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A CLINICAL AND LABORATORY STUDY OF PULMONARY INFILTRATES IN A SELECTED POPULATION OF AIDS AND ARC PATIENTS IN LUSAKA, ZAMBIA

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DEDICATION

This work is dedicated to my wife Pumulo and my son Litia.

ACKNOWLEDGEMENTS

In drawing up a list of those persons who have been of special help to me in the preparation of this dissertation, I live in fear of having forgotten someone. Only that individual will spot the inadvertent oversight and she or he will do me a great favour in bringing the omission to my attention, so I can correct it.

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Definition of Pulmonary Infiltrate

Pulmonary infiltrate refers to the presence of abnormal material spreading through the lung parenchyma or the abnormal distribution of the substances in the lung (1). The interstitial tissues of the lung may be primarily affected or the alveoli may be the target. Usually both are involved. Both infectious and non infectious agents may produce pulmonary infiltrates. Radiographically, infiltrates generally are poorly delinated unless pleural space produce boundaries. There are many radiographic patterns of infiltrate. The same pattern may be produced by a number of different diseases and one disease may manifest multiple appearances. Information in other portions of the film, the clinical history and pertinent laboratory data must be utilized to arrive at an informed differential diagnosis. The infiltrates are commonly refered to as alveolar or acinar if they are composed of poorly defined opacities 5 to 10mm in diameter, reminiscent of puffs of smoke and linear or reticular if they are scattered through out the lung (2). A combination of alveolar and reticular patterns is generally refered to as reticulo-nodular infiltrate.

1.2. Pulmonary Complications of Human Immunodeficiency Virus Infection

The spectrum of pulmonary disorders associated with human immunodeficiency virus infection include both infectious and non infectious diseases (3,4,5).

The lungs are the principal organ of infectious complications of the acquired immunodeficiency virus and a majority of patients with the acquired immunodeficiency syndrome (AIDs) will develop Pulmonary disease at some point during their course (6). Case reports of major pulmonary infections such as Tuberculosis, Cytomegalovirus, Pneumocystis carinii and other less common or exotic HIV associated infections can be found and more undoubtedly occur (5,6,7). Why the lungs are commonly infected is not entirely evident. Undoubtedly part of the explanation lies in the fact that the lungs are the portal of entry into the body of many infectious agents that either may cause acute illness or may cause latent infections that becomes the nidus for subsequent reactivation disease. It is well known that HIV infection can cause virtually every conceivable type of systemic immunologic deficiency (8). What is much less clear is whether the vulnerability of the lungs to infectious microorganisms is merely the regional manifestation of the systemic abnormalities or whether additional HIV induced factors affect the lungs complex system of local defence mechanisms. It would seem that pulmonary defences may be compromised by direct infection of alveolar macrophages as suggested by Salahuddin et al (9).

Several non infectious HIV-related pulmonary complications such as Kaposi's sarcoma (7,10), non-Hodgkins Lymphoma (11), lymphocytic interstitial pneumonitis (12) and non specific interstitial pnuemonitis (13) have been reported and were recently the subject of a review article (14).

The aetiology of pulmonary infiltrates in HIV infected patients with acquired immunodeficiency syndrome (AIDS) or AIDS related complex (ARC) especially those who are sputum negative for mycobacterium tuberculosis or those with non productive cough is relatively unknown in most African Countries, including Zambia. Most studies that have been done in Africa have concentrated on HIV and Tuberculosis (15, 16, 17, 18). The reason for this may be that most African countries lack the necessary diagnostic facilities required for further evaluation of AIDS/ARC patients with pulmonary complications. The further investigation of patients with pulmonary complications involves expensive equipment, which in most cases is beyond the reach of developing countries. The few studies using such facilities either did not demonstrate any other pathogens other than tuberculosis (19) or found pneumocystis carinii (20, 21).

Nebulized saline induced sputum has been used in the investigations of pulmonary infiltrates with variable results (19, 22, 23, 24). Bronchoscopy and bronchoalveolar lavage have been utilized over the years to investigate pulmonary conditions and have continued to enjoy a pivotal role, especially in the investigations of pulmonary infiltrates in HIV infected patients (21, 25, 26, 27). In the past 5 years studies have started to compare broncho-alveolar lavage with nebulized saline induded sputum because of the ease of performance of nebulized saline (28, 29).

However, only one study from South Africa has addressed the question of sputum negative pulmonary tuberculosis and investigated these patients (29). In addition no studies have been done to compare saline induced sputum with bronchoalveolar lavage in AIDS and ARC patients with pulmonary infiltrates who are either sputum negative for tuberculosis or who had non productive cough.

The aetiological factors for pulmonary infiltrates in patients with HIV infection can be classified as follows:-

A. Infections

(i) Viruses

Cytomegalovirus

Herpes simplex virus

Varicella - Zoster virus

Epstein Barr virus

Human immunodeficiency virus

(iii) Bacteria

Mycobacterium tuberculosis

Mycobacterium avium complex

Pyogenic bacteria such as Pneumococcus

Other mycobacteria

(iii) Fungi

Histoplasma capsulatum

Coccidioides inimitis

Cryptococcus neoformans

Candida species

Aspergillus species

(iv) Parasites

Pneumocystis carinii

Toxoplasma gondii

Cryptosporidia

Strongyloides stercoralis

B. Malignancies

Kaposi's sarcoma

Non Hodgkin's lymphoma

C. Others

Drug induced reactions

Adult respiratory distress syndrome

Secondary alveolar proteinosis

Pnuemocystis carinii pneumonia is the principal cause of pulmonary infiltrate in AIDS patients in Europe and North America (30). In contrast Mycobacterium tuberculosis often seems to cause pneumonia in African AIDS patients (31). This difference in pulmonary disease in AIDS patients may be environmental as African patients have been reported to have developed Pnuemocystis carinii pneumonia while in Europe (32). It is important to note that Pneumocystis carinii pneumonia is seen in 4 major categories of patients with some immunologic disturbance. These are organ transplant recipients on immunosuppressive therapy, patients with malignant diseases receiving immunosuppressive or cytotoxic therapy, children with congenital immunodeficiency and much more commonly patients with the acquired immunodeficiency syndrome (AIDS).

2. OBJECTIVES OF THE STUDY

MAJOR OBJECTIVE

To investigate pulmonary infiltrates in AIDS and ARC patients in Lusaka.

2.2 Minor Objectives

To explore further diagnostic methods for the investigations of direct smear negative for Mycobacterium tuberculosis and non productive cough in AIDS and ARC patients with pulmonary infiltrates.

3. PATIENTS AND METHODS

3.1 PATIENTS

A total of 32 consecutive patients with AIDS and ARC referred from general medical wards, the chest clinic, the immunodeficiency (ID) clinic and general medical clinics were studied. The 32 patients fullfilled the clinical definition of AIDS and ARC of the World Health Organisation and the Ministry of Health of Zambia (33, 34).

The 32 patients were sero-positive for human immunodeficiency virus (HIV) infection and had radiological evidence of pulmonary infiltrates. These patients were either direct smear negative for Mycobacterium tuberculosis or had a non-productive cough.

The patients gave a writ[illegible] they were informed about the nature [illegible] study. They were also told that the investigation[illegible] being undertaken were to try and explain further the nature of their illness.

They were also assured that the results were going to be made available to them. The investigative equipments were shown to the patients on the day of the procedure in order to allow the patient a second choice.

2.1 History

All cases were interviewed personally. The history was taken in detail and was divided into 2 sections, a personal history and a medical history.

2.2 Personal History

This included the name, age, sex, race, marital status, occupation, residence, home environment, smoking and drinking, religion , nationality; history of travel and contact with whites.

2.3 Medical History

The medical history included cough, its duration and productivity, haemoptysis, hoarseness of voice, chest pains, dyspnoea, wheeze, anorexia, weight loss, fever, night sweats, chest infections as described by patient, recurrent diarrhoea and duration, herpes zoster infection and when, menstrual disturbances (female patients only), antibiotic and steroid usage, previous history of tuberculosis, tuberculosis treatment, a family history of tuberculosis and BCG vaccination.

3.2.4 Physical Examination

All patients were examined personally and the findings were recorded. The examiner paid special attention specifically for AIDS/ARC features as described by WHO (33) and Ministry of Health of Zambia (34), and for the presence of other important clinical features. The features recorded were wasting, weight loss, pallor, lymphadenopathy, oral thrush, papular eruption, Herpes Zoster scar, chest findings, cardiac findings, hair and nail changes and presence or absence of Kaposi's sarcoma.

3.2.5 Investigations

Four main investigative procedures were performed on the patients. All patients had HIV results and a chest X-ray. The HIV results were positive. The chest x-ray was evaluated in terms of Cardiothorax ratio (CTR), hilar and Paratracheal lymphadenopathy, lung field infiltrates (nature and location) and pleural cavity disease. The patients either underwent bronchoscopy with bronchoalveolar lavage or inhaled saline sputum induction. The specimens obtained by either bronchoscopy with bronchoalveolar lavage or saline induction were recorded in millilitres. The specimens were divided into four sets for each patient. These were sent for direct smear for Mycobacterium tuberculosis (Zeihl-Nelsen Stain), Gram Stain and Culture, (for ordinary bacteria), Fungal and parasitologic study. The parasites that were looked for were Pneumocystitis carinii, Toxoplasma gondii and Entamoebae histolytica. Pneumocystis Carinii was detected by using the modified Toludine Blue Stain described by Gosey et al (35). Unusual fungi and parasites also were looked for. The sputum was cultured for Mycobacterium tuberculosis.

3.2.6 Bronchoalveolar Lavage

After an 8 hours fast (from midnight) the patient received Diazepam (valium) 10mg intramuscularly for sedation and Atropine 0.6mg intramuscularly to dry the secretions 30 minutes before Bronchoscopy. The vocal cords were anaesthesized using either a 10% lignocaine spray or 4% lignocaine solution. The bronchoscope was passed most of the time transorally but occasionally transnasally into the trachea. 1% lignocaine (2 - 3mls) was introduced into each main bronchus and this was allowed to act before passing the bronchoscope tube into the bronchi. 1ml of 1% lignocaine was introduced subsequently as required. The lignocaine was subsequently removed by aspiration as far as possible. Bronchoscopy was performed as described by Ikeda [36] (34). The bronchi were inspected and bronchoalveolar specimens were taken from the appropriate bronchial segment. To collect the sample the bronchoscope was wedged into the segmental bronchus and 20mls aliquots of warm normal saline were injected and aspirated. The bronchoscope was sterilized with 2% glutaralaldehyde. Bronchoscopic examination was performed by the Author.

3.2.7 Nebulised Saline Induced Sputum

Patients fasted overnight before sputum induction. To avoid contamination of the sputum specimen with oral debris, patients were asked to brush the buccal mucosa, tongue and gums with a wet tooth brush and rinse and the mouth thoroughly with water.

Sputum was then induced by inhalation of 20 - 30mls of 3% Saline through an ultrasonic nebulizer (NE-UiOB, OMRON, Fatersei electronic Company - Japan). The procedure was performed as described in 1986 by Bigby et al (23). Gentle chest percussion to aid expectoration was used when necessary. (This was performed by the Author and two Nurses with experience in the use of nebulizer.

3.3 Statistical Methods

The results were analyzed using percentage variables, the unpaired student t test and the chi-square (X^2). $P \leq 0.05$ was taken as significant.

3.4 Study Location

The study was done at the Bronchoscopy Clinic of the University Teaching Hospital, Lusaka, Zambia.

3.5 Study Authorisation

The study was authorised by the University of Zambia, School of Medicine Research and Ethics Committee.

4. RESULTS

4.1 PERSONAL HISTORY

A total of 32 patients with AIDS and ARC were studied. There were 31 Africans and 1 coloured and there were 23 males and 9 females. The age distribution was from 6 to 57 years. A total of 27 patients knew their ages, giving a mean (SD) of 33.4 ± 11.1 years. The age groups are shown on table 4.1. 18(56%) were married, 6(19%) were single, 5(17%) were divorced, 2(6%) were widows and 1(3%) was separated. The employed were 15(47%) and unemployed were 13(41%). There was an equal distribution of the patients in terms of residential status, which was 17(53.1%) from high density and 15(46.9%) from low density areas. 30 of 32(94%) of the patients were staying with somebody at home. Socially, 20(62.5%) took alcohol regularly, 12(37.5%) smoked cigarettes and 20(62.5%) were non smokers. 24(75%) of the 32 patients were from the Roman Catholic Church and the remainder were from the Protestant churches.

4.2 MEDICAL HISTORY

All patients presented with a cough, that was of insidious onset and of more than 2 weeks duration. Table 4.2 shows the duration of cough and number of patients. 7(21.9%) of patients had a cough of less than a month, 19(59.3%) had a cough of one month to one year and 6(18.8%) had a cough of more than one year.

Table 4.1

AGE DISTRIBUTION OF PATIENTS STUDIED

AGE	NUMBER OF PATIENTS	PERCENTAGE
0 - 10	1	3.1
11 - 20	1	3.1
21 - 30	9	28.2
31 - 40	8	25.0
41 - 50	6	18.8
51 - 60	2	6.2
Unknown	5	15.6
TOTALS	32	100

(Table 4.2) 17(53.1%) had a productive cough. There was no significant difference in the duration of cough between those with a productive cough and those with a non productive cough. Haemoptysis was documented only in 2 patients, some degree of dyspnoea was present in all 32 patients.

Varying degrees of chest pains, commonly pricking in nature, were present in all 32 patients. Wheeze and hoarseness of voice were notably absent. Malaise, anorexia and weight loss were present in all patients. 19 out of 32 patients had lost between 8 and 25 kilograms of weight. the remaining 13 patients did not know how much weight they had lost.
All patients gave a history of night sweats, fever and chest infections. Most patients had been on one or more antibiotics. The range of antibiotics was wide but commonly used were tetracycline, Trimethoprim-Sulfamethoxazole (Septrin), penicillin and chroramphenicol. Chronic diarrhoea was present in 9 patients. No patient was on steroid therapy and none of the female patients was pregnant. One female had delivered 3 weeks prior to entering the study. 6 patients had been treated for tuberculosis, mostly for tuberculous pleural effusion. 4 patients were on treatment for tuberculosis and 22 patients were not known to have had tuberculosis. A history of BCG vaccination was present in 20 patients. Most female patients had menstrual irregularities, 5 had amenorrhoea and 2 had irregular periods. One female was a child aged 6 years old and had post transfusion AIDS. 13 (40.6%) had had Herpes Zoster 1 to $4\frac{1}{2}$ years prior to entry in the study.

Table 4.2

DURATION OF COUGH

DURATION	NUMBER OF PATIENTS	PERCENTAGE
Between 2 - 4 Wks	7	21.9
1 month to 1 year	19	59.3
Greater than 1 year	6	18.6
TOTAL	32	100

4.3 PHYSICAL EXAMINATION

Wasting was noted in 25(78.1%) of the patients. The patients weighed between 14 and 68 kilograms. Pallor was observed in 24 (75%) of the patients. No patient had finger clubbing. 27 (84.4%) had lymphadenopathy, 18 (56.3%) had oral thrush, 13 (40.6%) had cutaneous papular erruptions, 8 (25%) had hepatosplenomegaly. 3 (8.4%) had Kaposi's sarcoma. 14 patients had BCG scars and 13 patients had Herpes zoster scars. Chest examination revealed bilateral mid and lower zone crackles in 12 (37.5%), unilateral crackles in 10 (31.3%) bilateral lower zone crackles in 8 (25%) upper lobe crackles in 1 (3.1%) and unilateral lower zone crackles with stony dullness in 1 (3.1%).

4.4 LABORATORY RESULTS

Chest X-ray revealed a cardiothorax ratio (CTR) ranging from 38 to 68% with a mean (SD) of 44.7 + 5.2%, hilar lymphadenopathy in 9 (28.1%), bilateral lower zone infiltrates in 15 (46.9%), bilateral mid and lower zone infiltrates in 6 (18.8%), unilateral lower zone infiltrates in 6 (18.8%), unilateral mid and lower zone infiltrates in 4 (12.5%) and unilateral upper zone infiltrates in 1 (3.1%). Perihilar infiltrates were observed in 16 (50%) of patients. 3 of the 9 patients with hilar lymphadenopathy had Kaposi's sarcoma. Bronchoscopic examination revealed lesions of Kaposi's Sarcoma in bronchi of 2 patients, ulcerating lesions in the upper lobe bronchi of 2 patients and these lesions were biopsed.

The Histology showed tuberculosis in one and non specific inflammation in the other. 17 of 32 patients (53.7%) underwent bronchoalveolar lavage. The age distribution was 17 to 56 years, with mean (SD) of 35.8 ± 10.3 years. 15 of 32 patients (46.9%) underwent nebulized saline induction. The age distribution was 6 to 57 years, with a mean (SD) of 30.8 ± 11.1 years. There was no age difference between those who underwent bronchoalveolar lavage (BAL) and those who had sputum induction (t_{10}, 5% = 2.0, P>0.5). 12 males and 5 females had BAL whereas 10 males and 5 females had induced sputum. There was no difference in the duration of cough between those who underwent bronchoalveolar lavage and saline induced sputum patients. 17 (53.1%) had a productive cough and 15 (46.9%) had a non productive cough. Out of the 17 who underwent bronchoalveolar lavage, 12 (70.6%) had productive cough and 5 (29.4%) had a non productive cough. Relatively more with productive cough had bronchoalveolar lavage. Out of the 15 patients who underwent saline induced sputum, 4 (26.7%) had a productive cough and 11 (73.3%) had a non productive cough. Inspection of bronchi during bronchoscopy revealed 2 with Kaposi's sarcoma, 2 with ulcerating lesions in upper lobe bronchi, 6 with inflammed bronchi, 2 with purulent secretion from the lower lobe bronchi, 5 without abnormalities and none with any proteinaceous material. The volume of specimen obtained by bronchoalveolar lavage varied from 15 to 50mls with a mean (SD) of 28.5 ± 7.2mls and the volume obtained through nebulized saline ranged from 3 to 25mls with a mean (SD) of 9 + 6.5mls.

The volume of specimen obtained by bronchoalveolar lavage was significantly more than saline induced specimen (t_{n-1} = 19.45, P 0.001).

Microbiological and parasitologic ..dy revealed 8 of 32 (25%) had Mycobacterium tuberculosis, 8 (25%) had candida, 4 (12.5%) had Pneumocystis carinii, 3 had Haemophilus influenzae, 1 had Ecchinococcus species, 1 had unidentified flagellate and no pathogens were found in 11 (34.3%) patients. These results are shown in table 4.3. Some patients had more than one pathogen. 3 patients with mycobacterium tuberculosis had candida albicans and all patients with Pneumocystis carinii had candida albicans and 1 patient with Mycobacterium tuberculosis also had Pneumocystis carinii. Some patients with certain pathogens had other causes of pulmonary infiltrates. Out of 2 patients with Kaposi's sarcoma one had Mycobacterium tuberculosis and the other had Ecchinococcus species. 1 patient with Pnuemocystis carinii had radiological evidence of pleural effusion and had received anti Tuberculous therapy.

Table 4.3

MICROBIOLOGIC AND PARASITIC PATHOGENS IDENTIFIED

PATHOGENS	NUMBER	PERCENTAGE
Mycobacterium Tuberculosis	8	25
Candida Albicans	8	25
Pneumocystis Carinii	4	12.5
Haemophilus Influenzae	3	9.4
Ecchinococcus Species	1	3.1
Unidentified Flagellate	1	3.1
No Pathogens identified	11	34.3

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17 of 32 had bronchoalveolar lavage and 15 had nebulized saline. A total of 8 cases of mycobacterium tuberculosis were identified, 5 through bronchoalveolar lavage and 3 through nebulized sputum, 8 cases of candida were identified (4 by bronchoalveolar lavage and 4 by nebulized sputum), 4 cases of Pnuemocystis carinii were identified, all through bronchoalveolar lavage. 2 of 3 cases of Haemophilus influenzae were identified by bronchoalveolar lavage and one by nebulized sputum. 1 case of Ecchinococcus species through nebulized sputum and 1 case of unidentified flagellate through bronchoalveolar lavage (Table 4.4).

There was no significant difference in the ability of the two procedures in the isolation of cases of tuberculosis and probably candida. However for Pneumocystis carinii, bronchoalveolar lavage was a more successful procedure. Previous antibiotic treatment did not have an influence on the yields.

TABLE 4.4 PULMONARY PATHOGENS IDENTIFIED BY SPECIFIC PROCEDURE

PATHOGENS	PROCEDURE		TOTAL
	BRONCHOALVEOLAR LAVAGE	NEBULISED SALINE	
Mycobacterium tuberculosis	5	3	8
Candida albicans	4	4	8
Pneumocystis carinii	4	0	0
Haemophilus influenzae	2	1	3
Ecchinococcus species	0	1	1
Unidentified flagellate	1	0	1
No pathogen identified	5	6	11

In summary, by extending diagnostic tests beyond the study procedure of direct sputum smear examination at the University Teaching Hospital (UTH) additional pathology and micro organisms has been identified in 17 of 32 patients (Table 4.5). The problems are grouped either singularly or in combination with the procedure for their identification.

Table 4.5

PROCEDURE AND PROBLEMS IDENTIFIED

SINGLE PROBLEM	BAL.	N.I.S.	TOTAL
M Tubercolis	3	0	3
C Albicans	0	0	0
H Influenzae	2	1	3
K Sarcoma	1	0	1
Unidentified flagellate	1	0	1
MULTIPLE PROBLEMS			
M Tuberculosis + K Sarcoma	1	0	1
M Tuberculosis + Candida + P Carinii	1	0	1
P Carinii + C Albicans	3	0	3
K Sarcoma + Echinococcus Species	0	1	1

Key: BAL - Bronchoalveolar Lavage
N.I.S - Nebulized Induced Sputum

DISCUSSION

The acquired immunodeficiency syndrome (AIDS) was first described in 1981 but it has since reached epidemic proportions throughout the world (37). AIDS is caused by the human immunodeficiency virus (HIV). The hallmark of the immunodeficiency in AIDS is the depletion of T4+ helper/inducer lymphocytes (39, 40). HIV is related to a group of nontransforming cytopathic retroviruses.

Pulmonary infiltrates in AIDS and ARC patients are common and pose a major diagnostic challenge in this group of patients in whom opportunistic infections are many and in whom a delay in diagnosis may mean life or death from a treatable condition.

Pulmonary disease in HIV infected patients is very common in Zambia and in the University Teaching Hospital in particular and as such clinical characteristics of patients with pulmonary infiltrates and an effective diagnostic approach may be important in order not to over diagnose tuberculosis, which may lead to enormous costs in the Tuberculosis Control Programme. At present pulmonary diseases account for about 50 percent of medical admission and they are a major cause of morbidity and mortality.

This study was undertaken to investigate pulmonary infiltrates in AIDS and ARC patients who were sputum smear negative by direct examination for mycobacterium tuberculosis and those who could not produce sputum. The study looked at patients characterists, radiological features and laboratory findings and tried to relate the features so as to assist in clinical diagnosis given minimal investigative procedures.

The study also analysed the findings according to the diagnostic procedure employed in order to find what may be an appropriate procedure or procedures for a specific clinical setting in a patient with AIDS and pulmonary infiltrates. In the present study, a total of 32 patients were enrolled. More males were enrolled than females, possibly reflecting the referral pattern. Most patients were young adults between the age of 20 and 40 years. This may be related to population demography or to the ages affected by AIDS as it has earlier been reported by Hira et al (41, 42).

There was no difference in terms of residual area of origin. Most of the patients (94%), stayed with somebody at home, possibly reflecting the extended family type of society. This, however, may be a risk factor in the development of chronic chest diseases such as pulmonary tuberculosis. In the present study, the Catholic Church was over represented. This may reflect the population of Catholics in the community studied, rather than a measure of promiscuity or susceptibility to HIV infection.

All the patients studied had a cough of insidious onset and 25(78.1%) had a cough of more than one month. The finding of prolonged cough of insidious onset in this population studied confirms earlier observations in the same community (16). The duration of cough however was not related to productivity. This has a major setback on the present method of direct sputum smear examination. All the patients had chest pains and dyspnoea.

These symptoms may hve no value in the making of a diagnosis of either pulmonary tuberculosis or any other pulmonary infections. Clinical examination was also less helpful in this highly selective population and raises doubts on relying a lot on clinical signs. Radiological finding were slightly helpful in that hilar nodes, especially asymmetrical hilar nodes were associated with either pulmonary tuberculosis or Pulmonary Kaposi's Sarcoma. It still was unable to differenciate these two conditions.

It has been stated that hilar and mediastinal lymphadenopathy are not part of HIV related generalized lymphadenopathy syndrome (43) and as such a patient with pulmonary infiltrations with the above findings should undergo further investigations.

In the present study, mycobacterium tuberculosis was detected in 8(25%), candida species in 8(25%), Pneumocystitis carinii in 4(12.5%), Kaposi's Sarcoma in 3(9.4), Haemophilus influenzae in 3(9.4), Echinococcus species in 1(3.1) and unidentified flagellate in 1(3.1) and no pathogens were identified in 11(34.3%).

The significance of these problems are discussed and clinical features are analysed further to try and find features which may help a clinician to formulate an intelligent approach to pulmonary infiltrates in AIDS patients in our community.

The aetiology of pulmonary infiltrates in acquired immunodeficiency syndrome (AIDS) and ARC vary in different parts of the world. In Europe and North America, pulmonary infiltrates are commonly caused by Pneumocystis carinii pneumonia (6, 44).

In Africa, pulmonary infiltrates are commonly due to Mycobacterium tuberculosis (19). Epidemiologic information suggests that there is a relationship between human immunodeficiency virus type 1 (HIV) infection and tuberculosis. In one study, 14% of HIV seropositive intravenous drug abusers with a positive tuberculin skin test developed tuberculosis over a 2 year period compared with none of similar group of HIV negative subjects (45).

Tuberculosis was the commonest cause of pulmonary infiltrates in the patients studied. It accounted for 8 patients, 5(29.5%) identified through bronchoalveolar lavage and 3(20%) by sputum induction. An earlier study using nebulized saline, but less selective than the present study, found tuberculosis in 11 of 22 patients studied (19). In the present study Mycobacterium tuberculosis was twice as common as Pneumocystis carinii as a cause of pulmonary infiltrate.

Tuberculosis is recognised as a major infectious complication of AIDS (16). Clinical studies have emphasized the early appearance of tuberculosis in the course of AIDS, the frequent extrapulmonary tuberculosis in patients with AIDS, the occurrence of non typical radiographic patterns in pulmonary tuberculosis patients with AIDS and the non specific presentation (16, 18, 45). It has also been reported that patients with pulmonary tuberculosis and AIDS may be less likely to have positive sputum smears than those who have pulmonary tuberculosis without AIDS (16). The above features were also observed in the 8 patients with tuberculosis, 5 were sputum negative, 3 had a non productive cough and all had atypical chest x-rays.

It is, however, rather difficult to accept the notion of sputum negativity as common finding because sputum smear positive in HIV seropositive is less dependent upon caseation. Rather as with other opportunistic infections in HIV seropositive patients, the profound immune defect alone may permit tubercule bacilli to multiply in great numbers in the airways. It is with this background that when a patient with AIDS/ARC with pulmonary infiltrate who is sputum negative and has a cough, that tuberculosis has to be excluded to avoid over diagnosis of tuberculosis and to guide therapy. Bronchoscopy with bronchoalveolar lavage or nebulized sputum should be undertaken in such patients. The x-ray was less informative and did not distinguish tuberculosis from Pneumocystis carinii or Kaposi's Sarcoma. It has been observed that the classical upper lobe disease caused by tuberculosis in seronegative patients is uncommon in patients with AIDS (16, 18, 45).

In the present study only one patient with tuberculosis had upper lobe disease confirming previous observations in this community and elsewhere in the world (16, 18, 45, 46).

Candida albicans was isolated in 8(25%) of the patients studied. This occured with most of the disorders detected. The role of candida albicans was not further analysed or assessed by lung biopsy, in order to attribute them, as the pathogens responsible for the pulmonary infiltrates. Candida albicans is a frequent saprophytic inhabitant of the human respiratory tract. However candida is also a recognised opportunistic infection in HIV (43).

Studies from the United States have noted that pulmonary candidiasis is a late or terminal manifestation of HIV infection, nearly always occurs in association with disseminated disease, frequently coexisting with other AIDS related opportunistic infections or malignancies (47). Thus the role of candida albicans in the present community will require another study. It may be a contaminant in the present study.

The role of Pneumocystis carinii in patients with AIDS in Africa may be underestimated. In an earlier study of pneumonia in HIV infected patients in Lusaka, using induced sputum, no Pneumocystis carinii cysts were detected (19). Pneumocystis carinii was also not found in limited autopsy material (48) and in 40 bronchoalveolar lavage of AIDS patients in Uganda (49). In contrast to the reports in Zambia (19) and Uganda (48, 49), Pneumocystis carinii was discovered in 8 of 37 (22%) AIDS patients in Zimbabwe (20) and Pneumocystis carinii pneumonia was detected in 5(11%) of the patients studied bronchoalveolar lavage in the Congo (50). These studies utilized bronchoalveolar lavage. Pneumocystis carinii infection has been diagnosed in African AIDS patients in Europe (51). It was earlier proposed that the infrequent reporting of Pneumocystis carinii pneumonia among AIDS patients in Africa may be due to lack of environmental exposure, early deaths due to other infections or limited resources, lack of methods of detection of parasite and possibly lack of motivation by researchers (32, 52). However, the present study found 4 cases of PCP suggesting that environmental exposure is present and may be as important as in Europe and North America where Pneumocystis carinii is common(3).

The environmental factor may be important in that the further one is from the equator the more likely for one to get this infection. The reports from Africa may suggest this geographical distribution (48, 49, 20). It may be possible that contact with whites may be important in the acquisition of the infection in that all 4 patients with PCP had been in contact with whites. It is also possible that early death due to infections and gastroenteritis may account for the observed low incidence of Pneumocystis carinii. In the present study 2 of 4 patients with Pneumocystis carinii had a history of treated tuberculosis and one patient had coexisting tuberculosis which may confirm the above speculation. The nonspecific nature of pulmonary infiltrates in patients with AIDS/ARC thus calls for a scientific approach to diagnosis. The success of each procedure however will depend on the availability of supportive facilities and experience of researchers (6, 14, 26).

3(8.4%) of the patients studied had Kaposi's Sarcoma. None of these patients had Pneumocystis carinii. This may reflect the fact that Kaposi's Sarcoma may be an early manifestation of AIDS while Pneumocystis carinii may be a late manifestation. 1 patient with Mycobacterium tuberculosis had co-existing Pneumocystis carinii suggesting that these organisms may cause pulmonary infiltrate in a single patient and that any patient in whom one of these organisms has been isolated and who does not respond well to appropriate therapy should undergo further investigations preferably bronchoscopy with bronchoalveolar lavage.

One of the patients with Mycobacterium tuberculosis also had Kaposi's Sarcoma strengthening the importance of diagnostic workup of pulmonary infiltrate. In patients with Kaposi's sarcoma with pulmonary infiltrate, sputum examination or bronchoalveolar lavage should be done prior to treatment or during the course of treatment to avoid missing coexisting tuberculosis. There were no previous reports on the coexistance of Pneumocystis carinii and tuberculosis or tuberculosis and Kaposi's sarcoma but it has been observed in Kaposi's sarcoma that prophylaxis for Pneumocystis carinii with Trimethoprim-Sulfamethoxazole prolonged life (47).

One patient with Kaposi's sarcoma was found to have coexisting ecchinococcus larval stages on nebulized sputum. The species of ecchinococcus could not be identified further but it was however smaller than the dog parasite. It was also unfortunate that when this patient died, the relatives could not consent to postmortem. This report may be the first report of this pathogen in AIDS patients with Kaposi's sarcoma isolated by nebulized sputum from the lungs. However this may not be surprising in view of the immunologic problems these patients have. The role of this pathogen awaits further studies.

One patient with sputum negative results was found to have flagellates in bronchoalveolar fluid. The flagellate could not be identified. The flagellate may have been a modified epithelial cell or a new pathogen. Earlier works by Urban and Michaelis (53) had noted the presence of these flagellates in 11 out of 24 patients with sputum negative pulmonary infiltrates.

The role of these flagellates or modified epithelial cells in HIV related pulmonary disease is at present unknown. These may be infected epithelial cells but their motile properties 18 to 24 hours after bronchoalveolar lavage may weigh against them being epithelial cells. This being the case, these flagellates may be a new pathogen in AIDS patients. This patient also died. From clinical observation patients with the flagellates, responded well to Metronidazole (53). However in the absence of tissue diagnosis, the pathogenic role of the echinococcus species and the unidentified flagellate are uncertain.

Mycobacterium tuberculosis, candida albicans and Haemophilus influenzae, bronchoscopy with bronchoalveolar lavage and nebulized saline induced sputum and with the limits of this study, the yields did not differ, however in the detection of Pneumocystis carinii and endobronchial lesion bronchoscopy with bronchoalveolar lavage was superior. The small numbers meditates against any further comments. However, in view of the lack of specificity and sensitivity of clinical features and radiology, bronchoscopy with bronchoalveolar lavage may be a procedure of choice in this environment in patients of suspected Pneumocystic carinii.

CONCLUSIONS

1. Mycobacterium tuberculosis is the most important cause of pulmonary infiltrate in community where tuberculosis and HIV are prevalent.

2. The radiological features of pulmonary tuberculosis in HIV are non specific and offer little help in the diagnosis and as such bacteriological proof is important if unnecessary antituberculous therapy is to be avoided.

3. Patients with HIV with pulmonary infiltration may have pulmonary tuberculosis despite being direct sputum smear negative or having a non productive

4. Pneumocystis carinii is uncommon but a definite cause of pulmonary infiltrate that must be looked for in HIV patients who are sputum negative for direct smear examination who have a non productive

5. The role of candida albicans may be commensal but it may contribute to the disease process.

6. A role of candida in pulmonary infiltrates in HIV requires further study.

7. Haemophilus influenzae, echinococcus species and unidentified flagellates may be important pathogens in AIDS, but their role is still not clear.

8. Bronchoalveolar lavage may be superior to nebulized saline in the investigation of pulmonary infiltrate in suspected cases of Pneumocystis carinii.

9. Nebulized saline induced sputum may be of value in the out patient investigation of pulmonary infiltrates and may be used as a screening procedure to reduce the number of patients undergoing bronchoscopy and broncho-alveolar lavage which is more invasive.

10. A large study is required to try and identify radiological patterns and arrive at definitive conclusion on the causes of pulmonary infiltrates in HIV in Lusaka.

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