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PULMONARY INFECTIONS IN ACUTE LEUKAEMIAS

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ABSTRACT

Pulmonary infections are frequent in acute leukemias, highly associated with death, often caused by organisms not pathogenic for immunocompetent patients. The management of pulmonary infection in acute leukemic patients, has evolved both conceptually and practically over the past few decades. The advent of cytotoxic therapy improved survival and even cure in some malignancies. With it, came an unprecedented and previously unrecognized abnormalities in host defense systems. And as a result bacterial and fungal infections complicating that, at first threatened to undermine the potential benefits of cancer treatment. The most important was neutropenia. Earlier it was recognized that successful management of neutropenic patient required new and unique therapeutic guidelines. The traditional approach for the treatment of infections in these patients, such as identification of a pathogen prior to institution of antibiotics and antifungal agents, led to disastrous consequences. As a result the concept of empirical antibiotic therapy emerged. Routine empirical therapy is now accepted as standard of care in a febrile neutropenic patient, A prospective study was carried out for analyzing the pattern of pulmonary infections in Acute leukemias at Tata Memorial Hospital, Parel, Mumbai, India from March, 1989 to June, 1989. A total of 71 consecutive patients who received cytotoxic chemotherapy for Acute Leukemias were included in the study. There were 56 episodes of Pulmonary infections, associated with Febrile neutropenia, in 36 patients. Bacteria was isolated in 18(32.2%) episodes and mixed bacteria and fungus 18(32.2%) episodes. In 20 episodes, no organisms could be isolated. The commonest bacterial isolated were Group A Streptococci (58.3%). The commonest fungus isolated was candida albicans (77.7%). Pulmonary infections, both bacterial and fungal were common in adults and were fatal. Early diagnosis by positive sputum culture, as a valid criteria for diagnosing Pulmonary infections is suggested. Early treatment of fungal infections may decrease the morbidity and mortality. Fungal infections, despite early diagnosis and treatment lead to substantial mortality.

Key Words: Pulmonary Infection, Acute Leukemia, Bacterial, Fungus.

INTRODUCTION

Infection is a major cause of death in patients with cancer, especially in those with haematologic malignancy and granulocytopenia [1]. The lung represents the single most commonly documented site of infectious disease [2] and pneumonia for as much as 25 to 50 percent [3,4] of all infectious deaths among patients with haematologic malignant disease. The spectrum of infective organisms is wide, including bacteria, mycobacteria, viruses, fungi, and protozoa.

The relative incidence of each of the infection varies in different parts of the world and at different periods in the natural history of the underlying primary disease. common fungal opportunistic invaders of the lung. Infection with more than one organism is common. The bacterial infection is the most frequent cause and streptococci, kleibseilla, Haemophilus influenza, E.Coli and staphylococci are the most common organisms [5,6]. Candida and Aspergillus probably are the most. The major mechanism protecting the body from infection are the mucocutaneous boundaries, polymorphonuclear leukocytes, circulating immunoglobulins and cellular immune mechanisms. Patients with acute leukemia tend to have severe impairment in both the number and functional capability of polymorphonuclear leukocytes [7,8].

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Pulmonary defense mechanisms are incompletely understood, but the alveolar macrophages, the minor initial line of defense against particles deposited on the respiratory membrane, and both humoral and cell mediated immunity appear important in protecting against pathogens⁹. Alteration in any of these sources of defense may lead to pulmonary infection.

MATERIALS AND METHODS

Patient Selection: Seventy one consecutive patients of acute leukemia were included in the study. Thirty six of them (50%) had 56 episodes of pulmonary infection. The study was carried out prospectively between 1st March 1989 to 30th June, 1989 at Tata Memorial Hospital, Mumbai, India. The treatment regimens used in acute leukemias produced bone marrow aplasia with severe granulocytopenia. The infection prophylaxis was given to all patients and consisted of Trimethoprim-Sulfamethoxazole and Candid orally. Hexidine mouth washes and Sitz baths were also given.

Before starting infection prophylaxis, surveillance cultures were sent. Cultures (blood, urine, sputum and stools) both for bacteria and fungi were also sent whenever the patient had fever. Repeatedly positive sputum cultures on three successive days were taken as diagnostic criteria for pulmonary infection, bacterial as well as fungal, in presence of febrile neutropenia, cytotoxic therapy, with pulmonary symptoms and signs, clinical as well a Radiological. Invasive procedures such as bronchoalveolar lavage, trans bronchial, transcutaneous and open lung biopsies were not done even in the sputum less patients, as they all had the risk of haemorrhage due to the presence of severe thrombocytopenia and also they had attended risk of pneumothorax besides their poor general condition. The severity granulocytopenia in the patients were graded as, Grade- I when neutrophil count was 500-1000 cells/mm³, Grade- II when the count was 100-500 cells/mm³ and Grade- III if count was less than 100 cells/ mm³.

In all the grades of granulocytopenia, the febrile illness was treated with Ceftazidime + Amikacin + Metronidazole in therapeutic doses till the neutrophil count is > 1000 cells/mm³ and fever subsides. If the fever doesnot subside, Amphotericin-B was added.

RESULTS

A total of 71 patients with acute leukemia were studied. Of the 71 patients, 41 were males and 30 were female, 32 were adults and 39 were children. Among these patients, 45 were diagnosed as Acute Lymphoblastic Leukemia (ALL) and 26 were diagnosed as Acute Non - Lymphoblastic Leukemia (ANLL).

A total of 56 episodes of pulmonary infections in 36 patients were diagnosed. Among these patients 10 had Grade- I, 33 had Grade- II and 13 had Grade- III neutropenia. (Table 2), Bacterial infections were evidenced in episodes while mixed bacterial and fungus in 18 episodes. In 20 episodes, patients could not produce sputum. (Table 7)

The commonest bacterial organisms isolated were Group A Streptococci 21/36 (58.3%) followed by Klebsiella pneumonia 6/36 (16.7%) and Staphylococcus aureus 5/36 (14.0%). (Table 3). The commonest fungal organism isolated was Candida albicans 14/18 (77.8%) followed by Aspergillus flavus 4/18 (22. 2%) (Table 4). Cough and chest pain were the commonest symptoms present. Twelve of these episodes had haemoptysis and all of them had fungal infections (Table 5).

There were 18 episodes of fungal infections, who had previously bacterial infection treated with broad spectrum antibiotics. The commonest radiological abnormality documented was Lobar consolidation. 20 episodes (35.7%) followed by bacterial Broncho – pneumonia 16 episode (28. 5%) (Table 6).

Overall the adult patients had more episodes of infections. Among ANLL patients, adults experienced maximum number of infectious episodes when compared to children. Similar is the case with fungal infections (Table4). Among all patients children experienced maximum number of infectious episodes when compared to adults but fungal infections were common in the adults (Table 4). This shows that the fungal Infections were exclusively common in adults, irrespective of the type of leukemia. Sixteen out of 18 deaths were due to mixed bacterial and fungal infections (Table 8). Only 2 out of 18 deaths were due to bacterial infections. None of the sputum negative patients who received empirical chemotherapy died.

Table 1. Showing Age, Sex, Type of leukemia among patients

Period of study	March 1989 to June 1989
Total no. of patients	71
Males	41
Females	30
Adults	32
Children	39
All	45
ANLL	26

Table 2. Severity of Neutropenia

Grade	Neutrophil Count (Cells/mm ³)	Number of Episodes
I	>500-1000	10
II	100-500	33
III	<100	13

Table 3. Showing split up of bacterial species in all & ANLL patients with polmonary infections

Species of Bacteria	No of Episodes (Total 36)	All (13)		ANLL (23)	
		Adults (5)	Children (8)	Adults (20)	Children (3)
1. Group A streptococci	21(58.3%)	2	8	12	2
2. Kleibseilla Pneumoniae	6(16.7%)	1	0	5	0
3. Staphylococcus aureus	5(14.0%)	1	2	1	1
4. E.Coli	2(12.5%)	1	0	1	0
5. Pseudomonas aeruginisa	2(12.5%)	0	1	1	0

Table 4. Fungal species isolated

Species	No.of Episodes (N=18)	All (4)		ANLL (14)	
		Adults (3)	Children (1)	Adults (14)	Children (0)
1. Candida albicans	14(77.8%)	3	1	10	0
2. Aspergillus flavus	04(22.2%)	0	0	4	0

Table 5. Presenting symptoms and signs

Symptoms	No.of Episodes
1. Cough	53
2. Chest Pain	22
3. Hemoptysis (These Pts.Later Developed Fungal Infections)	12
Signs	
1. Crepitations	55
2. Pleural Rub	12

Table 6. Radiological Features

Radiological Features	No. Of Episodes
1. Lobar Consolidation	20 (35.6%)
2. Bilateral Bronchopneumonia	16 (28.5%)
3. Patchy Infiltrates	15 (26.8%)
4. Pleural Effusion	04 (07.1%)
5. Pneumothorax	01 (02.0%)

Table 7. Outcome of Acute Leukamia Patients with Pulmonary Infections

Type of Infection	No.of Episodes (56)	Outcome	
		Recovered	Died
1. Pure Bacterial Infection	18	16	2
2. Fungal (Mixed With Bacteria)	18	2	16
3. No Organisms Isolated (Sputumless Pts)	20	20	0

Table 8. Infective organisms isolated in pulmonary infections with the type of Acute Leukamia and their outcome

Sl. No	Organisms Isolated	Total No. of Episodes (56)			Adults						Children					
					ANLL			ALL			ANLL			ALL		
		E	R	D	E	R	D	E	R	D	E	R	D	E	R	D
1	Pure Bacterial Infection	18	16	2	6	4	2	2	2	0	3	3	0	7	7	0
2	Fungal (Mixed With Bacteria)	18	2	16	14	01	13	3	0	3	0	0	0	1	1	0
3	NO organisms Isolated (Sputumless Episodes)	20	20	0	3	3	0	5	5	0	0	0	0	12	12	0

E= No. of Episodes, R= No. of Recovered, D=No. of Deaths

DISUSSION

Sputum culture positivity is regarded traditionally, as not useful for the diagnosis of pulmonary infections in acute leukemias. Isolation of an organism from sputum is virtually diagnostic of the pulmonary infection, especially in immunosuppressed patient who have prolonged granulocytopenia and who receive protracted courses of antibiotics [10,11]. Sputum less patients were treated empirically with broad spectrum antibiotics and antifungal agents.

In patients with acute leukemia, prolonged granulocytopenia is the major risk factor for developing pulmonary infections [12,13]. In our study, all patients were granulocytopenic and most of them (33 patients-59%) had Grade- II neutropenia.

The commonest organism that cause primary infection in the immuno - compromised host is the same as in the normal immunocompetent host, for example streptococcus pneumoniae or Haemophilus influenzae causing pneumonia. In the present analysis Group A streptococcus (58.3%) was the commonest bacterial

organism isolated. Other workers also found similar results [14-16]. Several investigators have noted a high incidence of fungal infections in patients with acute leukemia. Extensive use of broad spectrum antibiotics, steroids and anti-leukemic drugs have been implicated as the predisposing factors to fungal infections [17-21]. The fungal infections most commonly found were candida and aspergillus. This was also so in our cases. The pattern of radiological presentations in our study were similar to that reported by others, Lobar consolidation being the commonest [22,23].

Early initiation of treatment for pulmonary infection may decrease the morbidity and mortality with the need for establishing diagnosis early, a test with good specificity and ease of performance would be advantageous. In view of this, positive sputum culture (Bacterial and fungal) as a valid diagnosis criteria is suggested in immuno suppressed patients who have clinical and radiological evidence of pulmonary infection.

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