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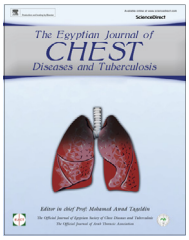

ORIGINAL ARTICLE

Perplexing pneumonia: Early anticipation and outcome

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KEYWORDS

Pneumonia;
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Abstract *Background:* Delayed resolving pneumonia represents a perplexing diagnostic dilemma. Many methods can lend a hand in diagnosis; however prediction of such a problem wishes a more precision.

Objectives: Define to what extent early anticipation of underlying causes of delayed resolving pneumonia via clinical, radiological and bronchoscopic markers would modify management plan and affect their outcomes.

Patients and methods: Prospective clinical study was conducted on 122 patients with delayed resolving pneumonia. They underwent chest X-ray, thoracic ultrasound, chest computed tomography (CT) and fiberoptic bronchoscopy (FOB). Tissue biopsy was taken for pathological examination.

Results: Studied cases were divided into two groups: group I included 58 patients with malignant etiology (49 cases with lung cancer and 9 cases with pulmonary metastasis) and group II included 64 patients with nonmalignant etiology (nonspecific pneumonia in 42 cases, specific forms of pneumonia in 14 cases, pulmonary sequestration in 4 cases and traction bronchiectasis in 4 cases). Sensitivity of clinical and CT chest markers of malignancy was 72.36% and 53.45% respectively however their specificities were 20.62% and 59.38% respectively. Thoracic ultrasound showed the highest sensitivity (75.86%) but lowest specificity (17.19%). FOB markers of malignancy were significantly higher in malignant than the non-malignant group ($p = 0.001$). Summation of clinical, FOB, CT chest and sonographic markers increased the probability of malignancy in 67.2% and excluded malignancy in 71.8% of cases with a success rate of 69.7%.

Conclusion: Early anticipation of what beyond delayed resolution of pneumonia can assist in earlier verification of causes and supervising course and guard against consequences.

Introduction

Pneumonia which resolves slowly after appropriate antibiotic therapy can be problematic. Richard Winterbauer et al. had empirically defined slowly resolving pneumonia in

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immunocompetent patients as either less than 50% radiological clearing at 2 weeks or less than complete clearance at 4 weeks in a patient who has defervesced and symptomatically improved with antibiotic therapy [1]. Normal resolution of pneumonia is not easily defined. It can vary depending on the infecting organism and the host immune status. Patients typically note subjective improvement within 3–5 days of initiation of treatment. Knowledge about factors causing nonresolution, will help to avoid unnecessary invasive diagnostic procedures [2].

The expected time of radiographic resolution is influenced by both host factors and the culprit pathogen. In a later review, Fein and Feinsilver [3] defined "a minimum of 10 days of antibiotic therapy and a radiographic infiltrate that is not resolving in an 'expected' period of time based on the presumed diagnosis. These criteria are admittedly arbitrary and lack precision. Nonetheless, in some patients, delayed radiographic resolution reflects derangements in host defenses, obstructing endobronchial lesions, pulmonary malignancies, metastatic pulmonary process or myriad alternative causes (both infectious and noninfectious). When patients with suspected pneumonia fail to improve within the expected time frame or deteriorate, alternative causes or factors contributing to delayed resolution must be assessed [4].

One must ask whether the antibiotic is inappropriate (because of antimicrobial resistance; inadequate bioavailability, penetration, or pharmacokinetics; noncompliance). Has a sequestered site of infection been overlooked (e.g., abscess and empyema)? Is failure related to impaired immune or host defenses? Are nonbacterial causes possible (e.g., viruses, fungi, mycobacteria and protozoans)? Noninvasive (e.g., serologic) and invasive (e.g., bronchoscopy) techniques are useful in establishing a specific diagnosis [5]. Noninvasive studies may include serologies or urinary antigen assays for *Legionella* [6]. Tuberculin skin testing and sputum smears and cultures for acid-fast bacteria may be indicated in patients with risk factors or clinical features suggestive of *Mycobacterium tuberculosis* [7]. Epidemiologic clues (e.g., travel history, hobbies and exposures) may suggest exposure to endemic fungi (*Histoplasma capsulatum*, *Coccidioides immitis* and *Blastomyces dermatitidis*) or unusual pathogens (e.g., Q fever, tularemia, psittacosis, leptospirosis, etc.) [4], in this situation, radiological investigations in the form of CT chest thoracic ultrasound pulmonary angiography or aortography may be enrolled in solving this issue. Bronchoscopy, with appropriate cultures and appropriate serologies, should be done. In other context, pulmonary embolism, congestive heart failure, atelectasis, malignancies and a host of immune mediated syndromes can masquerade as pneumonia [8].

Distinguishing noninfectious causes of pulmonary infiltrates from infection may be difficult. Noninfectious disorders often present with a more indolent course, less striking clinical presentation, and nonpurulent sputum or nonproductive cough [9]. Routine laboratory tests do not discriminate pneumonia from disease attributable to noninfectious causes. Leukocytosis may be present in diverse immune-mediated disorders; conversely, leukocyte counts may be normal in pneumonias caused by viruses, atypical agents, or bacteria [10].

Delayed resolution of pneumonia may reflect underlying malignancy with or without endobronchial occlusion. Bronchogenic carcinoma should be suspected in patients with specific risk factors (e.g., smoking history, advanced age, hemoptysis, and absence of fever). Other malignancies may present as focal alveolar opacities (mimicking pneumonia) [12]. Bronchioloalveolar cell carcinomas [11] and primary pulmonary lymphomas or lymphoproliferative disorders, occasionally present with focal, alveolar lesions, hence lung biopsies are required to substantiate the diagnosis [13]. Presentation of lung cancer in the form of non-resolving pneumonia is rather an atypical one and high index of suspicion is required for its diagnosis, especially in the young [14].

Aim of work

Define to what extent early anticipation of underlying causes of delayed resolving pneumonia via clinical, radiological and bronchoscopic markers would modify management plan and affect their outcomes.

Patients and methods

This prospective clinical study included 122 patients admitted in the chest department, Mansoura University Hospital in the period from June 2013 to August 2014 with delayed resolving pneumonia beyond 2 weeks in spite of optimal antibiotic therapy. They were divided according to final diagnosis into two groups:

Group I: included 58 patients diagnosed and known to be of malignant etiology.
Group II: included 64 patients diagnosed and known to be of non-malignant etiology.

Exclusion criteria: Patients with:

- Pneumonia before 2 weeks.
- Non compliant patients.
- Malignant lung from the start.
- Known to be immunocompromised from the start.
- Contraindication of biopsy procedure (bleeding diathesis).

Final diagnosis included pathological diagnosis by CT or US guided biopsy thoracoscopic, bronchoscopic or open biopsies and patient follow up.

All cases were subjected to full history taking, clinical examination, routine laboratory investigations, fiberoptic bronchoscopy and radiological investigation in the form of chest X-ray, computed tomography CT chest and transthoracic ultrasound. Clinical markers of malignancy according to Ferrer et al. [15] were age more than 50 years, positive smoking history, absence of fever, history of previous malignancy and duration of illness >1 month. Bronchoscopic signs suggestive of malignancy adopted in our study according to Tsaubi et al. [16] were four types of tumor–bronchus relationships. First, if the bronchial lumen is patent up to the tumor. Second, if the bronchus is contained in the tumor mass. Third, if the bronchus is compressed by the tumor with intact bronchial mucosa. Fourth, if the proximal bronchial tree is narrowed by peribronchial or submucosal spread of the tumor or by enlarged lymph nodes. Computed Tomography (CT) markers suggestive of malignancy adopted in this study according to Arenas et al. [17] were pleural nodules, pulmonary mass, mediastinal lymphadenopathy, chest wall invasion, pleural nodular thickening >1 cm and pulmonary cavity with shaggy irregular wall. Thoracic ultrasonographic