Pneumococcal pneumonia complicates presentation of pulmonary tuberculosis and pseudomembranous candidiasis, predictive of unknown HIV infection in Ekpoma Nigeria

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Abstract

This study outlined how pneumococcal pneumonia complicated the clinical presentations of pulmonary tuberculosis and showed the predictive value of Pseudomembranous candidiasis (PC) in detection of unknown Human immunodeficiency virus (HIV) infection in Ekpoma. Out of 510 sputum samples analyzed, bacteria and fungi were identified using standard microbiological methods and sera of 240 patients, with undiagnosed PC, whose sputum had Candida albicans, were screened for HIV. Exactly 44.1% were co-infected with Streptococcus pneumoniae and Mycobacterium tuberculosis while 40.2% had M. tuberculosis and C. albicans. Out of 260 patients clinically diagnosed with pulmonary tuberculosis, 23.1% had Streptococcus pneumoniae, while 69.3% of 150 patients clinically diagnosed with pneumonia had M. tuberculosis. Exactly 79.2% of 240 patients with PC, had undetected HIV. Pneumococcal pneumonia complicated the clinical diagnosis of pulmonary tuberculosis. PC was 79.2% predictive of undiagnosed HIV infection. Full laboratory investigation remains invaluable in the management of mixed infections.

INTRODUCTION

In most developing countries like Nigeria, the problem of inability to find out the exact cause of infection before commencement of treatment is high especially in remote rural areas. This could be due to lack of good health facilities with standard diagnostic equipments and qualified laboratory staff. This has promoted over-dependence on presumptive diagnosis and treatment of infectious agents based sorely on clinical findings. Consequently many infectious agents are either misdiagnosed or undiagnosed.

Streptococcus pneumoniae is the most frequent etiologic agent of bacterial pneumonia (Herffelfinger et al., 200) and S. pneumoniae pneumonia develops when encapsulated (virulent) S. pneumoniae are inhaled into the alveoli of susceptible host, multiply rapidly and cause an inflammatory response. Serum and phagocytic cells pour into the air sacs of the lungs causing difficulty in breathing and sputum production (Nester et al., 1998). On the other hand, the pulmonary form of tubercle bacilli after inhalation multiplies within the lower respiratory tract. There is an inflammation of lung tissues leading to the initial formation of exudative lesions. These lesions contain the mycobacteria, phagocytic leukocytes and an area of non specific inflammation (Murray et al., 1998, Nester et al., 1998). Pneumonia often occurs as a complication of secondary infection which typically occurs when an individual is run down and his or her physiological state depresses the effectiveness of the immune response system. This may happen after surgery or during the course of treatment of another disease (Murray et al., 1998). Immunodeficiency can result in activation of latent tuberculosis and over 5% of AIDS patients have developed active tuberculosis (Murray et al., 1998). Both S. pneumoniae and Mycobacterium tuberculosis produce infections that affect the lobes of the lungs producing lobar pneumonia and pneumonitis respectively. When there is co-infection of pneumonia and tuberculosis in patients with S. pneumoniae pneumonia as the underlying disease, undiagnosed underlying S. pneumoniae pneumonia could pose health management problems if tuberculosis alone is diagnosed. This may be true in rural settings where poverty, illiteracy, and cultural beliefs scare people away from few available hospital services, and those who manage to go to the hospital expects quick recovery.

Preliminary survey reveal that increasing evidences of

recurrent lower respiratory tract (LRT) infection among patients attending tuberculosis clinics in Ekpoma suggest other microbial etiology in addition to Mycobacterium tuberculosis. In a previous report (Agwu et al., 2006), it was outlined that occupation, age and sex affects prevalence of S. pneumoniae infections in patients attending chest clinics in this region. Ekpoma has few private clinics with no specialist hospital and these private clinics are mostly owned by general practitioners who may not be willing to send samples for analysis in a German Tuberculosis center housed in Irrua Specialist Hospital located in a nearby community. The trend of empirical clinical diagnosis of pulmonary infections and commencement of treatment without resort to laboratory investigations has remained a common practice in this region. The recurrent situation of LRT infections compels most patients to resort to herbal mixtures which in most case lack scientific proof of efficacy and fitness for human consumption.

This study which is entirely laboratory based, was therefore designed to show the role of underlying pneumococcal pneumonia in complicating LRT (tuberculosis) infections among patients attending tuberculosis clinics in Ekpoma Nigeria and to re-emphasize the significance of laboratory investigations in the management and control of infections.

MATERIALS AND METHODS

SAMPLING AREA

Ekpoma and its environs in Esan West Local Government Area of Edo State, Nigeria were the main study areas. It is a University town situated 120km north of Benin, the capital city of Edo State Nigeria. It has few private clinics with no specialist or referral hospital. Four private clinics and one General Hospital, all in Ekpoma, served as the major sites for sample collection. Informed consent of the patients were sought and obtained in writing.

INCLUSION CRITERIA

There were respiratory symptoms suggestive of pulmonary infections which were used as criteria for inclusion of patients in this investigation. The characteristics of patients enrolled in this investigation included: prolonged chronic productive cough, constant weight lost, fever, loss of appetite, weakness, night sweats, malaise, pulmonary inflammation and necrosis, peripheral adenopathy, general chest pain and difficulty in breathing. Pseudomembranous candidiasis was detected on visual inspection of the oral cavity in the Laboratory. There was no chest X-ray for patients to have guided the use of radiographic resolution in the diagnosis of lobar pneumonia and no facilities for cultural isolation of Mycobacterium tuberculosis in Ekpoma. Lack of X-ray for patients may either be because patients could not afford the services or the few available X-ray services were not reachable because of poor power supply.

SELECTION OF SUITABLE SAMPLES FOR ANALYSIS

Smears of the purulent parts of the specimens were made on a glass slide for Gram-staining before transportation to Search-Light Medical Diagnostic Center Ekpoma for further processing. Direct examination of samples by the Grams staining technique was adopted in selecting ideal samples for culture (Agwu et al., 2006). Purulent or blood flecked portion of the submitted specimens were subjected to direct gram staining, for epithelial cells and leucocytes. Specimens having less than 10 epithelial cells and more than 25 leukocytes were selected for this investigation and others were rejected as recommended our earlier (Agwu et al., 2006). Five hundred and ten (510) early morning sputum samples were collected over a period of one year in a clean sterile dry wide-necked leak-proof universal container from patients sent to Search-light Medical Diagnostic Center, Ekpoma, Nigeria for investigation.

STAINING AND CULTIVATION OF SAMPLES FOR MICROBIAL ETIOLOGY

The Ziehl Nielsen technique of staining for M. tuberculosis was adopted in the identification of acid and alcohol fast bacilli (Raphael, 1986). All media used (Blood agar, Chocolate agar, and Sabouraud Dextrose agar), were prepared using standard procedures and according to manufactures instructions. Sheep blood which does not contain streptococcal inhibitor was used for blood and chocolate agar preparation (Agwu et al., 2006). Five microgram per mil of gentamicin was added as selective inhibitor and duplicate non-selective media were used as control (Agwu et al., 2006). All sputum specimens for culture were homogenized gently with 2 ml sterile normal saline by refluxing the sputum saline mixture in a small syringe without a needle attached. Homogenized samples were streak-stabbed onto freshly prepared media for the determination of streptococcal hemolysis. Streak-stabbed plates were incubated in a candle extinction jar. Control Streptococcus pneumoniae supplied by the National Veterinary Research Institute, Vom, Plateau State, Nigeria was added to all sets of culture. Alpha hemolytic isolates

with other cultural characteristics consistent with S. pneumoniae were picked and identified using standard techniques including bile solubility and optochin sensitivity test (Barrow and Feltham, 1993; Hadie, 1986). Samples suspected to be Candida albicans on Sabouraud Dextrose agar (SDA) were identified by the germ tube test, chlamydospore test and growth at 45oC (Emmanuel et al., 1998).

SEROLOGICAL DETECTION OF HIV AMONG PATIENTS WITH ORAL THRUSH

Sera of the patients whose sputum samples yielded significant growth of C. albicans were screened for HIV 1 and 11 antibodies, using the immunocomb II kit. The procedure for the test as directed by the manufactures (Orgenics Limited) was carefully followed and the results of our investigation recorded.

RESULTS

The result of this survey reveals that out of the 510 sputum samples analyzed, 225 (44.1%) were co-infected with both S. pneumoniae and M. tuberculosis while 260 (51.0%) samples were co-infected with S. pneumoniae and C. albicans. Two hundred and five 205 (40.2%) samples were positive for M. tuberculosis and C. albicans whereas 240(47.1%) of the total 510 patients were positive for visible oral lesion (Pseudomembranous candidiasis) respectively as shown in (Table I). No sample was positive for all 3 organisms; S. pneumoniae, M. tuberculosis and C. albicans.

S. pneumoniae was isolated from sputum samples of 60 (23.1%) out of the 260 patients clinically diagnosed with Pulmonary tuberculosis and 104 (69.3%) M. tuberculosis obtained out of the 150 sputum samples whose patients were clinically diagnosed with Pneumonia. (Table II). Specimens sent for AFB/MCS screening were from those patients whom the clinicians suspected either pulmonary tuberculosis or pneumonia (Table II).

Oral lesions (pseudomembranous candidiasis) were also observed in the oral mucosa of the patients whose samples yielded significant growth of C. albicans. One hundred and seventy 170 (70.8%) of 240 samples, who had oral lesions (pseudomembranous candidiasis), tested positive for HIV I, 18 (7.5%) tested positive for HIV II, 2 (0.8%) were positive for both HIV I & II, while 50 (20.8%) were negative for HIV I & II respectively (Table III). Thus, the predictive value of oral pseudomembranous candidiasis for new previously undiagnosed HIV infection in the studied population was 79.2%. Table (III).

Figure 1

Table 1: Distribution of Microorganisms in The Sputum Samples of Patients Examined. n=510.

Microorganism	No (%) positive
S. pneumoniae and *M. tuberculosis*	225 (44.1)
S. pneumoniae and *C. albicans*	260 (51.0)
M. tuberculosis and *C. albicans*	205 (40.2)
M. tuberculosis, C. albicans and *S. pneumonia*	0. (0.0)
Oral lesions (Pseudomembranous candidiasis)	240(47.1)

n= total number of patients examined

Figure 2

Table 2: Prevalence of S. pneumonia and M. tuberculosis from the 510 sputum samples analyzed.

		n=510	
Examination requested	No of samples	No (%) of samples positive for:	
		S. pneumoniae	*M. tuberculosis*
AFB/MCS	100	70 (70.0)	60 (60.0)
AFB	260	60 (23.1)	146 (56.2)
MCS	150	56 (37.3)	104 (69.3)

Keys

MCS:	=	Request for Microscopy Culture and Sensitivity
AFB:	=	Request for Acid Fast Bacilli Staining
MCS/AFB	=	Request for both MCS and AFB.
n	=	Total Number of samples examined

Figure 3

Table 3: HIV screening of sera samples from 240 patients with pseudomembranous candidiasis with sputum samples yielding growth of .

HIV type	Number (%) positive
HIV I	170 (70.8)
HIV II	18 (7.6)
HIV I & II	2 (0.8)
Negative to HIV I & II	50 (20.8)

HIV = Human Immunodeficiency Virus.

DISCUSSION

Lack of adequate health care facilities in Ekpoma is a major health concern for Esan West Local Government (Edo State Nigeria) and the inhabitants of Ekpoma community. Presumptive disease diagnosis and empirical treatment are

therefore on the increase in the private health sector predominant in Ekpoma. The co-infection of S. pneumoniae, M. tuberculosis and C. albicans observed in this survey (Table I) are highly considered defining disease of Acquired Immunodeficiency Syndrome (AIDS) (CDCP, 1996). Their establishment in any individual depends on if certain conditions are favorable such as smoking, crowded environment, use of drugs, malnutrition and use of steroids (Al-Bayati, 1999). Health care providers should therefore be reminded that low immunity in patients may be indicated by co-infections of S. pneumoniae, M. tuberculosis and C. albicans and this should be confirmed by screening for HIV infection. This may help to identify a population of unknown HIV patient. This population if undetected posses a public health problem especially in the epidemiology of HIV infection and they are also a problem in the control of opportunistic infections in HIV/AIDS disease (Atlas, 1995, CDCP, 1996). Thus, early detection of HIV in this population with new HIV cases may help them to seek medical attention, encourage behavioural change and may ultimately minimize spread of HIV.

Table II shows undiagnosed but detected infections of pneumococcal pneumonia and pulmonary tuberculosis. In brief, out of 260 patients clinically diagnosed with pulmonary tuberculosis, 60 (23.1%) harbored S. pneumoniae as confirmed by the isolation of S. pneumoniae from their sputum samples. Another 150 patients clinically diagnosed with S. pneumoniae pneumonia also haboured 104 (69.3%) M. tuberculosis, confirmed by their sputum samples testing positive for M. tuberculosis using the Ziehl Nielsen technique of staining for acid fast bacilli (Table II). Our observations in this study depict a high incidence of undiagnosed pulmonary tuberculosis 104 (69.3%) and undiagnosed pneumococcal pneumonia 60 (23.1%). The presence of under-lying diseases like HIV infections, sickle cell disease, and other predisposing factors may activate asymptomatic or latent infectious agents.

Furthermore, most of the clinical diagnosis made based on the observable signs and symptoms of lower respiratory tract (LRT) infections were inaccurate. It is therefore important for rural health-care providers to note that significant percentage of empirical diagnoses made based on clinical manifestation of LRT infections and other diseases may be unreliable as the sole bases for treatment. This re-emphasizes the non-specific nature of most clinical manifestations of lower respiratory track infection and portrays the danger of relying only on clinical findings as sole basis for disease management without necessary laboratory investigations. For improved and effective empirical management of pulmonary tuberculosis and S. pneumoniae pneumonia, even while full laboratory investigation is being awaited, more emphasis should be placed on other quicker diagnostic protocols (if available), like Radiographic resolution of S. pneumoniae and M. tuberculosis which can be completed within 24hrs (Benzo and Sahn, 2000).

The observed diagnosis of pulmonary tuberculosis and subsequent request for detection of acid and alcohol fast bacilli while leaving other underlying infections such as pneumococcal pneumonia may be as a result of bizarre clinical presentation or asymptomatic infection. This point is supported by our former report that about 95% of tuberculosis infections may be asymptomatic and 70% of S. pneumoniae infections in apparently healthy children may also be asymptomatic (Agwu et al., 2004). Again underlying pneumococcal pneumonia could pose a problem in treatment of tuberculosis patients and also progression from asymptomatic to symptomatic tuberculosis could complicate pneumonia cases if undetected. Etiologic agent of under-lying infections may as well develop antibiotic resistance because while treating clearly diagnosed infection, an etiologic agent of underlying or asymptomatic infection may develop resistance after prolonged exposure to antibiotics. Thus, prolonged usage of these antibiotics may lead to development of multidrug resistance in an organism. An example is in our earlier report of the emergence of multi-drug resistant S. pneumoniae in this region (Agwu et al., 2004). However, we had reported an exception as well in which streptomycin antibiotic which is one of the drug regimens in tuberculosis management was also found to be sensitive to Streptococcus pneumoniae isolated from patients attending chest clinics (Agwu et al., 2005). Thus, streptomycin could serve a dual purpose of being used against tuberculosis and pneumococcal pneumonia. This implies that under-lying etiologic agent of disease may respond to drugs used in treating symptomatic infections at the onset before developing resistance after prolonged exposure.

The clinical relevance of the C. albicans isolated was established by screening for HIV, the patients whose sputum samples yielded growth of C. albicans. There is little or no literature regarding the pattern of oral manifestations in

Ekpoma HIV/AIDS patients and to the best of our knowledge the frequencies and pattern of oral disease have not been established in Ekpoma region. However, the result in (Table III) depicts 79.2% predictive value of oral lesions (Pseudomembranous Candidiasis) in the diagnosis of new cases of HIV/AIDS disease. The observed 79.2% positive predictive value of oral lesions for new HIV disease is higher than 43% oral Candidiasis in Lagos Nigeria reported to herald the emergence of HIV disease (Agbelusi and Wright, 2005). This might be connected to genetic component, geographical setting and socio-economic class of people found in Lagos metropolis compared to Ekpoma which is a rural small university town.

Available reports from different African geographical regions differ on the positive predictive values of the different clinical presentations of Candida infection for underlying HIV disease. The presence of any form of Candidosis was significantly associated with HIV infection in subjects, from various clinical settings, in Tanzania (Shiodt et al., 1990). These findings were supported by further studies in Tanzania and Uganda (Miller et al., 1995, Matee et al., 1999, Mayanga et al., 1999). Despite the frequent occurrence of pseudomembranous candidiasis in Dar Es Salaam, Matee et al, (1999) only consider it to be strongly suggestive of HIV infection if other factors such as xerostomia or therapy with antimicrobials, corticosteroids or other immunosuppressive drugs are excluded. The positive predictive value of oral pseudomembranous candidiasis for associated HIV infection in Dar Es Salaam HIV population was 87.5%. This is higher than 79.2% observed in this study. This difference may have geographical interpretation and underlying infections should be excluded according to Matee et al., (1999), to rule out false positive predictive values of oral lesions in detection of undiagnosed HIV infection. Significant infection by any of S. pneumoniae, M. tuberculosis and C. albicans in a patient is highly indicative of low immunity (HIV infection) since immune status of the patient is a factor in disease establishment (Fauci et al., 1998).

Pneumococcal pneumonia complicated the diagnosis of pulmonary tuberculosis in Ekpoma due to lack of modern diagnostic facility for full cultural and radiographic resolution of the two infections. On the other hand, pseudomembranous candidiasis was highly predictive (79.2%) of new HIV infection among the studied population. Full laboratory investigation remains invaluable in the management, prevention, and control of infectious agents, especially in conditions where underlying etiologic agents of diseases may pose a public health problem. The role of the laboratory is therefore very important in the diagnosis of mixed, dual, or double infections. Further study would be needed to establish the predictive value of other oral lesions so as to develop simple diagnostic algorithm to help healthcare providers in detection of new HIV disease. Nigerian Government is hereby advised to improve the condition of services at primary health centers, make the services affordable and extend such services to more remote villages where the ordinary citizens can access it.

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