Bacterial pneumonia in the AIDS patients

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Summary

Objective: **To determine the incidence, microbiological pattern and prognostic factor of bacterial pneumonia in AIDS patients.**

Study design: **Prospective study of AIDS patients from July 2001 to Dec 2002.**

Methodology: **Adults AIDS patients on HAART drugs that develop acute fever, cough with bronchial breathing or lung crepitations had diagnostic evaluation that included chest x-ray, paired sputum microscopy, culture and sensitivity, paired blood culture and haematological profiles including CD4⁺ cell count.**

Results: **Twenty-one patients (22.6%), 9 males and 12 females developed community acquired pneumonia during this 16-month period. Pneumonia was confirmed in 9 patients (42.9%), presumed in 4 (19%) and probable in 8 (38%). *Streptococcus pneumoniae* accounted for 22% of the cases when immunity was less impaired. *Staphylococcus aureus* accounted for another 22% while *Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Escherichial coli* were isolated in 11% each when immunity was severely compromised. Fifteen patients (71.4%) were successfully treated with routine antibiotics. Six cases (28.6%) died. All had anaemia, leucopoenia and low CD4 cell count. Four (66.7%) of this had positive bacterial culture with bacteremia in three of them.**

Conclusion: **Bacterial pneumonia in HIV-infected patients has similar presentation to that in the general population, *Staphylococcus aureus* and gram-negative bacilli especially *Klebsiella pneumoniae* were seen in a good proportion of the cases. Outcome of treatment was poor in the presence of positive bacterial culture, anemia, leucopoenia and very low CD4⁺ lymphocytes.**

Key-words: ***AIDS, Pneumonia, Bacterial pathogen and Prognostic factors.***

Résumé

Objectif: Décider l'incidence, tendance microbiologique et la prognostique factorielle de la pneumonie bactérielle chez des patients atteints du SIDA.

Plan d'Etude: Etude prospective sur des patients atteints du SIDA du juillet 2001 au décembre 2002.

Méthode: Patients adultes du SIDA avec l'utilisation de la drogue du HAART qui provoque une fièvre aigue, la toux avec une respiration bronchique ou une crépitation du poumon avaient eu une évaluation diagnostique y compris rayon x de la poitrine, microscopie crachat par paire, culture et la sensitivité, culture sanguine par paire et des profiles hématologiques y compris compte cellule CD4+.

Résultats: Vingt et un patients soit 22,6%, 9 du sexe masculin et 12 du féminin avaient contracté la pneumonie communautaire acquise au cours d'une période de 16 mois. La pneumonie a té confirmée chez 9 patients soit 42,9%, présumée chez 4 soit 19% et probable chez 8 soit 38%. Streptococcie pneumonie constitue 22% des cas dans le cas ou l'immunité était moins détériorée, Staphylococcus aureus constitue un autre 22% tandis que la klebsiella pneumonae pseudomonas aeruginosae et Escherichio coli ont été isolés en 11% chacun quand l'immunité était gravement compromisée. Quinze patients soit 71,4% ont été soignés conu du succès avec antibiotiques de routine. Six cas soit 28,8% mortalités. Tous les patients ont eu leucopoenie anamie avec un bas niveau du compte de la cellule CD4. Donc, quatre soit 6,7% avaient eu la culture bactérienne avec bactèremie dans trois d'entre eux.

Conclusion: Pneumonie bactérienne chez des patients infectés du VIH a une présentation semblabe par rapport à la population générale. Staphylococcus aureus et bacili gram-négatif surtout Klebsiella pneumonae ont été vus dans une très bonne proportion dans les cas. Le résultat de la prise en charge était mauvais dans la présence de la culture bactérienne positive, leucopoenie anamie et un niveau très inférieur de lymphocytes CD4+.

Introduction

Bacteria pneumonia is frequent in HIV positive patients[1] being 5-15 times more common in them than in HIV negative ones[2,3] and even more common in HIV-infected drug users[4,5,6]. Unlike in the early part of the epidemic when *Pneumocystic carinii* pneumonia was very common, bacterial pneumonia is now the most common cause of pneumonia requiring hospitalization in HIV-infected patients[5]. It is caused by both classic and opportunistic organisms[7]. Alteration in the host T-cell function is responsible for the increased susceptibility to opportunistic infection caused by Mycobacteria, viruses, fungi and protozoa.[8] Impaired phagocytic response of neutrophils and macrophages to mitogens,[9] and failure of B-cells to produce specific and rising antibody[10] to microbes are responsible for the increased risk of bacterial infection. Increased rate of community

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acquired and nosocomial pneumonia have been reported in AIDS patients[2,3] especially when the $CD4^+$ cell count is below 400/μl[11,12]. When pneumonia is recurrent in them it becomes a marker of severe immunosuppression and a sign of bad prognosis[1]. *Streptococcus pneumonae* and *Haemophillus influenzae* are the most common pathogen isolated[1,2,13]. However, varieties of other bacteria like, *Staphylococcus aureus*[14] and group B *streptococcus* have been identified to cause community-acquired pneumonia in these patients. So are Gram-negative pathogens such as *Pseudomonas aeruginosa* and *Klebsiella pneumonae*[15,16]. The outcome of treatment of bacterial pneumonia in HIV patients is good when diagnosis is accurate and made on time[1,2]. This paper presents the incidence, microbiological pattern and prognostic factors of bacterial pneumonia in AIDS patients under our care.

Methodology

Symptomatic adult HIV positive patients on treatment with twice daily oral highly active anti-retroviral (HAART) drugs comprising Nevirapine 200mg, Starvudine 40mg and Lamivudine 150mg and on follow-up care in the department of medicine between July 2001 and Dec 2002 were recruited into this study. A diagnostic evaluation for bacterial pneumonia was conducted on any of them that develop acute fever and cough and were admitted to the hospital. Questions were asked about pleurisy and dyspnea. Each patient was then examined generally and for respiratory signs such as; tachypnea, dull percussion note, bronchial breath sounds and lung crepitations. Afterwards a chest x-ray was done and paired sputum specimens were submitted for microscopy, culture and sensitivity on the day of the hospital visit. A smear of the purulent part of the sputum was made on a slide for gram staining and inoculated in three culture media; blood, chocolate and MacConkey agar for bacteria isolation[17]. These were incubated aerobically at 37 0^c for 24hours. Paired blood specimens were taken from two different sites for culture using thioglycollate broth medium. The sensitivity pattern of the bacterial isolates was done on a sensitivity agar. Haemogram studies including $CD4^+$ cell count was also done before commencement of empirical broad-spectrum antibiotic treatment. This was modified according to the sensitivity result. Diagnosis of positive HIV infection has been described elsewhere[18]. Pneumonia was classified into three groups[11,19] viz: confirmed pneumonia, when respiratory symptoms and signs were compatible with the radiological findings and a likely pathogen was isolated from the sputum, or blood, presumed pneumonia, when clinical features were compatible with radiological signs and a likely pathogen was suggested on Gram staining of a sputum smear, probable pneumonia, when clinical features that were compatible with radiological signs responded to empirical antibiotic therapy.

Analysis: The frequencies, mean ±SD and the percentages of all the variables were generated on an Epi-info software package.

Results

Ninety-three HIV positive patients; 44 males and 49 females, aged 19-55 years with a mean age of 37±5.8 years were on follow-up care in the out patient unit of our department at the time of this study. Twenty-one (22.6%) of these, 9 males and 12 females developed community acquired pneumonia over a 16-month period, all of them had fever and cough, while 11 (52.4%) had associated dyspnea and 6(28.6%) had pleurisy. On physical examination, 18 patients (86%) had pyrexia (38.8±1.6), 17 (81%) had tachypnea (27±4cycles/min) and 16 (76.2%) had tachycardia (108±9beats/min). Bronchial breath sounds occurred in 6 (28.6%) patients and crepitations occurred in some other 14 (66.7%) (Table1). Non-respiratory signs like rash occurred in 3 (14.3%) patients and splenomegaly in one (4.8%). Pneumonia was confirmed in 9 (42.9%) patients, it was presumed in 4 (19%) and probable in 8 (38%). Sputum specimen yielded

Table 1 Clinical and laboratory features of bacterial pneumonia in HIV- infected patients

Variables	No (%)
Respiratory symptoms at presentation	
Fever	21 (100)
Cough	21 (100)
Dyspnea	11 (52.4)
Chest pain	6 (28.6)
Respiratory signs at presentation	
Tachypnea	17 (80.1)
Tachycardia	16 (76.2)
Pyrexia	18 (85.7)
Crepitations	14 (66.7)
Bronchial breath sounds	6 (28.6)
Laboratory and radiological findings	
Haematology	
Mean WBC	8.5 2.7x10^9/l
Range	1.4 –19.4x10^9/l
Left shift	5 (23.8)
CD4 lymphocytesμl	
Mean	215 ± 45
Range	80-510
Positive culture result	
Sputum	9 (42.8)
Blood	3 (14.3)
Pleural fluid	1 (5)
Chest x-ray pattern	
Focal consolidation	4 (19)
Unilateral infiltrate	9 (42.8)
Bilateral infiltrate	6 (28.6)
Bilateral consolidation	3 (14.3)
Pleural effusion	3 (14.3)

Table 2 Haematologic variables and outcome of culture-positive pneumonia in AIDS Patients

PCV(%)	WBC(10^9/l)	$CD4^+$(ul)	Neutrophil(%)	Left shift	Organism	Source	Outcome
26	13.2	390	70	+	*S.pneumonae*	sputum	improved
24	2.5	140	60	+	*K.pneumonae*	blood	died
37	16.7	240	63	-	*K. pneumonae*	sputum	improved
13	2.4	90	42	-	*S.aureus*	blood/pleural fluid	died
14	1.7	80	56	-	*E.coli*	sputum	died
29	1.3	200	61	-	*P. aeruginosa*	sputum	improved
21	2.0	110	32	-	*S.aureus*	blood	died
35	14.2	470	87	+	*S. pneumonae*	sputum	improved
19	4.0	210	72	-	*K. pneumonae*	blood	improved

Table 3 Haematologic variables and outcome of culture-negative pneumonia in AIDS patients.

PCV (%)	WBC(x10^9/l)	$CD4^+$(ul)	Neutrophil (%)	Left shift	Outcome
20	3.2	390	78	-	improved
34	19.4	200	59	+	improved
15	2.3	130	44	-	died
33	17.1	150	52	-	improved
21	1.8	90	63	-	died
22	1.7	240	58	-	improved
29	2.3	170	66	-	improved
33	13.6	420	82	+	improved
41	12.2	510	67	-	improved
27	2.5	190	81	-	improved
38	11.2	160	74	-	improved
32	15.3	290	63	-	improved

Streptococcus pneumoniae in 2 (22%) cases; *Staphylococcus aureus* in another 2 (22%) while *Klebsiella pneumoniae*, *Pseudomonas aureginosa* and *Escherichial coli* were isolated in 1 (11%) case each (Table 2). Two (22%) patients had multiple pathogens isolated from sputum, but blood culture yielded Klebsiella spp in both. Patients with *Staphylococcus aureus* pneumonia had associated bacteremia and one of them had *Staphylococcus aureus* cultured also from pleural fluid twice. Two each of the patients with presumed pneumonia had clusters and chains of gram-positive cocci on Gram staining of their sputum smears. The white cells count (WBC) ranged from 1.3-19.4 X 10^9/L with a mean of 8.5±2.7 X 10^9/L. Leucocytosis; WBC ≥ 11 X 10^9/L occurred in 9 (42.8%) patients out of which 5 (23.8%) had left shift with toxic granulation of the neutrophils. The range of $CD4^+$ cell count was 80-510/ul and the mean was 215±45/ul. Thirteen of 21 patients (62%) had PCV less than 30% (anaemia), 8 (38.1%) had WBC less than 2.5 X 10^9/L (leucopoenia) and 15 (71.4%) had $CD4^+$ lymphocytes count below 250/ul. Chest x-ray showed unilateral lobar consolidation in 4 (19%) patients one of which had air-fluid level. Patchy lobar infiltrates was seen in 9 (42.8%), bilateral lobar consolidation occurred in 3 (14.3%) cases and diffuse infiltrates in 6 (28.6%). A case (4.7%) of pleural effusion was clinically demonstrable, 2 (9.5%) others were revealed on chest x-ray. Culture negative pneumonias are illustrated in table 3. Sixteen patients (76.2%) were treated with single antibiotic comprising intravenous (iv) ciprofloxacin 200mg twice daily in 6 (28.6%) patients, iv cefuroxime 750mg 8hourly in 5 (23.8%), iv amoxicillin/clavulanic acid 1.2gm 8hourly in 3 (14.3%) and iv ceftriaxone 1gm daily in 2 (9.5%). Another 5 patients (23.8%) were treated with combination therapy that included iv gentamycin 80 mg 8 hourly and iv cefuroxime 750mg hourly in 2 (9.5%) patients, iv gentamycin 80 mg hourly and iv ceftriaxone 1gm daily in another 2 (9.5%) and iv gentamycin 80mg hourly and oral sultamicillin 750mg 8 hourly in one (4.7%). Fifteen patients (71.4%) were successfully treated and discharged. The average length of hospital admission was 10.7 days. Six cases (28.6%) died. They all had anaemia, leucopoenia and $CD4^+$ cell count below 150/ul. Four (66.7%) of these had positive bacterial culture with associated bacteremia in 75% of them.

Discussion

$CD4^+$ cells regulate B-cells differentiation and antibody production as well as phagocytic function of the neutrophils. These regulatory roles are impaired in

HIV-infected patients and they exhibit a number of immunologic defects such as ineffective polyclonal hypergammaglobulinaemia[20] and abnormal phagocytosis by the polymorphonuclear cells as well as impaired local pulmonary defenses[21,22]. These factors predispose them to increase risk of bacterial infection, especially the encapsulated ones. The incidence of bacterial pneumonia in this study was 22.6%. Fever and cough were universal to all the patients, however, pleurisy and dyspnea were found in 28.6% and 52.4% of them. Of note also was the normal temperature, respiratory and pulse rates in about a quarter of the patients on physical examination even though they reported fever and had respiratory features that necessitated diagnostic evaluation for pneumonia in them. Likely causative bacteria were isolated from only 9 of the cases (42.9%), in keeping with reports[23,24,25] on pneumonia from the general population where etiologies were not found in substantial number of cases. Microscopic examination of the sputum was suggestive of bacterial infection in 19% (4 patients) and probable diagnosis of pneumonia was made in 38% of the cases (8 patients) based on response to antibiotic treatment. *Streptococcus pneumoniae* was the most common (22.2%) Gram-positive bacteria isolated from the sputum when the immune status was mild to moderately compromised; $CD4^+$ lymphocytes of 390-470 cells/ul, while *Staphylococcus aureus* and Gram-negative rods comprising *Klebsiella pneumoniae*, *Escherichia coli* and *Pseudomonas aeruginosa* were recovered from those whose immune status was moderate to severely compromised; $CD4^+$ lymphocytes of 80-240 cells/ul. This observation probably suggests that *Streptococcus pneumoniae* is ordinarily more pathogenic and could cause chest infection in a relatively less compromised state of immunity. This is in conformity with several studies that have reported *Streptococcus pneumoniae* as the most common cause of bacterial pneumonia with or without bacteremia in HIV–infected patient[6,26,27] and one of the causes of severe community acquired pneumonia even in immunocompetent patients[28]. Recovery of bacterial pathogen from sputum was not remarkable in this report partly, because of indiscriminate use of antibiotic by the patients before seeking hospital consultation. The tendency of commencing antibiotic therapy before obtaining sputum for laboratory studies was discouraged in this study and was therefore not a contributing factor. In keeping with some earlier studies[28,29] and as found in five of our patients, two of which had associated *Klebsiella pneumoniae* bacteremia, Gram-negative bacilli became an important cause of community-acquired pneumonia when immunity was severely compromised. Gram-negative bacilli are therefore, opportunistic bacteria that are less pathogenic outside the hospital environment. This fact has also been recognized in Nigeria and there is increasing reports of gram-negative bacilli as a community acquired pathogen in a number of infections including pneumonia, especially among those with underlying immunity disorders[30,31,32].

Multiple-partner heterosexual practice was the most likely risk of exposure to HIV infection in most of our patients and *Staphylococcus aureus* was isolated from two of them, both of whom had associated bacteremia. It is also likely that *Staphylococcus aureus* was the causative organism in about 2 of those with presumed diagnosis of pneumonia. Therefore, high prevalence of *Staphylococcus aureus* pneumonia with bacteremia that is often found among injection drug users[1] and homosexuals[13], may not be limited to these group of patients alone as we observed 19% (4) of all the pneumonias in this series to be due to *Staphylococcus aureus*. Our experience is supported by other studies[11,14,33] that have earlier reported *Staphylococcus aureus* bacteremia in HIV-infected patients without any obvious predisposing factor. Positive bacterial culture, anaemia, leucopoenia and low $CD4^+$ count represented poor signs of prognosis. Four (66.7%) of the six deaths in this report had positive bacterial culture with bacteremia in 75% of them. All the six deaths had PCV less than 24%, leucocytes count below 2.5×10^9/l and $CD4^+$ cells count less than 150/ul.

In conclusion bacterial pneumonia in HIV-infected patients has similar presentation to that in the general population. Normal vital signs could be observed in a few of them in spite of other evidence of pneumonia. The usual community acquired *Streptococcus pneumoniae* was the common causative bacteria in the early part of the disease when the immunity was less impaired while *Staphylococcus aureus, Klebsiella pneumoniae* and other gram-negative bacilli were the responsible pathogens at the advanced stage of the disease. Outcome of treatment was, however, good with routine antibiotics therapy except in a few cases with anemia, leucopoenia and very low $CD4^+$ lymphocytes where the risk of mortality was high.

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