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Community Acquired Pneumonia - Radiological And Microbiological Diagnosis

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Abstract

This article addresses the role of radiological and microbiological tests in community acquired pneumonia (CAP). The main utilities include diagnosing the presence of CAP, assessing its severity and identifying the causative agent. Plain chest radiograph (CXR) remains the conventional imaging modality for establishing the diagnosis of CAP. However, it is not 100% sensitive and lacks specificity to identify the microbiological cause. Presence of specific patterns on CXR can suggest the likely etiological agent(s). Identifying the causative organism in blood and/or sputum cultures can help to narrow down the spectrum of antibiotic(s) to be used and thus reduce the risk of development of antibiotic resistance. However, problems with sample collection, storage, processing and isolation techniques limit their sensitivity and specificity. The etiology of CAP is often difficult to establish since the most effective methods are often invasive and serological methods yield results that are too late to be of any therapeutic use. Even after extensive evaluation, the causative agent remains unknown in about 50% of cases. Current recommendations therefore suggest that various microbiological and serological tests should be used only in patients with CAP who have severe disease, are hospitalized, have comorbidities and do not respond to empiric antibiotic therapy.

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Introduction

Pneumonia is a microbial infection involving the terminal airways and alveoli of the lung (1). Community acquired pneumonia (CAP) remains a common and serious illness with significant morbidity and mortality (2). In U.S. it results in more than 5 millions hospital admissions annually and is the sixth leading cause of death (3). The problem is even greater in developing countries where it is the most common cause of hospital attendance in adults (4). Despite its high incidence and availability of large number of studies on this common entity, there are still controversies about certain issues of evaluation and management. The cause of CAP is often difficult to establish. The most effective methods are often invasive and serological diagnosis is too late to be of any therapeutic use (5). It takes few days to identify the causative organism in blood or sputum and even after extensive evaluation, causative agent remains unknown in about 50% of cases (3,6). Diagnostic tests have a role in three aspects of CAP namely (i) to diagnose presence of CAP, (ii) to assess the severity and (iii) to identify the causative agent of CAP. This article addresses the radiological and microbiological tests for CAP.

Radiological Diagnosis

The reference standard for diagnosis of CAP is Chest X-ray. However it is not 100% sensitive and lacks specificity to identify the microbiological cause. Usually alveolar densities indicate presence of typical pneumonia (i.e. bacterial) and patchy or interstitial densities suggest atypical infection. But this categorization is not always accurate (7). Nevertheless they can suggest a microbiological differential diagnosis (Table 1).

Non-segmental air space (focal or lobar) pneumonia is seen on radiographs as homogenous consolidation having sharp demarcation. Patent large bronchi are seen as classical *air bronchogram sign*. The fissure may bulge if exudate is extensive. This is classically seen in Pneumococcus and *Klebsiella* infections. Necrosis (pulmonary gangrene) is seen as small lucent areas within consolidation; if extensive they may coalesce resulting in large cavity (Fig.1).

Bronchopneumonia classically caused by *Staph. aureus* is seen as focal, peribronchial or peribronchiolar areas of consolidation which may be bilateral (Fig.2).

Table 1. Radiographic Presentations of Common Etiologic Agents

Chest Radiographic Pattern	Pathogen
Focal; large pleural effusion	Usually bacterial
Cavitary	Bacterial abscess, fungal, acid-fast bacilli (AFB), *Nocardia*
Miliary	AFB, fungal
Rapid progression/multifocal	*Legionella,* pneumococcal, staphylococcal
Interstitial	Viruses, *Pneumocystis, Mycoplasma, C psittaci*
Mediastinal widening without infiltrate	Inhalation anthrax

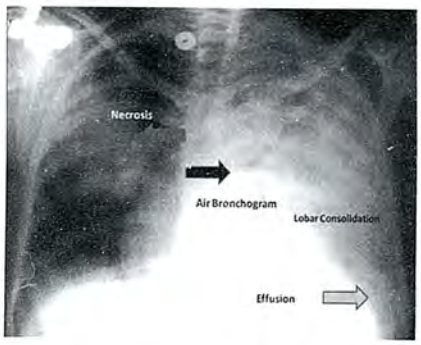

Figure 1

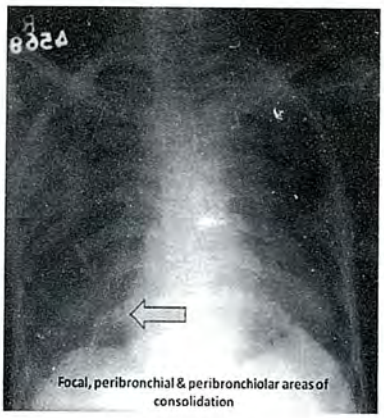

Figure 2

Interstitial pneumonia is seen as reticular or reticulonodular opacities. There may be prominent septal lines (Fig. 3).

Lung abscess is seen as single or multiple masses with cavitations which may have air fluid levels. The inner wall

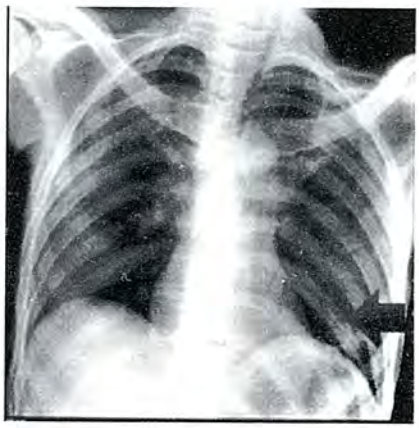

Figure 3. Interstitial pneumonia with ground glass haziness in *P. jirovecii* infection in a patient of AIDS

is relatively smooth with surrounding area of consolidation (Fig. 4).

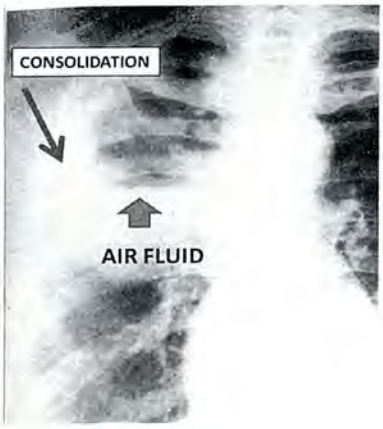

Figure 4

Fig. 5 depicts multiple small lung abscesses in both lung fields without air fluid levels usually seen with staphylococcal infection.

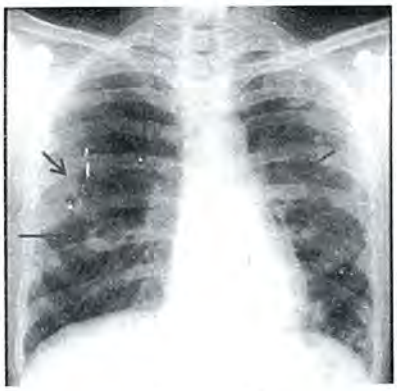

Figure 5

CT scan is not required in most cases. However it can be helpful in more complex situations such as strong suspicion of pneumonia clinically but no opacity on chest x-ray, complication of CAP like bronchial obstruction, lymphadenopathy or empyema, delayed resolution or in immunocompromised patients. Fig. 6 displays interstitial infiltrates with ground glass haziness more clearly seen than in Fig. 3. Further CT scan helps in excluding alternative diagnosis like pulmonary embolism.

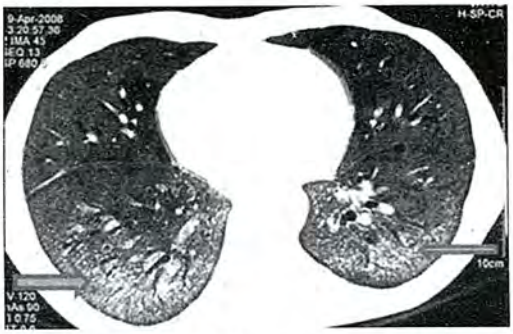

Figure 6. HRCT scan of the same patient as in Figure 3 showing clear-cut interstitial infiltrates (arrows)

Resolution of radiological opacities usually takes place in 10-14 days. In a series complete radiographic clearing of pneumonia occurred in 50% at 2 weeks and in 66.7% at 4 weeks (8). However a gamut of host and pathogen related factors affect resolution rates. Advanced age, smoking and various co-morbid conditions like diabetes, congestive heart failure, COPD, renal failure, malignancies, steroid use and immunosuppression all serve to delay resolution of pneumonic process (9). Likewise resolution was delayed in in-

hospital treated patients (Vs OPD patients), in patients with co-existent bacteremia and with multilobar involvement (9). Resolution time also varies depending uon the infectious agents causing pneumonia. Pneumococcal pneumonia usually gets resolved within 6 weeks whereas *Legionella* pneumonia may take 2-6 months to resolve. *Mycoplasma* infections usually resolve quicker than pneumococcal infections (10).

Radiography also provides a clue to the severity of the disease. Multilobar distribution and presence of complicating factors like pleural effusion and abscess formation indicate severe disease. It should be however noted that radiographic manifestations of chronic diseases such as congestive heart failure, COPD or malignancies may confound the infiltrate of pneumonia.

Microbiological Tests

Ideally speaking, identification of causative agent of pneumonia has many beneficial implications. It results in targeted narrow spectrum antibiotic treatment and hence less chances of antibiotic resistance, determines appropriate duration of treatment and provides accurate data for epidemiological studies. But because of delay in initiating treatment, various complications of invasive procedures in collecting samples and often unneeded antibiotic changes their cost effectiveness is debated. Currently available diagnostic tests for microbiological diagnosis include Sputum Gram Stain, Blood Culture, Sputum Culture, Serological studies, Antigen studies, Polymerase Chain Reaction (PCR).

These tests may be carried out on expectorated sputum or material obtained by invasive methods such as bronchoscopy on transthoracic needle aspiration of lung.

Sputum Gram Stain

The value of sputum gram stain is considerable but controversial. It is a cheap, readily available and rapid technique that may provide a tentative identification of pathogen and helps in guiding initial use of antibiotics. The main problem with gram staining of sputum is that due to contamination from upper respiratory tract sputum may not accurately represent lower respiratory tract infection. Murray and Washington (11) have suggested that presence of <10 squamous epithelial cells and >25 PMN's per low power (10X) field in sputum specimen is highly suggestive of secretions from lower respiratory tract. Interpretation of findings of gram stain is also difficult.

Sputum positivity has been defined on finding a predominant organism, an organism present in greater than 10 oil immersion fields, an organism that account for >50% of those seen or a combination of last two criteria (12). Some organisms like *Haemophilus* and *Neisseria* are difficult to identify on gram stain. Moreover gram stain fails to detect atypical organisms. Keeping in view these drawbacks, sputum gram stain should be used in a targeted fashion particularly in patients with severe CAP, immunosuppression, or in those who fails to respond to initial antibiotic treatment.

Blood Culture

Blood culture has low diagnostic yield (5-16%) (13) but high specificity. It must be done before the start of treatment. As many cases of CAP are due to mixed infections, it also misses the co-infection with atypical agents. Despite these limitations ATS & IDSA recommend that blood culture should be included in diagnostic work up if patient requires hospital admission.

Sputum Culture

This procedure encounters same problems as with gram stain such as inability of many patients to expectorate sputum and contamination of sputum with oropharyngeal secretions. This leads to low sensitivity and specificity of sputum culture results. Also isolation techniques for atypical pathogens and viruses are not easily available. To improve sensitivity and specificity of culture results comparison with gram staining is advisable. Although washing of sputum with saline before culture and quantitative culture techniques have been advocated by some, they are time consuming and are not widely available (12).

Serological Studies

These tests are more relevant for atypical pathogens like *Legionella, Mycoplasma* & *Chlamydia* which are not detectable by gram stain or routine cultures. They add little to management decisions because to be positive they require a four fold rise in acute and convalescent phase sera. Their main value is in collection of epidemiological data.

Antigen Studies

Various tests are available which can be performed on sputum, urine or serum. Prior antibiotic therapy does not affect results and they remain positive long after treatment. But these are rapid, simple and have high specificity. Urinary antigen test for *L. pneumophilia* type I has sensitivity of 70% & specificity of 100% (14). These tests are also available for *S. pneumoniae* and can be performed on sputum, urine or serum and its specificity is >90%.

Polymerase Chain Reaction

It can detect even minute quantities of organisms in various samples like sputum or serum. The results are not affected by prior antibiotic therapy. Also it can detect the antibiotic susceptibility of microbes by noting differences in DNA sequences of antibiotic susceptible and resistant strains. However it is a complex and time consuming technique which is not easily available. False positive results may be obtained if contamination occurs in laboratory or from upper respiratory tract. Until recently the only PCR assay for respiratory pathogens that was approved by US FDA was for diagnosis of *M. tuberculosis* on specimens which are positive for AFB (9). FDA has recently approved a new PCR assay for detection of all serotypes of *Legionella* in sputum (IDSA/ATS 2007) (15). Still in the developmental stage, PCR may become the ideal diagnostic test for CAP giving accurate identification of pathogen & finding its antibiotic susceptibilities.

Invasive Procedures

These include thoracocentesis, transtracheal aspiration, fibreoptic bronchoscopy, transthoracic needle aspiration, open lung biopsy and thoracoscopic biopsy. Generally they require consideration of risk-to-benefit and cost-to-benefit ratio and are reserved for patients with severe CAP particularly who are immuno-compromised. Thoracocentesis is required in patients with significant pleural effusion regardless of severity of CAP.

Recommendations

As already mentioned the diagnostic tests for CAP fall into three categories helping in diagnosis, assessment of severity and identification of causative agent. If a patient is suspected of having CAP, he/she should have a chest x-ray to confirm the diagnosis. Assessment of severity should be done using Chest x-ray, CBC, blood chemistries, oxygen saturation and blood gas analysis. As most patients do well on empirical treatment (16), there is absence of any statistically significant difference in mortality rates or duration of hospital stay between those receiving pathogen directed and those receiving empirical therapy (17). Because of lack of an ideal test till date, the identification of causative agent is the most difficult and controversial aspect. The intensity of diagnostic work up should take into account the following aspects: (1) severity, (2) response to treatment, (3) level of immune competence and (4) factors related to patients and environment. A general guideline is presented. (Table 2)

Table 2 : Diagnostic Tests for CAP (15)

Patient Category	Chest x-ray	Sputum Gram Stain & Culture	Blood Culture	Urinary Legionella/ Pneumo. Antigen	Serologic studies	Invasive Procedures
Ambulatory	√					
Hospitalized	√	√	√			
Severe CAP	√	√	√	√	?	?
Immuno-compromised	√	√	√	√	?	√
Treatment Failure	√	√	√	√	?	√

? = may be appropriate depending on clinical picture

Conclusion

Diagnostic tests play an important part in evaluation and management of CAP. There is still a lack of ideal diagnostic test for microbial diagnosis but when applied to properly selected group of patients, these tests may prove more cost-effective.

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