Bronchoalveolar Lavage (BAL) and Tropical Lung Disease

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Abstract
The advent of fiberoptic bronchoscopy permitted bronchoalveolar (BAL) to become an easily performed well-tolerated diagnostic and investigative tool. The technique has opened up a helpful new window to the lungs. Changes in the quantity and pattern of BAL fluid and analysis of cells, cytokines have enabled us to broaden our understanding of respiratory and multisystem disorders. For obvious reasons of cost and availability he technique, to a large extent, has remained limited to the developed world and the vast tropical and subtropical land masses have not had benefit of BAL analysis. Although many investigators have reported the range and cellular content of Bal fluid in normal individuals, the usefulness of such an evaluation in tropical lung diseases is over due.

Key-words: Bronchoalveolar lavage (BAL), Paragonimiasis, tropical eosinophilia, leptospirosis, Bronchial Lavage (BAL) in Tropical Lung Disease

In tropical medicine, perhaps more than any other medical specialty, a complete history and physical examination are of paramount importance. In an average outpatient department, 20-40% of patients come with respiratory complaints; whereas, 20-30% of hospital medical admissions are for disorders affecting the lungs. When medicine is practiced in rural areas of Asia and Africa, with little or no laboratory tests and radiological facilities, medical acumen is the only tool used in establishing the correct diagnosis. In a poor country chest x-ray films are expensive; a single chest x-ray film may cost as much as much more the entire health budget for a year for four people. Even when a few of

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the modern diagnostic technologies are readily available, the clinician should learn to use them with discretion. It is neither helpful nor economical to obtain a chest x-ray in order to demonstrate what can clearly be deduced from history and physical examination including e.g., pulmonary consolidation, pleural effusion, sputum-positive tuberculosis. Bronchoalveolar lavage (BAL) is a basic technique used to collect cells and non-cellular material from the surface of the respiratory tree. Although various conduits have been used to obtain BAL samples, the fiberoptic bronchoscope is the most common. Since its introduction in the 1970, particularly in the developed countries, BAL has become an important tool for diagnosing, assessing activity, and monitoring a large number of pulmonary diseases. The instrument is expensive, but each procedure can be performed with minimal expense. BAL and brushing can identify acid-fast bacilli in sputum-negative patients, Pneumocystis carinii, fungi, parasites, and foreign-body particles. Although, a physician can quite readily learn the procedure after a period of instruction by an expert, the value of BAL is limited by the quality of laboratory facilities. BAL is useful in the following tropical lung diseases.

1. Bacterial infection

(a) Tuberculosis
More than 8 million new cases of tuberculosis occur each year, nearly 95% are in developing countries. The acquired immune deficiency syndrome (AIDS) epidemic has had a major impact on the incidence and clinical manifestations of tuberculosis. Because tuberculosis is common disease, especially among HIV-infected individuals, many patients with other chronic respiratory illnesses suffer from unwarranted lengthy therapeutic trial of anti-tuberculosis drugs. In South Africa as many as half of the patients considered “unresponsive pulmonary tuberculosis”, seen in a tuberculosis hospital, did not have tuberculosis; the correct diagnoses included non-tuberculous bronchiectasis, lung abscess, congenital cystic lung, hydatid disease, sarcoidosis, and foreign bodies. Diagnosis of tuberculosis is confirmed by sputum examination. Typically 10,000 organisms per ml of sputum are needed for smear positivity. Bronchoscopic examinations including washings, brushings, and biopsy specimens establish the diagnosis in 55-96% (average rate of 725). In a study of 1734 patients who had bronchoscopy and bronchial cultures 8.3% had tuberculosis; amongst those who with tuberculosis, 82.6% had positive bronchial cultures. The positive BAL cultures was the only means of diagnosis in 44% of the patients. Transbronchial biopsy increases the diagnostic yield by identifying caseating granulomas.

(b) Melioidosis
Melioidosis is caused by Burkholderia pseudomallei, a gram-negative aerobe and facultative anaerobe that occurs in muddy water and soil in the endemic areas in Vietnam, Cambodia, Laos, Thailand, the Philippines, India, Malaysia and Australia. It causes both acute and chronic, un-resolving pneumonia, particularly affecting the upper lobes. The infection may remain dormant and reactivate only during periods of stress and immunosuppression, particularly the HIV-infection. Tuberculosis, fungal diseases, lung cancer, and paragonimiasis are in the differential di-
agnosis. Bronchoscopic biopsy, brushing and BAL provide material for culture and tissue to definitely rule out tuberculosis, cancer, and other granulomatous diseases.\(^7,8,9\)

(c) Leptospirosis
Leptospirosis is a re-emerging tropical disease with large epidemics all around the world. The disease, caused by a spirochete of the genus Leptospira, has the clinical spectrum that ranges from sub-clinical benign illness to fatal respiratory failure. The disease has two classical forms of presentation: icteric and anicteric. The anicteric form is common, benign, and self-limiting; whereas, the icteric form tends to be multisystem with a mortality rate of 15% or more. Hemoptysis, the main pulmonary symptom, varies from a blood-tinged sputum to a fatal massive alveolar hemorrhage. The radiographic pattern is similar to that of alveolar hemorrhage caused by other conditions. Alveolar bleeding, due to diffuse capillary damage, is present in almost all cases with signs of pulmonary involvement and in 70% of those without any pulmonary signs. Serology with macro- or microscopic agglutination is the most common way of diagnosing leptospirosis. A four-fold increase in titers between paired sera is accepted in confirming the current case. Detection of specific IgM antibodies by ELISA is more sensitive than the detection of agglutinating antibodies. The definitive diagnosis depends on finding Leptospira in blood, cerebrospinal fluid, or BAL fluid cultures. Leptospira can also be detected by dark-field examination of bronchoalveolar lavage fluid. PCR methods have been applied to rapid detection of Leptospira DNA in specimens of serum, urine, CSF and aqueous humor.\(^10,11,12\)

(d) Brucellosis
Brucella melitensis has a worldwide distribution but found predominantly in Middle Eastern and Mediterranean countries. The infection is acquired by ingestion, inhalation, and by skin. Pulmonary infections occur after ingestion of the bacteria with resulting septicemia and pulmonary involvement. Pulmonary findings include cough, pleuritic chest pain, and fever. Miliary infiltrate, nodules, consolidation, hilar adenopathy, and pleural effusion have all been reported. The organism has been isolated from sputum; however, there is no clear role for bronchoscopy.\(^3\)

2. Fungal infection
(a) Cryptococcosis
Cryptococcus neoformans is a fungal infection acquired by inhalation of the organism commonly found in pigeon droppings and in geographic areas that support growth of the red river gum tree (sub-Saharan Africa, Southern California). Most pulmonary infections are asymptomatic and self-limiting in immunocompetent host. The disease may be difficult to diagnose because fungal smears and cultures of expectorated sputum are positive in less than 25% of patients. In immunocompromised hosts the diagnosis of cryptococcosis can be made in more than 90% of patients. Transbronchial biopsies are diagnostic in less than 35%, cultures of BAL fluid are positive in 60-90% of patients. Cytologic studies of BAL fluid demonstrates the organism in 36-62% of the cases. The latex agglutination assay for cryptococcal antigen is highly sensitive and may be present in more than 90% of immunosuppressed patients with pulmonary cryptococcosis.\(^13,14,15\)
(b) Histoplasmosis
It is a common fungal infection with a broad spectrum of pulmonary manifestations ranging from acute pneumonitis, disseminated military disease, extensive calcifications, fibrosing mediastinitis, and cavitations. Serologic tests may be useful, but BAL and biopsy are more sensitive and easily available. In patients with disseminated disease, particularly in AIDS patients, detection of Histoplasma antigen in urine by enzyme immunoassay is a sensitive and specific test. Bronchoscopy established the diagnosis in 71 of 469 patients with histoplasmosis. In 11% of these, bronchoscopy was the only diagnostic method.

(c) Coccidioidomycosis
Caused by Coccidioides immitis, this fungal infection has numerous pulmonary manifestations, but most patients do not require any treatment. Two skin antigens, coccidioidin and spherulin are available. Skin tests are most beneficial in patients who are not from the endemic areas, but have recently travelled through the endemic area, and have symptoms consistent with acute clinical syndrome with erythema nodosum and pulmonary infiltrates. BAL and a transbronchial lung biopsy may show typical cocci spherules clinching the diagnosis particularly in immunosuppressed patients with diffuse lung disease. BAL fluid should always be sent for cytology (Papanicolaou stain), fungal stains (KOH, silver stain) and culture.

(d) Pneumocystis jiroveci (carinii)
Is a common cause of severe pneumonia among immunosuppressed patients both in tropical and temperate countries. The epidemiology of the disease has changed with the HIV epidemic. Common symptoms include fever, dry cough and dyspnea. Diagnosis is established by nebulized sputum and BAL fluid examination. Both silver stains and direct fluorescent antibody test are useful for detecting the organism. Transbronchial lung biopsy may be utilized if the BAL examination is negative and the diagnosis is in question. Bronchoscopic examinations have a sensitivity of 55-95%.

3. Parasites (Table I)

(a) Amebiasis
Entamoeba histolytica infests approximately 10% of the world’s population. It is the third leading parasitic cause of death worldwide. 90% of patients are asymptomatic; 10% have amoebic colitis. Other organs, particularly the liver, lung, and CNS are involved in 2-20% of patients. The different forms of pleuro-pulmonary amebiasis include:

(i) Hematogenous pulmonary involvement without hepatic abscess.
(ii) Independent hepatic and pulmonary involvement
(iii) Direct extension of the liver abscess into the lung pleura or pericardium. Most patients with pulmonary disease have negative stool studies. Sputum examination or BAL may demonstrate trophozoites and establish the diagnosis; role of BAL is limited. The sensitivity of pleural fluid test is less than 10%. Serologic diagnosis with ELISA is useful.

(b) Schistosomiasis
Schistosomiasis, also called bilharziasis, is one of the most prevalent infectious diseases in the world. It is endemic in more than 70 de-
Table 1. Pulmonary symptoms caused by common parasites

<table>
<thead>
<tr>
<th>Species</th>
<th>Cough</th>
<th>Wheezing</th>
<th>Dyspnea</th>
<th>Pnunonitis</th>
<th>Hemoptysis</th>
<th>Chronic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascaris</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>–</td>
</tr>
<tr>
<td>Hookworm</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Strongyloides</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Visceral larva migrans</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Pneumocystis</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Toxoplasma</td>
<td>+</td>
<td>–</td>
<td>+++</td>
<td>+++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Entameba histolytica</td>
<td>++</td>
<td>–</td>
<td>+++</td>
<td>+++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Filaria</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Schistosoma</td>
<td>++</td>
<td>–</td>
<td>++</td>
<td>++</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Paragonimus</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>+++</td>
<td>+++</td>
<td>–</td>
</tr>
<tr>
<td>Echinococcus</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

– Usually absent; ++++ Key symptom

Table 1I. Acute and chronic pulmonary schistosomiasis

<table>
<thead>
<tr>
<th>Features</th>
<th>Acute pulmonary disease</th>
<th>Chronic pulmonary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset after exposure</td>
<td>Weeks (4-8)</td>
<td>Years</td>
</tr>
<tr>
<td>Population at risk</td>
<td>Non-immune (travelers)</td>
<td>Immune (living in endemic areas)</td>
</tr>
<tr>
<td>Pathogenesis</td>
<td>Immune-complex disease</td>
<td>Glanuloma formation</td>
</tr>
<tr>
<td>Clinical features</td>
<td>Cough, fever, eosinophilia</td>
<td>Dyspnea, cor-pulmonale</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>Nodules, infiltrates</td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Ova in stools and urine</td>
<td>Ova in stools, urine, lung biopsy tissue</td>
</tr>
<tr>
<td>Serology</td>
<td>Helpful</td>
<td>Unhelpful</td>
</tr>
<tr>
<td>Treatment</td>
<td>Praziquental, Arthemeter</td>
<td>Arthemeter</td>
</tr>
<tr>
<td>Outcome</td>
<td>Good</td>
<td>Only partially reversible</td>
</tr>
</tbody>
</table>

developing countries. The most prevalent area is Africa. The number of people affected is more than 200 million. Although the lungs are not an end organ in the life cycle of schistosome infection in man, lung can be involved. Early and late pulmonary Schistosomiasis are two different types of disease with different clinical and radiological man-
N. Cotrim et al.

1. Introduction

Pulmonary eosinophilia is a clinical syndrome characterized by the presence of a high number of eosinophils in the blood or sputum, with no apparent cause. It is often associated with various infections, particularly helminthic parasites.

2. Helminthic pulmonary eosinophilia

(a) Strongyloides stercoralis

Strongyloides stercoralis is a roundworm that infects the human small intestine and can cause a chronic, recurrent infection. It is characterized by eosinophilia, pulmonary infiltrates, and skin lesions.

(b) Schistosoma spp.

Schistosoma is a genus of parasitic trematodes that infect humans and cause liver and lung problems. It is transmitted through snails and can cause pulmonary eosinophilia.

(c) Paragonimiasis

Paragonimiasis is a lung fluke disease caused by the ingestion of undercooked crustaceans. It is endemic in Asia and is characterized by eosinophilia, pulmonary infiltrates, and eosinophilic pneumonia.

(d) Echinococcosis or Hydatid Cyst disease

Echinococcosis is a parasitic infection caused by the Echinococcus granulosus or Echinococcus multilocularis worms. It can cause pulmonary lesions, and the diagnosis is often made through imaging studies and serology.

3. Pulmonary eosinophilia and tropical lung disease

Bronchoalveolar lavage (BAL) and transbronchial biopsy have been used to diagnose respiratory infections in the setting of eosinophilia.

4. Pulmonary eosinophilia (PIE) syndrome

The association of pulmonary infiltrates and eosinophilia is recognized as pulmonary eosinophilia (PIE) syndrome. PIE results from the introduction of foreign material into the human body by different routes: ingestion, infection, inhalation, skin contact, and vaginal absorption. The parasitic causes of PIE are Filariasis, Strongyloides, Schistosoma, Ascariasis, Trichinellosis, Ancylostomiasis, and Paragonimiasis spp. The pulmonary infiltrates occur during larval migration through the lungs and are usually transitory. BAL during the stage may reveal eosinophils as well as larval parasites.
5. Tropical pulmonary eosinophilia
Can cause cough, wheezing, dyspnea, fever, night sweats, weight loss, fatigue, peripheral eosinophilia, and diffuse miliary or nodular pulmonary infiltrates. The disease occurs predominantly in males, with a male: female ratio of 4:1, mainly in ages of 15 to 40 years. It is caused by immunologic hyper-responsiveness to filarial parasites and is prevalent in filarial endemic areas of the world, especially South East Asia and South Pacific Islands. In many countries including India the efficient control of filariasis has drastically reduced the incidence of tropical eosinophilia.

Tropical granulomas
In the tropics there are numerous causes of pulmonary granulomas ranging from live replicating intracellular organisms (bacteria, mycobacteria, fungi, viruses) to non-replicating metazoans (helminths) to inanimate substances (metals, chemical agents) and organic (animal and plant proteins) antigens. Parasitic causes of lung granulomas are visceral leishmaniasis (kalaaz), metazoan tissue parasites such as Trichinella spp., nematodes such as Ascaris lumbricoides, Toxacara canis and trematodes such as Schistosoma mansoni.

Conclusion
The spectrum of tropical lung disease is vast. It is a significant cause of morbidity and mortality in the developing countries. Most of these illnesses are preventable if appropriate clinical and laboratory tools are available. Social upheavals, economic failures and political crusades have destroyed the infrastructure needed to provide the most basic medical necessity.

References