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Review Article

What Does It Mean When a Child is Diagnosed with Pneumonia?

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Abstract

Pneumonia is a frequent diagnosis without adequate consideration of the etiology. Pneumonia implies the presence of inflammation of the lung parenchyma with consolidation. That inflammation may be from infectious or noninfectious causes. Radiologic diagnosis of pneumonia is subject to interobserver interpretation and may misdiagnose noninflammatory radiological opacifications as pneumonia. The common diagnosis of community-acquired pneumonia in children most commonly has a viral rather than bacterial etiology. Antibiotics should be reserved for those where the clinical course, laboratory measure of biomarkers, and radiology are consistent with the diagnosis of pyogenic bacterial pneumonia.

Keywords: Antibiotics, bacterial infection, pneumonia, pseudopneumonia, viral infection

Introduction

The World Health Organization (WHO) describes pneumonia as the single largest infectious cause of death in children worldwide.[1] Diagnosis of pneumonia is described by the WHO as "the presence of either fast breathing or lower chest wall indrawing where the child's chest moves in or retracts during inhalation." Under the heading, "Treatment," the WHO states, "Pneumonia should be treated with antibiotics." However, the same WHO document acknowledges that "Pneumonia is caused by a number of infectious agents, including viruses, bacteria and fungi."

The WHO therefore provides the clinician with ambiguous recommendations. Is the observation of fast breathing or thoracic retractions sufficient for decision-making of the diagnosis and treatment of pneumonia? Diagnosing by observing chest movement and treating unreservedly with antibiotics is not consistent with the acknowledgment of the various etiologies of pneumonia. This review of pneumonia presents 6 cases illustrating various examples of children diagnosed with pneumonia. These contrasting cases set the stage for an evidence-based discussion of pneumonia diagnosis and treatment. The result is a more nuanced justification for treating pneumonia with antibiotics that that recommended by the WHO.

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Cases with a Diagnosis of Pneumonia

Case number 1

An 8-year-old boy presents with acute-onset fever and left-sided chest pain. He appears toxic and has rapid breathing. There are mild intercostal retractions but no supra- or sub-sternal retractions. There are diminished breath sounds on the left [Figure 1].

He is treated with antibiotics. One week later, his X-ray looks worse and he is still febrile [Figure 1].

Diagnosis

Pyogenic pneumonia (most commonly *Streptococcus pneumoniae*) complicated by a parapneumonic pleural effusion.

Comment

This is a typical clinical course of *S. pneumonia* exhibiting rapid onset of high fever, toxic appearance, and tachypnea, but respiration is not usually labored. There is a risk of fatality if not treated with an antibiotic to which the organism is sensitive. The fever may initially improve from the antibiotic, and the

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patient may become less toxic in appearance before return of fever and increased radiologic opacification. This indicates a parapneumonic effusion. Although a parapneumonic effusion can be associated with fever, it is generally not infected and can eventually resolve on its own. A diagnostic tap can sample the fluid and determine if there is infection. If substantial mediastinal shift with increasing respiratory distress from compression of the right lung occurs, removal of the fluid may become necessary.

Case number 2

An 8-year-old girl presents with cough, low-grade fever, malaise, and sore throat for a week. She is alert and in no major distress. Chest X-ray shows infiltrates [Figure 2].

Diagnosis

Mycoplasma pneumonia.

Comment

This is a classic example of pneumonia from *M. pneumoniae*. While this will resolve on its own, more rapid improvement may occur from use of a macrolide antibiotic.

Case number 3

A 6-year-old girl presents with worsening cough for the past 2 days. It was preceded by rhinorrhea with an initial low-grade fever 3 days ago. She is now afebrile and not toxic appearing, but she has labored breathing. She has had multiple prior similar episodes and many diagnosed as pneumonia. She has intercostal and supra- and sub-sternal retractions. She has decreased breath sounds throughout but no localizing signs [Figure 3].

Diagnosis

Viral respiratory infection-induced asthma exacerbation manifested by hyperinflation and right middle lobe atelectasis.

Comment

This is a common presentation of a young child with an asthma phenotype characterized by recurrent exacerbations of asthma initiated by a common cold viral infection, rhinovirus being the most common. Wheezing may be absent where there is severe airway obstruction. Treatment with a bronchodilator aerosol will provide some short-term relief of symptoms, but a short course of an oral corticosteroid is important to stop progression and shorten the course. Antibiotics are not indicated.

Case number 4

A 3-year-old boy presents with tachypnea and cyanosis for several weeks with gradual worsening. He is afebrile, has mild intercostal, but has no supra- or sub-sternal retractions. Pulse oximeter reads 80%, and arterial blood pCO_2 is 30 mmHg [Figure 4].

Additional history identifies pink doves (a type of pigeon) raised in the front room of his house [Figure 4].

Diagnosis

Pigeon breeder's lung disease, an allergic alveolitis.[2]

Comment

Hypoxemia without ventilatory insufficiency is characteristic of interstitial lung diseases. There are multiple antigens that can cause allergic alveolitis. Ouchterlony double gel diffusion identifies precipitins to pigeon serum antigen [Figure 4]. Treatment requires avoiding pigeon exposure. He improved slowly to normal physiology once no longer exposed to pigeons. The radial diffusing serum containing high levels of pigeon-specific antibody in the center well meets and interacts with the radial diffusing pigeon antigens. Precipitation of antigen-antibody complexes occurs that is visible in the gel. Treatment requires avoiding pigeon exposure. Continuous or repeated exposure may cause pulmonary fibrosis.

Case number 5

A healthy infant had this chest film taken during a febrile illness that subsequently self-resolved [Figure 5].

Diagnosis

A chest CT identified left upper lobe agenesis.

Comment

This is an example of pseudopneumonia. No treatment is indicated. Disability is unlikely in the absence of other abnormalities.

Case number 6

A healthy infant had this chest film taken during a period of prolonged cough that subsequently self-resolved [Figure 6].

Diagnosis

This is thymus exhibiting a classic "sail sign." Another potential pseudopneumonia.

Comment

The thymus may be a visible part of the mediastinum in infants. The radiologic shadow can vary and occasionally requires a chest CT scan to distinguish it from a pathologic mediastinal shadow. Older literature attributed the thymus as a cause of respiratory distress under the diagnostic name of "thymus status lymphaticus."[3] That diagnosis has long since been discarded.

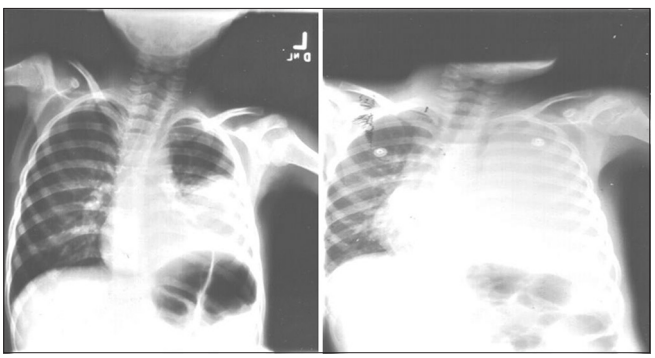

Figure 1: (left) First x-ray of Case number 1; (right) One week later.

What is "Pneumonia"?

Case number 1 is a classic bacterial pneumonia requiring urgent antibiotic treatment. A parapneumonic effusion can occur even when appropriate antibiotic treatment is provided. This child with bacterial pneumonia appeared toxic and was tachypneic. The clinical appearance of the patient justified the chest X-ray that demonstrated a consolidated left lower lobe. If measured, an elevated C-reactive protein (CRP), and procalcitonin would likely have been present.

Case number 2 is a typical clinical course of what used to be called atypical pneumonia that we know now is generally caused by Mycoplasma pneumoniae. Despite the segmental consolidation apparent on the chest X-ray, low-grade fever, and malaise, the relatively benign clinical appearance of this patient contrasts with the toxic appearance of the first case. Spontaneous improvement is typical but macrolide antibiotics may shorten the course.

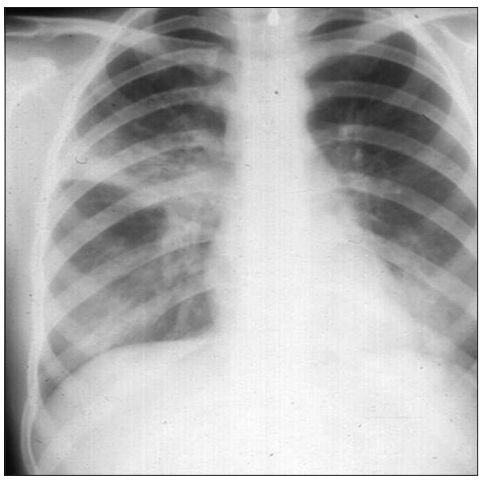

Figure 2: Chest X-ray of Case number 2.

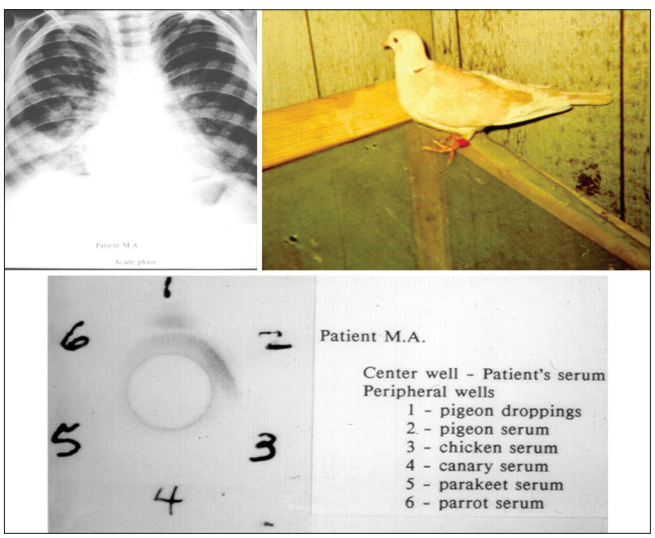

Figure 4: (upper left) Initial chest x-ray; (upper right) One of the pink doves, a type of pigeon, that were raised in the front room of their house; (lower) Ouchterlony double-gel diffusion plate with precipitin lines for pigeon droppings and pigeon serum.

Case 3 illustrates a child with recurrent episodes of increased work of breathing as manifested by suprasternal, substernal, and intercostal retractions. Those observations are consistent with airway rather than the parenchymal disease of pneumonia. Common cold viruses are the etiologic agents. In susceptible patients with this common asthma phenotype, rhinovirus and other common cold viruses cause inflammation of the airways resulting in airway narrowing from mucosal edema, excess mucous secretions, and bronchial smooth muscle constriction. The resulting airway obstruction causes increased work of breathing and expiratory wheezing. The inflammation typically does not involve the lung parenchyma, so a diagnosis of pneumonia is not appropriate. Opacities seen on chest X-ray are most likely from atelectasis resulting from mucous plugging of an airway. The lingula and right middle lobe are most commonly affected. The opacities from atelectasis are frequently misdiagnosed as pneumonia, but the clinical history and symptoms are consistent with airway, not parenchymal, disease from a respiratory viral illness.

Case 4 is an example of an interstitial lung disease. There are many causes of interstitial lung disease. The evidence

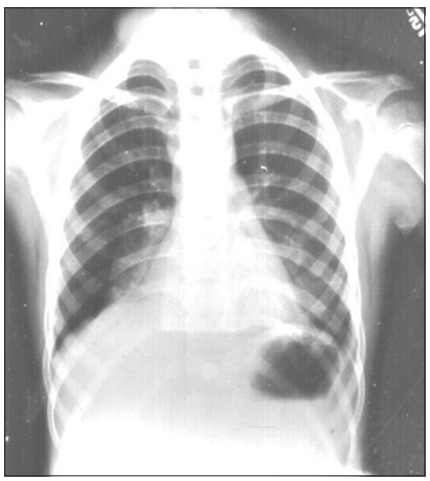

Figure 3: Chest X-ray of Case number 3.

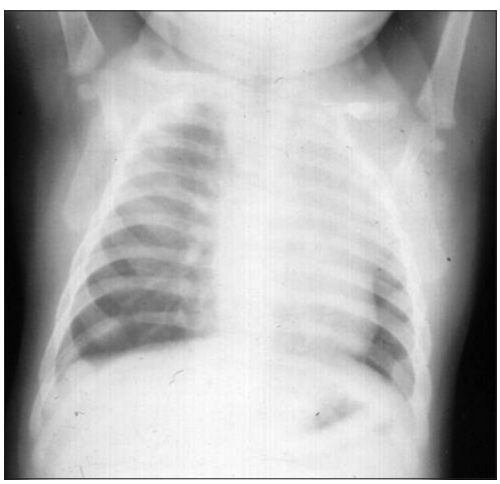

Figure 5: Ches X-ray of Case number 5.

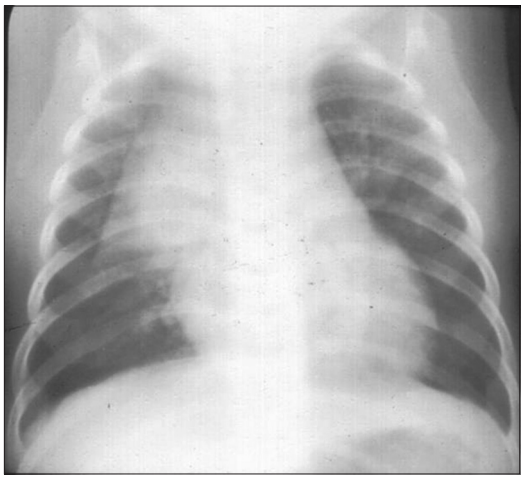

Figure 6: Chest X-ray of Case number 6.

Table 1: Pseudopneumonia areas of opacification on a chest film from consolidation not from inflammation of the lung parenchyma may result in misdiagnosis as pneumonia

Thymus	Atelectasis
Pulmonary sequestration	Pulmonary hemosiderosis
Bronchogenic cysts	Neoplastic disease
Lung agenesis	Congenital cystic adenomatoid malformation
Asthma	Congenital pulmonary airway malformation

Table 2: Descriptive terminology for pneumonia

By location	Epidemiological
Bronchopneumonia	Congenital
Lobar	Nosocomial
Segmental	Community acquired
Interstitial	Hospital acquired

While these diagnoses may have implications regarding the etiology, they lack the specific etiology that provides the best option for treatment

Table 3: Specific etiologic causes of pneumonia

Infections	Aspiration
viral	foreign body
bacterial	chronic aspiration
mycoplasma	acute hydrocarbon aspiration
chlamydia	
rickettsia	Hypersensitivity
fungal	allergic bronchopulmonary aspergillosis
protozoan	allergic alveolitis
spirochetal	

of precipitating antibody to an allergen that corresponds to environmental exposure identified an allergic mechansim as the cause of the parenchymal lung inflammation. The pneumonia in this case is known as allergic alveolitis from exposure to pigeon antigen.

Cases 5 and 6 illustrate opacities unrelated to any disease process that may initially be misdiagnosed as pneumonia based on a chest X-ray taken during an incidental illness. There are several of these radiologic observations that may initially be read as pneumonia [Table 1].

These cases illustrate that an opacity on a chest-ray cannot, by itself, make a diagnosis of pneumonia, nor can it identify the etiology of pneumonia if present. The inflammatory process that results in pneumonia may be from infectious agents or immunological reactions. The infectious agents may be viral, fungal, or bacterial infection. A treatment decision therefore ideally requires an etiologic diagnosis. The reality facing the clinician who encounters a suspected pneumonia is that there are many pneumonias. In addition to acute pneumonias there are chronic pneumonias, and pneumonias not caused by an infectious agent. Pneumonias are sometimes described in terms of anatomical location or epidemiological characteristics [Table 2]. While that descriptive term may have some utility in suspecting etiology, a specific etiology is more useful for providing the most specific treatment [Table 3].

What Causes Pneumonia?

A common diagnosis is "community-acquired pneumonia." That is defined as an acute infection of the pulmonary parenchyma in a patient who has acquired the infection in the community. For children, this essentially includes any previously healthy child where a diagnosis of pneumonia is made. A comprehensive assessment of the etiology of children with community-acquired pneumonia requiring hospitalization was performed at three hospitals in different major U.S. cities.[4] A viral or bacterial pathogen was identified in 81% of 2222 children with radiographic evidence of pneumonia. The radiographic evidence varied. Descriptions included the presence of consolidation (58%), linear and patchy alveolar or interstitial densities (51%), or pleural effusion (13%). Forty-five percent of the children were <2 years of age and 25% were of ages 2–4 years. Interestingly, 33% had asthma or asthma-like symptoms (Case number 3). At all ages, viral pathogens were identified as the major etiology associated with pneumonia in those children [Figure 7].

Respiratory syncytial virus (RSV) was the most common isolate in children <4 years of age and continued to be identified in older children. Human rhinovirus was the second most common isolate, only somewhat less frequent than RSV in children under 4 years of age. Rhinovirus was the most common isolate in the 5–9-year-old group and second in frequency only to *M. pneumoniae* in those 10–17 years old. *M. pneumoniae* became an increasing etiology of pneumonia with age. *S. pneumonia*, the most serious etiology, made up a small fraction of pneumonia at all ages.

Diagnosing Pneumonia

The diagnosis of pneumonia is commonly made or confirmed radiologically. While consolidation can certainly be seen

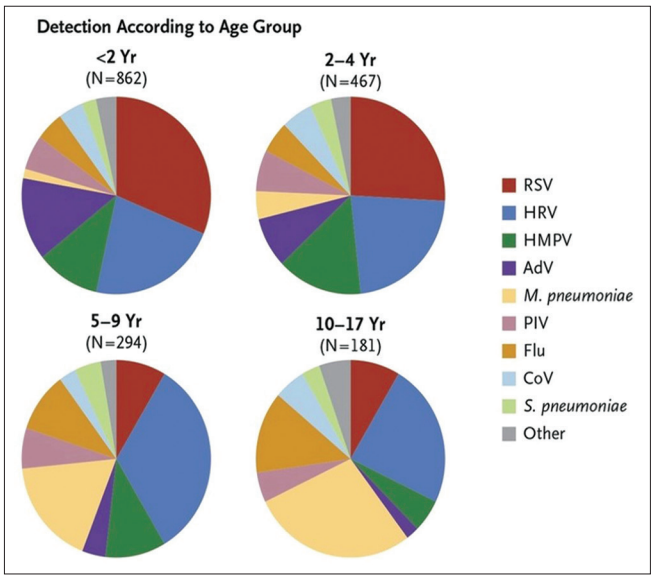

Figure 7: The proportion of pathogens for each age group. RSV: Respiratory syncytial virus; HRV: Human rhinovirus; HMPV: Human metapneumovirus; ADV: Adenovirus; *M. pneumonia*: *Mycoplasma pneumoniae*; PIV: Parainfluenza virus; Flu: Influenza A or B virus; CoV: Corona virus; *S. pneumonia*: *Streptococcus pneumoniae*.[3] Reproduced with permission from Jain S *et al*. N Engl J Med 2015;372:835-845.

radiologically, the best radiograms with the best radiologists can not identify inflammatory cells in the lung parenchyma, nor can the various etiologic agents be distinguished. A chest X-ray is essentially a shadowgram. Areas of localized atelectasis and anatomical anomalies may all result in opacities that could be misinterpreted as a pneumonic infiltrate [Table 1].

Moreover, there is a degree of subjectivity involved in the interpretation of chest X-rays. In an evaluation of the World Health Organization criteria for diagnosing pneumonia from a radiograph, this subjectivity was apparent in the lack of uniformity in interpretation, particularly for patchy and perihilar changes.[5,6] It is among children under age 6, the age with the highest frequency of pneumonia diagnoses, that the radiologic interpretation is most likely to suffer from such variability in interpretation. A critical commentary on chest radiographs for childhood pneumonia agreed that a negative chest film, i.e., the absence of consolidation, excludes pneumonia, but the presence of areas of consolidation alone should not dictate treatment.[7]

Over-diagnosing of pneumonia is common, especially among children under age 6. At a university hospital outpatient clinic in Turkey, 126 children diagnosed as pneumonia and prescribed antibiotics were subsequently reevaluated in a Pediatric Chest Disease Department of the same hospital.[8] That reevaluation determined that the diagnosis of pneumonia was not supported in 40% of the patients, and antibiotics were judged to be unnecessary in 85%. An observational study at four hospitals in India of 516 children under 5 years of age found that 43% had what was called "wheezy disease" consistent with asthma or bronchiolitis, neither of which requires antibiotics.[9]

Because of the history of a high fatality rate from pneumonia in less developed countries, especially before *S. pneumonia* and *Haemophilus influenzae* immunizations, the World Health Organization guidelines had recommended empirical treatment with antibiotics, based on the clinical presentation.[10] A placebo-controlled clinical trial of amoxicillin in children who met the criteria for that guideline was performed in 1126 Malawian children <6 years old.[11] Treatment failures were 4% and 7% in the amoxicillin and placebo group, respectively. No treatment failures by day 4 occurred in over 90% of the children, and there were no differences in the frequency of treatment failures or relapses by day 14 in those without treatment failures by day 4. Thus, most of the patients improved without antibiotics.[12] This was consistent with the relative infrequency of bacteria as a cause of pneumonia seen in the U.S., Turkey, and India.[4,8,9]

How to Determine Who to Treat

The question is not whether the child has pneumonia, as defined by radiologic imaging, but does the child have pneumonia due to bacterial infection. To identify those with bacterial pneumonia from the majority with viral etiology, efforts have been made to examine the value of biomarkers, white blood cell count and differential, C-reactive protein (CRP), and procalcitonin. Of those inflammatory markers, CRP values are significantly higher in the presence of bacterial infection, but some degree of overlap has been seen.[13] There is general agreement that procalcitonin is the most useful biomarker for identifying those with bacterial infection.[14]

Antibiotics therefore should be considered primarily after careful clinical assessment of how sick the child appears, the presence of fever, an elevated CRP, an elevated procalcitonin, and a radiologic image of a distinct lobar or lobular infiltrate. Fever and a toxic appearance may be the exception where antibiotics are appropriate without further initial assessment. While there also may be cases where the clinical and laboratory data are equivocal, the great majority of what has been called pneumonia does not justify more than supportive treatment without the use of antibiotics.

Summary

Pneumonia is a generic term for inflammation of the lung parenchyma with consolidation. Pneumonia may be acute or chronic, from various types of infectious or noninfectious causes or inflammation. Various respiratory diseases or abnormalities can be misdiagnosed as pneumonia. Few common acute pneumonias of children have bacterial infection. Overuse of antibiotics for "pneumonia" results from inadequate diagnostic consideration before a treatment decision. Identifying those patients with bacterial etiology of pneumonia is important because of the morbidity and occasional fatality that can occur from pyogenic bacterial pneumonia. A combination of clinical assessment, laboratory obtained biomarkers, and radiology can generally distinguish

pneumonia with bacterial infection requiring antibiotic treatment from the majority that are viral and not likely to benefit from antibiotics.

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Conflicts of interest

There are no conflicts of interest.

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