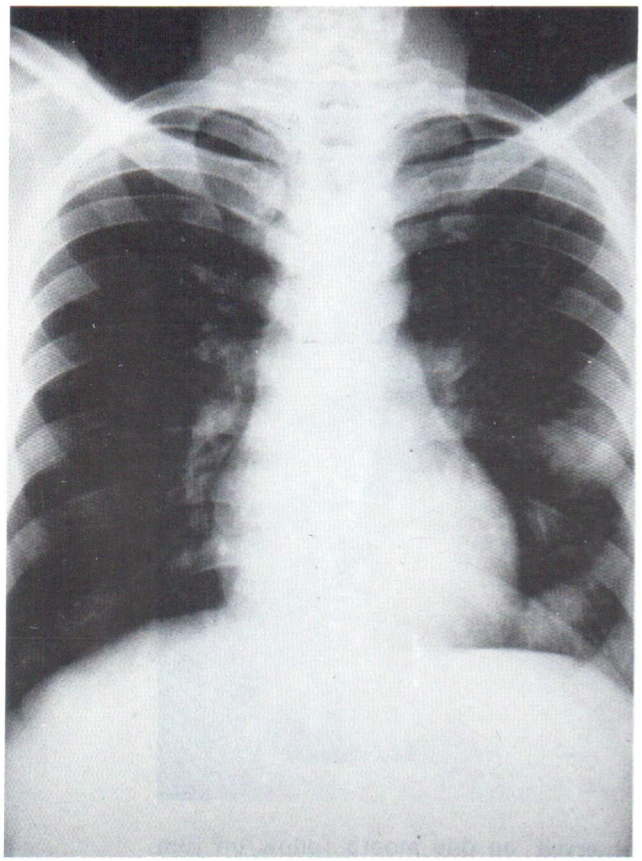

Fig. 2 A few cavitary nodules were noted at hilar region and left lower lung field.

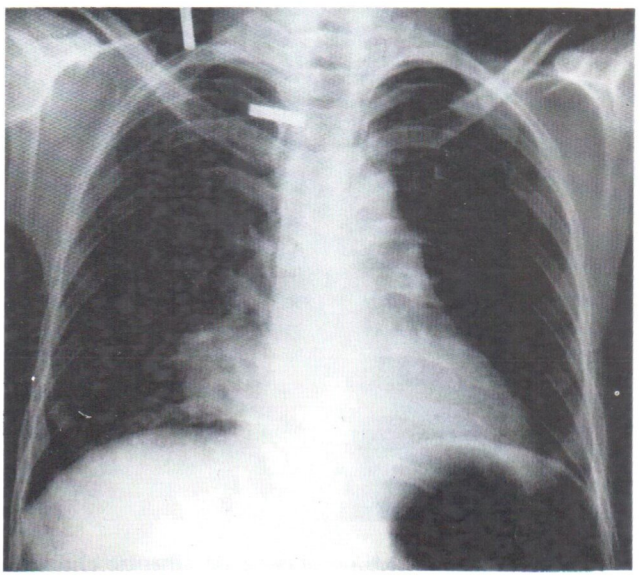

Fig. 3 Single cavitary mass lesion was noted on RML.

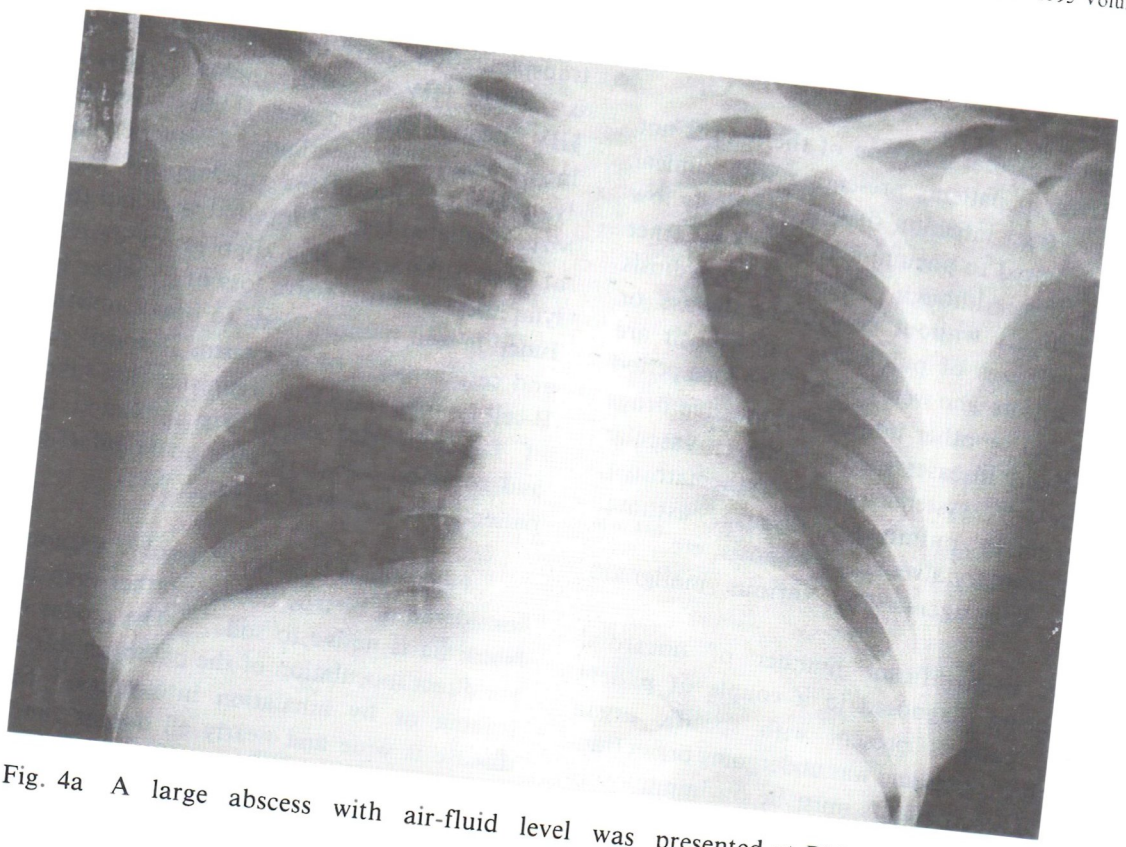

Fig. 4a A large abscess with air-fluid level was presented at RUL.

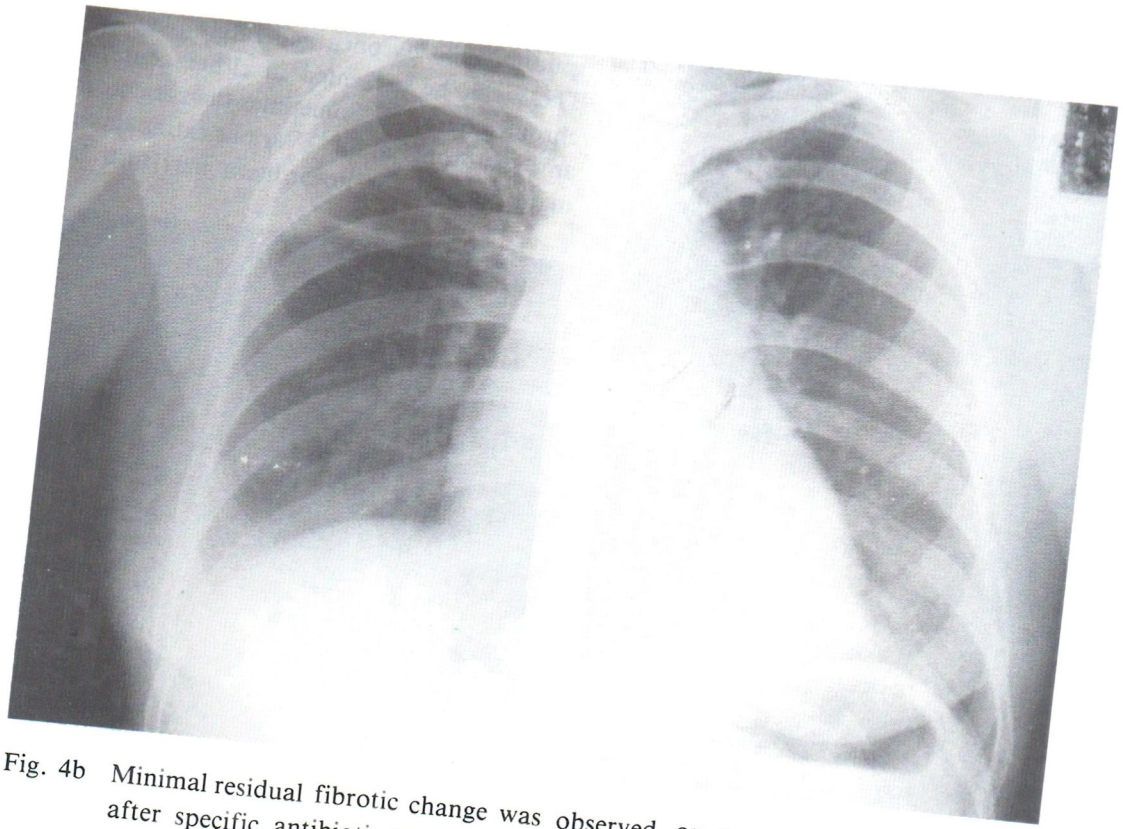

Fig. 4b Minimal residual fibrotic change was observed on one month follow up film after specific antibiotic treatment.

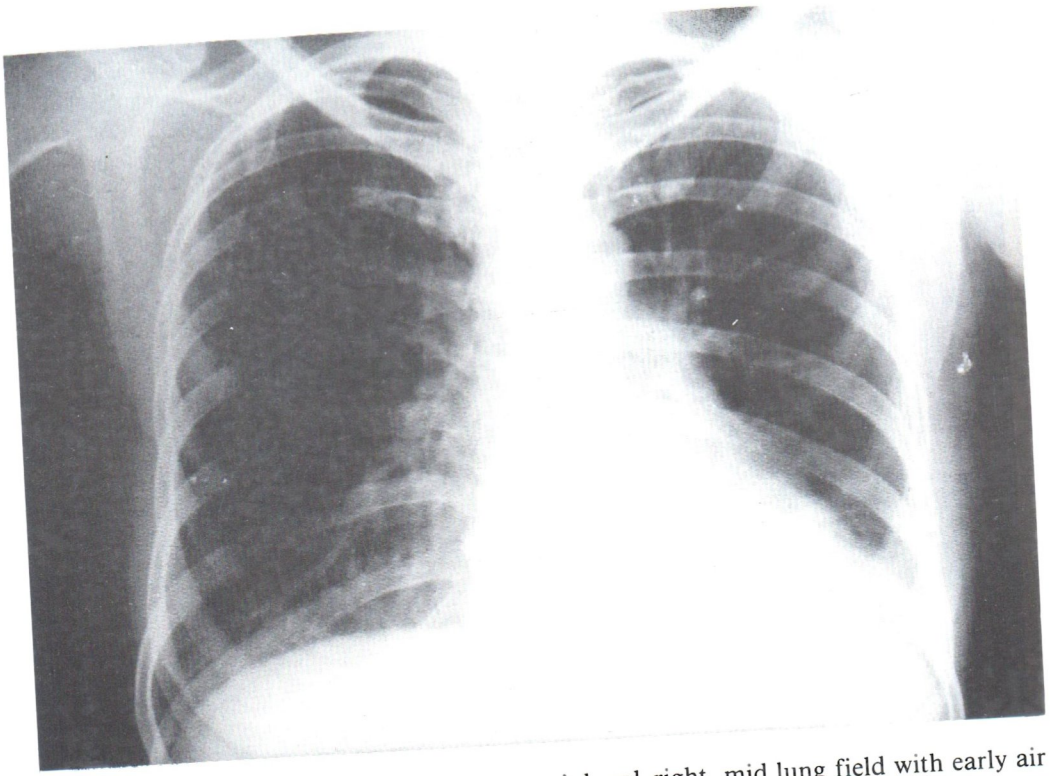

Fig. 5a Single pulmonary nodule at peripheral right mid lung field with early air space infiltration at bilateral basal lungs were noted on this initial film.

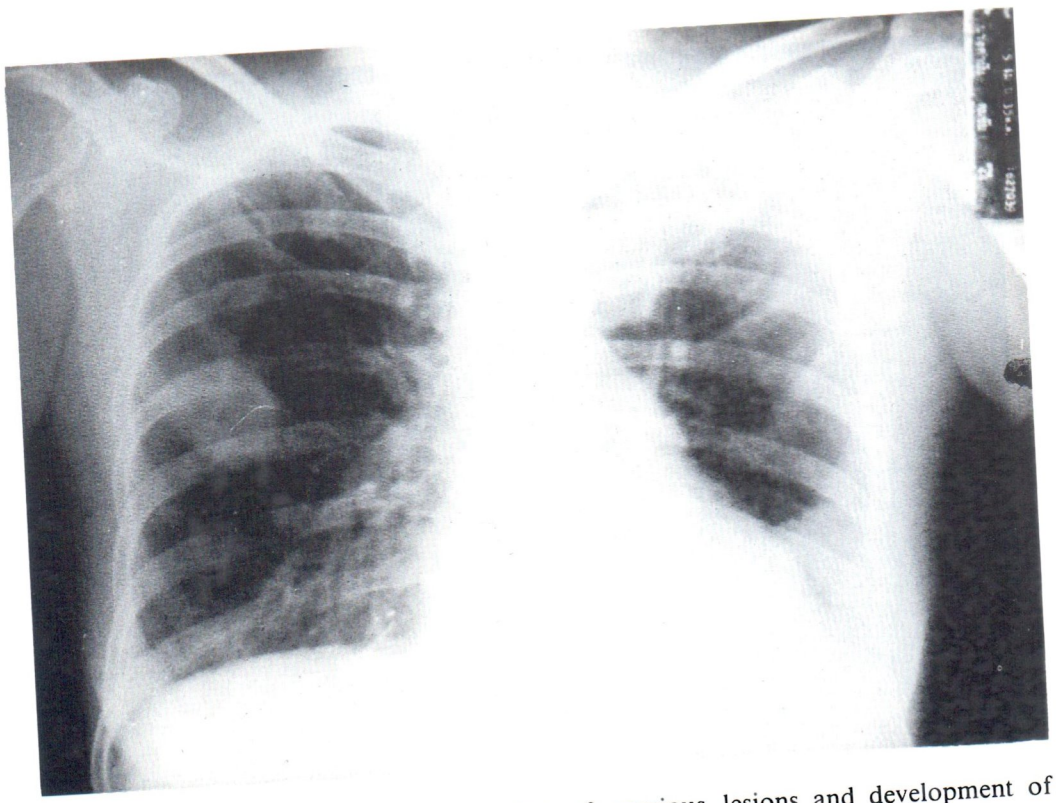

Fig. 5b Three weeks later; progression of previous lesions and development of new pulmonary mass at LUL and LLL. Left pleural effusion was also presented.

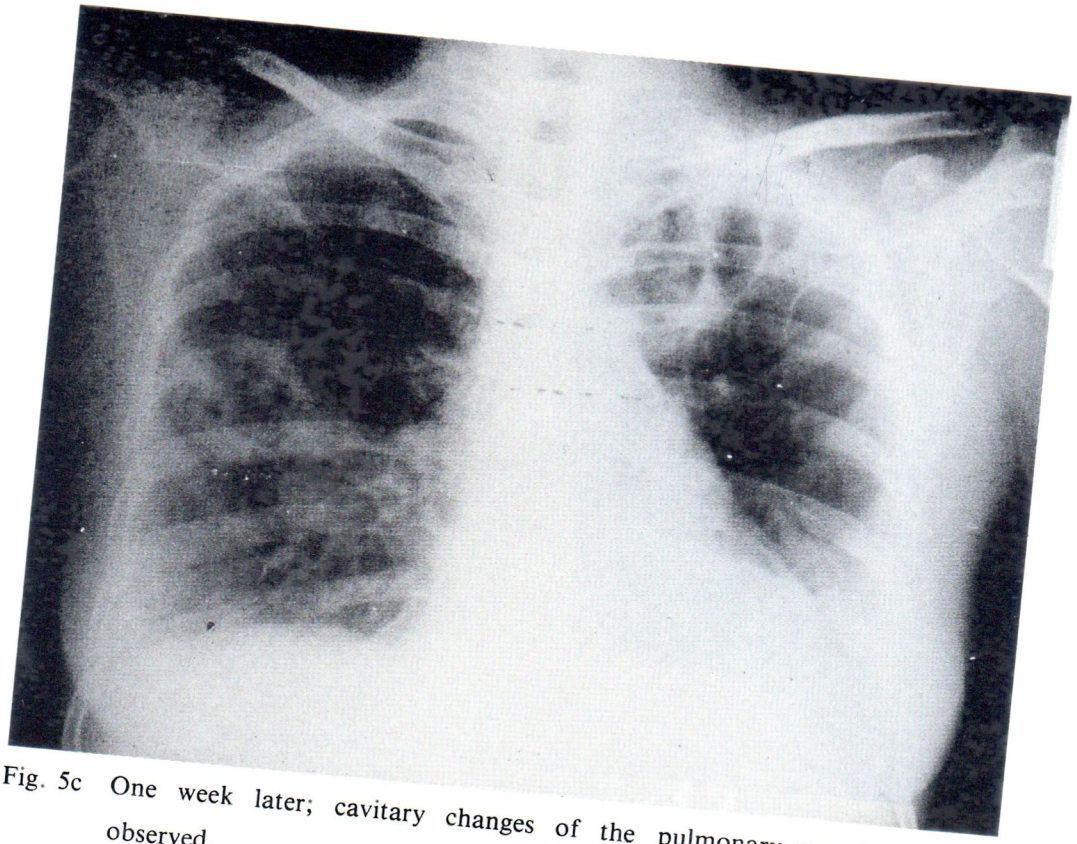

Fig. 5c One week later; cavitary changes of the pulmonary mass lesions were observed.

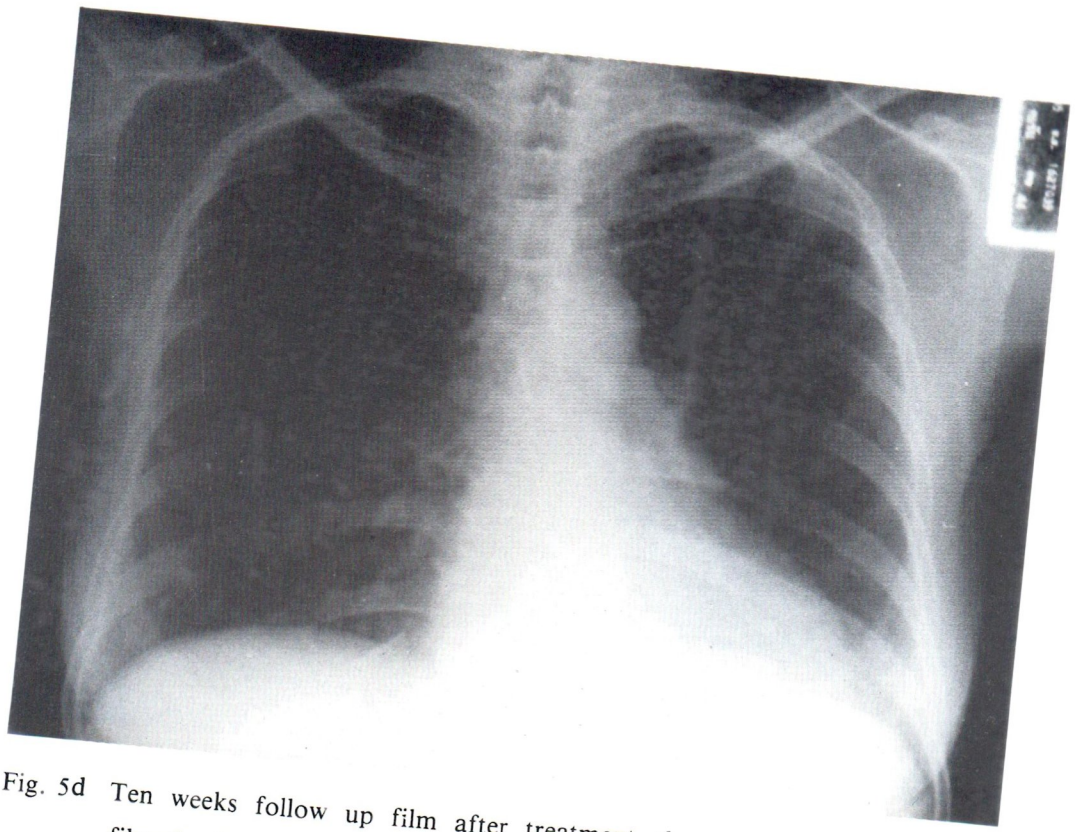

Fig. 5d Ten weeks follow up film after treatment shown only minimal residual fibrotic change at RML and LUL. Left pleural effusion was disappeared.

depend upon what organ is involved. Extrapulmonary manifestations of nocardiosis include skin lesion (especially subcutaneous abscess), liver abscess, brain abscess and abscess formation in any other organs.[10,11,15,19,22] Disseminated disease is not uncommon. The risk of metastatic infection did not seem to be related to patients' underlying immune status.[10,23] Poor prognostic factors in nocardiosis are (1) acute fulminant infection with an incubation period of less than 3 weeks. (2) Cushing's syndrome (3) central nervous system dissemination (4) those receiving corticosteroid or antineoplastic therapy.[10,14,22] Death by nocardial infection usually from sepsis, brain abscess and overwhelming pneumonia.[22]

Nocardial pulmonary infection can produce a variety of radiographic abnormalities.[1,9,10,11,13,17,18] Pulmonary consolidation in large area usually is the most common pattern in many previous reports.[1,13,14,15,17-19] Other radiographic patterns are solitary or multiple irregular masses or nodules, reticulonodular pattern, pleural effusion with or without pleural plaque, mediastinal or hilar lymphadenopathy. The frequency of cavitary lesions within the consolidated area or within the solitary nodules or masses are variable and range from 15-62%. The highest incidence of cavitation is in the series of pulmonary nocardiosis associated wih AIDS. Extension of pulmonary lesion into the pleural space with chest wall involvement occured in 8-10% of cases.[10,14] However, chest radiograph may appear normal despite sputum culture positive for nocardia. These patients usually have mild symptoms and recover without treatment. The saprophytic role of nocardia is still questionable.[11]

From our study, the consolidation (usually inhomogeneous rather than homogeneous in appearance) is also the most frequent pattern seen. Pulmonary nodules, masses or reticulonodular infiltrative pattern are commonly less seen. Multiple cavitary changes developed within the consolidation, nodules or masses either on initial or follow up radiographs are very pertinent character. They occur in higher percentage than previous reports.[1,13,14,17,18] Pleural effusion and hilar lymphadenopathy are often less seen. Solitary large abscess formation with air fluid level is seen in chest radiograph in only one case. Spontaneous pneumothorax presented in case of polymyositis could be due to the underlying disease itself or rupture of pre-existing subpleural bleb rather than the nocardiosis.

The morphology of nocardia is rather characteristically different from most of other bacteria, fungi and mycobacteria. Nocardia is seen as non-spore forming, filamentous Gram positive branching rod on usual sputum Gram stain and weakly acid fast branching filamentous organism on modified Ziehl-Neelsen staining method. The typical appearance of nocardia on sputum examination in combination with the compatible chest radiographic pattern in immunocompromised patients should suggest nocardial pulmonary infection and presumptive diagnosis can be made. Prompt and appropriate treatment should be initiated since therapeutic response is usually effective even in these compromised hosts. Although some other organisms of the family Actinomycetaceae have been reported to be positive with modified Ziehl-Neelsen staining method[23] but these occurance are not common. Moreover, nocardial infection of the lung is much common than the actinomycoses in the immunocompromised patients. However; sputum, pleural fluid, pus or any tissue preparations that are obtained should be sent for culture confirmation. Nocardia can grow on many kinds of culture media but isolation of nocardia is relatively difficult because it rerely grow on within the first 48 to 72 hours and the culture plates or tubes may have been discarded before any growth can be detected. In addition; there may be overgrowth of other more rapidly growing mouth flora which may interfere with the culture result.[12,14] Growth of nocardia usually require two or more weeks and suspecious nocardial infection should be informed upon request. False negative sputum culture may be as high as two third of all cases,[11] therefore; invasive procedure as tranbronchial biopsy, percutaneus needle aspiration or open lung biopsy may be required for definite tissue diagnosis.

As a radiologist, the consideration of pulmonary nocardiosis should be considered if the appearance of multiple cavitary changes are seen in the area of consolidation, nodules or masses with or without pleural effusion on chest radiograph of immunocompromised patients. Pulmonary tuberculosis or other atypical mycobacterial pneumonia, pyogenic pneumonia and unususal pattern of pneumocystis carinii pneumonia in HIV infected patients can also be presented in such radiographic patterns and should be included in the differential diagnosis.[24-27] In the same population of advancing age, single or multiple, cavitating or noncavitating nodule (s) or mass (es) with or without adjacent rib destruction should be differentiated from primary or metastatic lung cancer and histologic proof should be obtained.

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Table 1. INITIAL CHEST RADIOGRAPHIC ABNORMALITIES.

CASE	UNDERLYING DISEASE	CONSOLI-DATION (S)	NODULE (S)	MASS (ES)	R N.	CAVI-TIES	ABSCESS	HILAR LN.	PLEURAL EFFUSION
1.	HIV infection	+ (I,S)	+ (M)	—	—	+	—	+	—
2.	HIV infection	+ (I,S)	—	—	+	—	—	—	—
3.	HIV infection	+ (H,S)	—	—	—	—	—	—	—
4.	HIV infection	—	—	+ (S)	—	+	—	—	—
5.	HIV infection	+ (I,S)	—	—	—	+	—	—	—
6.	HIV infection	+ (I,S)	—	—	—	+	—	—	—
7.	HIV infection	+ (I,S)	—	—	—	+	—	—	—
8.	HIV infection	+ (I,S)	—	—	—	+	—	—	+ (U)
*9.	polymyositis	+ (I,M)	+	—	+	+	—	—	—
10.	overlapped syndrome	—	+ (S)	—	+	—	—	—	—
11.	SLE	—	—	—	—	—	+	—	—
	TOTAL	8	3	1	3	7	1	1	1
12.	HIV infection	+ (H,S)	—	—	+	—	—	—	—
13.	HIV infection	+ (I,S)	+ (M)	—	—	+	—	—	—
14.	HIV infection	+ (I,M)	—	—	—	+	—	—	—
15.	HIV infection	—	+ (M)	—	—	+	—	—	—
16.	HIV infection	+ (I,M)	+ (M)	—	—	+	—	—	+ (B)
17.	HIV infection	+ (I,M)	—	—	—	+	—	—	—
18.	SLE	+ (I,S)	—	+ (M)	—	+	—	—	—
	TOTAL	6	3	1	1	6	0	0	1

CASE 1-11 = definite pulmonary nocardiosis,
CASE 12-18 = presumptive pulmonary nocardiosis
RN. = Reticulonodular infiltration, HILAR LN. = Hilar lymphadenopathy
I = inhomogeneous, H = homogeneous, S = single area, M = more than one area
U = unilateral, B = bilateral
* = spontaneous right pneumothorax with parital right lung volume loss.

TABLE 2. INFECTIOUS COMPLICATION OF AIDS : ORGANISMS THAT TAKE ADVANTAGE OF T-CELLS DEFECTS

BACTERIA	FUNGI	VIRUSES	PARASITES
M. Tuberculosis M. avium intracellulae Salmonella Legionella Nocardia Listeria	Candida albicans Cryptococcus neoformans Histoplasma capsulatum Coccidioides immitis	Cytomegalovirus Herpes simplex virus JC virus ? adenovirus	Pneumocystis carinii Cryptosporidia Isospora belli

TABLE 3. CAUSES OF PULMONARY INFECTION IN AIDS PATIENTS

ORGANISMS TAKING ADVANTAGE OF T-CELL DEFECT	ORGANISMS TAKING ADVANTAGE OF B-CELL DEFECT	OTHER ORGANISM
Pneumocystis carinii Cytomegalovirus M. tuberculosis Legionella Nocardia asteroides ? M. avium intracellularae ? Adenovirus	Streptococcus pneumoniae Hemophilus influenza	Staphylococcus aureus Gr. B streptococcus Branhamella catarrhalis

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