Diagnostic Approach to Pediatric Recurrent Pneumonia

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Abstract

Recurrent pneumonia (RP), i.e., at least two episodes of pneumonia in one year or three episodes ever with intercritical radiographic clearing of densities, occurs in 7.7%–9% of children with community-acquired pneumonia. In RP, the challenge is to discriminate between children with self-limiting or minor problems, that do not require a diagnostic work-up, and those with an underlying disease. The aim of the current review is to discuss a reasoned diagnostic approach to RP in childhood. Particular emphasis has been placed on which children should undergo a diagnostic work-up and which tests should be performed. A pediatric case series is also presented, in order to document a single centre experience of RP. A management algorithm for the approach to children with RP, based on the evidence from a literature review, is proposed. Like all algorithms, it is not meant to replace clinical judgment, but it should drive physicians to adopt a systematic approach to pediatric RP and provide a useful guide to the clinician.

Keywords: pediatric, recurrent, pneumonia

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Introduction

Lower respiratory tract infection (LRTI) is an inflammation of the airways (pulmonary tissue), due to viral or bacterial infection, below the level of the larynx. LRTI includes various diseases such as: bronchiolitis, wheeze-associated LRTI, bronchopneumonia, Lobar pneumonia and Empyema. LRTI is one of the serious illnesses requiring hospitalization especially in children under 5 years of age. It accounts for 30% of deaths annually worldwide mostly due to pneumonia as the leading cause [1].

Epidemiology

Pneumonia continues to be the biggest killer worldwide of children under five years of age. Although the implementation of safe, effective and affordable interventions has reduced pneumonia mortality from 4 million in 1981 to just over one million in 2013, pneumonia still accounts for nearly one-fifth of childhood deaths worldwide [2].

Furthermore, pneumonia continues to be the leading cause of morbidity for young children outside the neonatal period, particularly in low-and-middle-income countries (LMICs) [3]. Understanding the current epidemiology, and diagnostic and management strategies in these settings may improve preventive, diagnostic and treatment approaches.

Pneumonia is a major problem in children and has been estimated by the World Health Organization (WHO) to occur in around 156 million children (151 million in developing countries and 5 million in developed countries) resulting in 935,000 deaths each year. It has been estimated that Egypt has about 2 million cases of pneumonia every year and 42,000 Egyptian children under 5 years die every year with pneumonia [2]. Around 6% of infants experience at least one episode of pneumonia during the first two years of life [4].

Risk factors

Risk factors for pneumonia incidence and severity include:

• Infancy, lack of immunization.

• Malnutrition and chronic underlying diseases.

• HIV infection and HIV exposure in young infants.

• Young maternal age, low maternal education, low socio-economic status.

• Smoke exposure/indoor air pollution [5].

Aetiology

Pneumonia is caused by several infectious agents, including viruses, bacteria and fungi. The most common are the following:

• Streptococcus pneumoniae is the most common cause of bacterial pneumonia in children.

• Haemophilus influenzae type b (Hib) is the second most common cause of bacterial pneumonia.

• Respiratory syncytial virus is the most common viral cause of pneumonia.

In infants infected with HIV, Pneumocystis jiroveci is one of the most common causes of pneumonia, responsible for at least one quarter of all pneumonia deaths in HIV-infected infants.

The increased use of pneumococcal conjugate vaccine (PCV) and Haemophilus influenzae type b (Hib) vaccine has changed pneumonia aetiology, with Staphylococcus aureus and H. influenzae non-type b now the commonest bacterial pathogens and viruses most common as pathogens [6].

However, the identification of aetiological pathogens may be difficult as distinguishing colonizing from pathogenic organisms can be difficult on respiratory specimens and multiple co-pathogens are common [7].

Common aetiology of pneumonia in children in LMICs in table :

A. Bacteria	**Staphylococcus aureus** **Haemophilus influenzae** **Streptococcus pneumoniae** **Mycobacterium tuberculosis** **Bordetella pertussis** **Klebsiella pneumoniae**
B. Viruses	Respiratory syncytial virus Influenza , Parainfluenza virus Human metapneumovirus Adenovirus , Rhinovirus Measles, Herpes viruses – CMV, EBV
C. Fungi	*Pneumocystis jirovecii*

Transmission

Pneumonia can be spread in several ways. The viruses and bacteria that are commonly found in a child's nose or throat can infect the lungs if they are inhaled. They may also spread via air-borne droplets from a cough or sneeze.

In addition, pneumonia may spread through blood, especially during and shortly after birth. More research needs to be done on the different pathogens causing pneumonia and the ways they are transmitted, as this is of critical importance for treatment and prevention.

Prevention

Preventing pneumonia in children is an essential component of a strategy to reduce child mortality.

Preventive interventions that include childhood and maternal immunization, and optimizing nutrition are listed in Table . [8]

Recurrent Pneumonia

Definition

Recurrent pneumonia (RP) is defined as at least two episodes of pneumonia in one year or three episodes ever, with intercritical radiographic clearing of densities [9].

Sometimes, it is difficult to determine whether pneumonia is persistent or recurrent, unless there has been a symptom-free interval during which chest radiographs have documented clearing of the pneumonia infiltrations [10].

In RP, the challenge is to discriminate between children with self-limiting or minor problems, that do not require a diagnostic work-up, and those with an underlying disease.

Epidemiology

Recurrent pneumonia is a challenge for our children. Incidence data indicate that RP occurs in 7.7%–9% of all children with community acquired pneumonia [9].As a result , it represents a frequent presenting manifestation in the general pediatric practice and is a very common reason for referral to pediatric chest physicians [11].

There are limited studies in our locality that reported the prevalence of recurrent pneumonia in children, although Morcos et al ,2016 reported that 12% of children with pneumonia had the risk for developing recurrent pneumonia.

In another study ,El–Saied et al,2019 reported that approximately 1 in every 12 children with pneumonia had recurrent pneumonia with percentage of 12.61%.

Risk factors for recurrent pneumonia in children

Healthy children, particularly of a preschool age, are at risk of pneumonia during autumn and winter, when multiple respiratory viruses spread [12].

In the evaluation of children with RP, the first step is to distinguish between otherwise healthy “but unlucky” subjects, and those with an underlying disorder that requires further investigation.

A thorough diagnostic work-up is not required when: infections are self-limiting; other organs or systems are not involved; there are relatively long periods of clinical wellness, at least during the

summer; the child has normal growth and a normal physical examination; the family history for genetic or infectious respiratory disorder is negative; there is a quick response to treatment and a complete recovery after the episode [13].

The presence of any risk factor for RP should be ruled out by a careful recording of the clinical history (Table 1), as cases presenting risk factors may experience earlier and more severe episodes.

There are limited data on the underlying risk factors that predispose to the recurrence or persistence of pneumonia in children [14].Moreover, only few reports had studied this problem in developing countries [15].

Table (1): Risk factors for recurrent/persistent pneumonia in children.[16]

Condition	Proposed Underlying Mechanisms
Prematurity/ bronchopulmonary dysplasia	• Inadequate immunity due to low maternal antibodies levels. • Impaired lung function. • Altered innate immunoregulatory response of the lungs to respiratory pathogens secondary to neonatal hyperoxia
Atopy	• Defective innate immuresponse of epithelial cells • Interleukin 13-dependant reduced mucociliary clearance
Tobacco smoke exposure	• Neonatal low lung volume and impaired toll-like receptor-mediated immune response . • Suppressed phagocytic activity of neutrophils and monocytes/macrophage cells secondary to reduced production of oxygen radicals. • Increased bacterial adherence. • Impaired lung function

Over-crowding	Increased exposure to respiratory pathogens
Indoor and outdoor pollution	Distal bronchial and alveolar inflammation

Underlying causes of recurrent pneumonia in children

There are limited data on the underlying diseases which predispose children to recurrent pneumonia. However, few studies in the developing world have addressed this problem [17].

The underlying causes of RP in some studies were identified in more than 80% of children, It was due to recurrent aspiration, congenital malformations of the upper or lower respiratory tract , immunodeficiency, the presence of unusual organisms or resistant bacteria, neglected foreign body, defects in clearance especially cystic fibrosis or ciliary dyskinesia [18].

Localized intraluminal obstruction, extra luminal focal compression or congenital airway abnormalities should be suspected when densities recur in the same area. Neglected foreign body is the most frequent cause of intraluminal obstruction in children [19].

The occlusion of the segmental bronchus with mucus plugs may lead to recurrent pulmonary infiltrations. Middle lobe syndrome is the most frequent cause of focal RP in the clinical practice . Middle lobe syndrome is characterized by a spectrum of clinical and radiographic presentations, from persistent or recurrent atelectasis to bronchiectasis of the right middle lobe and/or lingula [9].

This is due to the fact that the middle lobe bronchus is relatively narrow and long, and arises from the bronchus intermedius with an acute angle. Moreover, it can be compressed by enlarged adjacent lymph nodes and no collateral ventilation is present between the middle lobe and other lobes, and this decreases the likelihood of reinflation after the development of atelectasis. In these patients, repeated episodes of infection/ inflammation and obstruction often institute a vicious cycle that may eventually lead to bronchiectasis. FOB and CT scan are important diagnostic tools for the diagnosis of middle lobe syndrome [18]. It is well recognized that the most common cause of right middle lobe syndrome is asthma [20].

Congenital structural airway anomalies include focal bronchomalacia or bronchial stenosis,Pulmonary sequestration, cystic adenomatoid malformation, and bronchogenic cysts represent the most frequent causes of bronchopulmonary malformations which may cause RP[21]. Although rare in childhood, endobronchial tumours (i.e., bronchial carcinoid, hemangiomas, papillomas, and mucous gland tumors) may result in RP [22].

Extraluminal compression may be caused by enlarged lymphnodes, and/or enlarged or aberrant vessels. Also, tuberculosis infection is re-emerging as a cause of severe pneumonia, that might also causes recurrent pneumonia [13].

A group of genetic disorders that primarily involve the respiratory tract and the host's defense against pathogens, i.e., cystic fibrosis (CF), primary ciliary dyskinesia (PCD), and primary immune defects (ID) may present with RP in different areas. When RP is associated with chronic wet cough, pancreatic insufficiency, rectal prolapse, electrolyte disorders, liver disease or nasal polyps, CF should be excluded by sweat chloride test and/or genetic analysis [23].

Suspected features of PCD include neonatal respiratory distress, situs inversus, persistent rhinorrhea, recurrent otitis media with hearing loss, chronic wet cough due to recurrent airway infections, and a positive family history for PCD [24].

The presence of severe infections in multiple organs (e.g., skin, gastrointestinal tract or pneumonia sustained by atypical bacteria or prolonged clinical course) indicate that immunodeficiency should be ruled out [25].

Bronchial asthma was reported as an important underlying cause of recurrent pneumonia in children [26]

A clinical clue to RP associated with Idiopathic pulmonary haemosiderosis is the triad of haemoptysis, diffuse parenchymal infiltrates on chest radiographs and iron deficiency anaemia [24].

Chronic neurological disorders frequently predispose to recurrent respiratory symptoms and signs [27], through many causative mechanisms as recurrent aspiration, secondary to gastroesophageal reflux and/or uncoordinated swallowing, and reduced mucociliary clearance, due to hypotonia and an impaired cough reflex that may be worsened by chronic administration of antiepileptic drugs [9].

Chronic aspiration may also result in the progressive loss of the cough reflex. Therefore, a careful history of recurrent choking should be recorded [28]. Finally, obesity in children which becomes a common problem, increases the risk of aspiration pneumonia [29].

Even after taking into account all of the possible underlying diseases, the etiology of RP in a proportion of children may remain obscure [19].

In a study in Egypt, The most frequent underlying causes for recurrent pneumonia in children were aspiration syndrome, followed by pulmonary TB followed by Bronchial asthma & congenital heart diseases [29].

In another study in Egypt, the most frequent underlying causes for recurrent pneumonia were congenital heart diseases followed by immunodeficiency diseases followed by bronchial asthma [4].

Causes of RP in the same lung lobe differs from RP that affects different or multiple lung lobes .The causes are summarized in figure 1 and table 2.

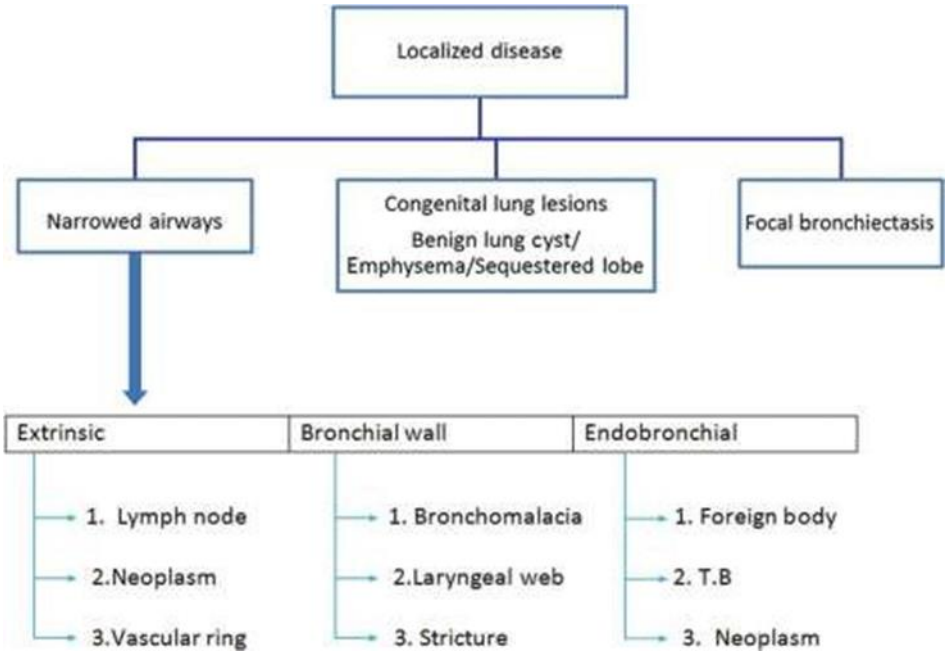


Figure (1): Underlying causes of recurrent pneumonia in the same lobe or segment [30]

Table(2):Underlying causes of recurrent or persistent pneumonia affecting different or multiple lung lobes [19].

Systemic Immune Disorders	• **Primary immunodeficiency** • **Acquired immunodeficiency**
Local immune disorders	subtle abnormalities of mucosal defense.
Genetic diseases	• Cystic fibrosis • Primary ciliary dyskinesia
Neuromuscular disorders	• Central neurologic disease • Peripheral nerve or muscle disease • Conditions causing weakness of expiratory muscles

Airway anomalies	• Post infective or idiopathic bronchiectasis • Multiple complete cartilage rings. • Generalized bronchomalacia
Major airway obstruction	Airway compression by enlarged heart or great vessels. Vascular rings and slings
Recurrent aspiration	• Severe gastro-esophageal reflux Isolated, late-presenting H-type fistula • Esophageal dysmotility syndromes • Laryngeal cleft
Recurrent pulmonary edema	cardiac left-to-right shunting; heart failure.
Autoimmune diseases	
Allergic bronchopulmonary aspergillosis	
Granulomatous lung disease	
Pulmonary hemorrhagic syndromes	
Drug toxicity	

Diagnostic Approach to pediatric recurrent pneumonia

Evaluation of patients with recurrent pneumonia is a challenge and requires an aggressive approach to prevent the delay in the diagnosis and treatment. Some children with RP do not need a thorough investigation, as pneumonia episodes are not frequent and/or severe, or they stop reoccuring over time.

Determining which case should be investigated relies on clinical judgment, a careful history and physical examination, whether the child is improving clinically and whether there is any pointers to the underlying condition. Several signs in the medical history or the physical examination suggest the presence of an underlying disease and thus should lead to a specific further investigations (Table 3).

Table (3): Pointers that should lead to further investigations in a child with recurrent pneumonia [19]

Abnormalities	Duration
Fever	2 – 4 days
Cough	4 – 9 days
Tachycardia	2 days
Hypotension	2 days
Tachypnea	3 days
Crackles	3 – 6 days
Leukocytosis	3 – 4 days
C-reactive protein	1 – 3 days
Chest X-Ray abnormality	4 – 12 weeks

There is no evidence base to inform the pulmonologists of the optimal timing of investigations or the optimal sequence of the diagnostic work-up in children with RP [31].

Ideally, the diagnosis should be confirmed or excluded with the minimum number of minimally invasive confirmatory tests. Some Patients may need laboratory tests to assess their immune status (i.e., blood cell counts, serum immunoglobulins, total IgE, IgG sub-classes, lymphocyte sub-populations, C3, C4, CH50, and specific antibody responses .

Sweat chloride test and genetic analysis for CF, 24-h esophageal pH monitoring, tuberculosis screening may be needed in suspected cases. Nasal fiberoptic endoscopy, nasal nitric oxide measurement, and ciliary motility/ultrastucture study may also be ordered [32].

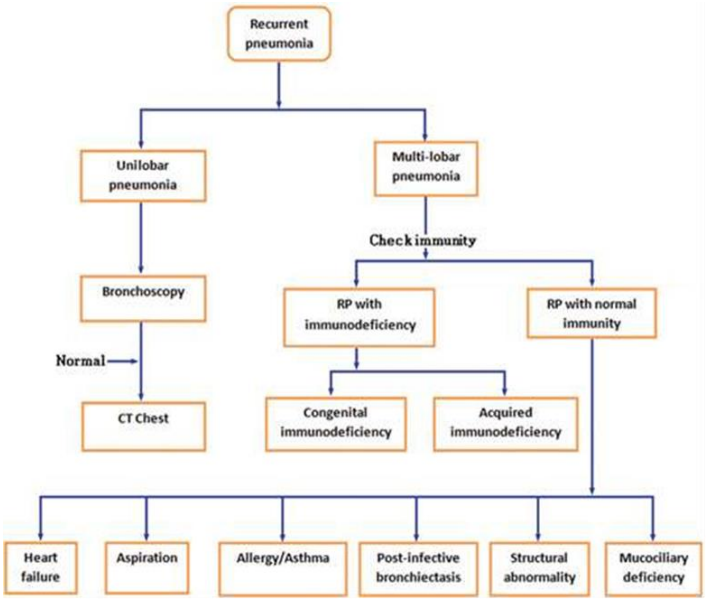
If the same lung lobe is involved in RP, or if recurrent abnormal localized chest findings are detected , diagnostic tests are indicated as chest X-Ray or high resolution computed tomography (HRCT), to

rule out focal parenchymal disease and fiberoptic bronchoscopy to exclude focal airway disease as neglected foreign bodies, intraluminal obstructions, mucus plugs or extrinsic compressions [13].

During bronchoscopy, samples from airways or alveolar spaces can be obtained for culture and cytological examinations.[33].

The differential diagnosis of RP involving different lung lobes is wide.Hence, the number of possible tests is great. Therefore, a targeted diagnostic approach based on clinical suspicion, driven by the clinical history and physical exam, is strongly recommended [19].

Diagnostic approach to identify the etilogy of recurrent pneumonia according to the lung lobes involved shown in figures 2 .



Figure(2):Diagnostic approach to identify the etiology of recurrent pneumonia according to the lobe involved [30]

Screening for pulmonary TB is very important. This includes sputum or gastric aspirate analysis, ZN staining and culture. Manteaux test and even bronchoscopy and bronchoalveolar lavage may be indicated. Flexible bronchoscopy helps in capturing the diagnosis by identifying endobronchial calcification and granuloma, which can be confirmed by cytology. In some cases, interferon gamma release assay (QuantiFERON) is available and would add an important diagnostic value.[34].

An echocardiogram is an essential tool for diagnosis of suspected congenital heart diseases or enlarged cardiac chamber compressing the bronchus that predispose to recurrent or persistent pneumonias [35].

Pulmonary function testing (PFT) can be applicable from the school-age. Much useful information can be obtained from spirometry, in addition to lung volumes, if the child is able to perform these

tests. However, PFT only provides a global assessment of lung function, contributes no clues to the specific contribution of each lung or lobe, and is not sensitive enough to distal airway diseases [36].

Pulmonary alveolar hemorrhage can be diagnosed by the presence of hemosiderin-laden macrophages at BAL. However, this test can not discriminate between the different causes of pulmonary bleeding. If there is no evidence of an underlying predisposing disease, the condition is usually considered to be idiopathic pulmonary hemosiderosis and a confirmatory lung biopsy is not required [37].

Screening tests as the erythrocyte sedimentation rate, circulating immune complexes, complement studies, rheumatoid factor, anti-neutrophil cytoplasmic antibodies, double-stranded DNA, and anti-glomerular basement membrane antibody (for children with pulmonary hemorrhage and renal disease) are indicated, if a connective tissue disease is suspected [13].

Diagnostic work-up for children with recurrent pneumonia is shown in figures 3.

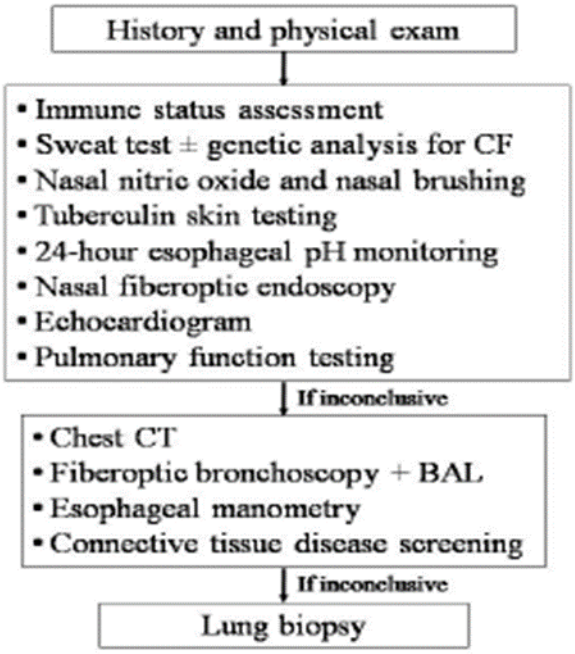


Figure (3): Diagnostic work-up for children with recurrent pneumonia [19]

Treatment

Recurrent pneumonia was considered as a risk factor for development of bronchiectasis in 6.7%- 8.5% of cases [38],so early and accurate diagnosis is essential , Also early treatment of the child's underlying condition is crucial in order to stabilize lung disease and thus prevent progressive pulmonary function deterioration [39].

Persistent Pneumonia

Definition

The term non resolving or persistent pneumonia (NRP) has been used to refer to persistence of radiological abnormalities beyond expected time of course [7]. It was also described as the persistence of symptoms and radiographic abnormalities in a LRTI child for over a month, despite a 10-day course of antibiotic therapy [8].

Slow resolving pneumonia (SRP) defined as pulmonary consolidation that persists for more than 21 days.

It is also defined as persistence of symptoms and radiographic abnormalities for more than 1 month ; however, some authors prefer to use the cut off of 3 months.

As there is no standard definition for NRP, the most accepted definition is the persistence of clinical symptoms and signs (cough, sputum production, with or without fever more than 100°F), failure of resolution of the radiographic features by fifty percent (50%) in two weeks or completely in four weeks on serial chest radiographs (indicated in at least 2 consecutive chest radiographs) in spite of antibiotic therapy for a minimum period of ten days, and sputum for acid fast bacilli (AFB) smear negative for two consecutive days [40].

Epidemiology

Persistent pneumonia or Non-resolving pneumonia (NRP) in children is a challenging issue to the pediatricians . It accounts for about 10% to 15% of nosocomial pneumonias and estimated to be responsible for approximately 15% of inpatient pulmonary consultation and 8% of pediatric bronchoscopies [40].

The mortality in persistent pneumonia increases three-fold in community acquired and five-fold in nosocomial pneumonia compared with global mortality in hospitalized patients [7].

NORMAL RESOLUTION OF PNEUMONIA

Normal resolution of pneumonia is difficult to define and the estimated resolution time is controversial [41].

It depends upon the underline causes. Patients typically note subjective improvement within three to five days of treatment; more specific clinical criteria for resolution include improvement in tachycardia and hypotension, which are expected to improve in two days; fever, tachypnea, and arterial oxygenation (PaO2), which are expected to improve within three days; and cough and fatigue, which may take 14 days or longer to improve [42]

It is known that radiological abnormalities of pneumonia may take even longer than 12 weeks before the clearing of densities occurs. Therefore, determining which child should be investigated relies on severe symptoms and signs, any systemic involvement or serious local complications are reported or when unusual causative pathogens are isolated and any symptoms and/or signs indicating the presence of an underlying disease [29].

Most studies of the natural history of pneumonia have focused upon the resolution of radiographic abnormalities and "slow resolution" often was defined as the persistence of radiographic abnormalities for greater than one month in a clinically improved host [43].The period of radiographic resolution depends mainly on the causative agent; this may vary from 2 weeks with (RSV) or Para influenza virus infection to as long as 12 months with adenovirus infection[44].

Causes of non resolving pneumonia in children

Inaccurate diagnosis, inappropriate antibiotic therapy, immunocompromised child, atypical microorganisms, resistant pathogens, non-infectious causes of pneumonia,Pulmonary tuberculosis, endobronchial lesions are the common causes of nonresolving pneumonia or slowly resolving pneumonias[46].

Some studies reported that aspiration syndromes (Gastro-esophageal reflux , Swallowing abnormalities, Foreign body, Anomalies of the upper airways) were the most common cause of persistent pneumonia in children [47].

Aspiration syndromes include all causes of inhalation of oropharyngeal contents into the lungs [48]. Anatomical disorders associated with an increased risk of aspiration include esophageal atresia, trachea-esophageal fistula, cleft palate, laryngeal cleft, duodenal obstruction or malrotation [49].

In our locality, around 1 in 10 children with pneumonia in our locality had the risk of recurrent/persistent pneumonia. In a study done in Upper Egypt, aspiration syndrome was the most frequent underlying cause for persistent pneumonia in children, followed by pulmonary TB followed by congenital heart diseases and immunodefeciency[29].

The underlying factors associated with persistent pneumonia can be broadly classified into the following categories: [7]:

A) Resistant or highly virulent organisms or atypical organisms.

B) Inadequate antibiotic therapy. C) Complicated infections :

Empyema , lung abscess.

D) Congenital malformations:

1- Airways: Cleft Palate, Pierre Robin syndrome, Tracheoesophageal fistulae , Tracheomalacia

2- Lungs: (Pulmonary hypoplasia, Pulmonary sequestration, Congenital adenomatoid malformation , Bronchogenic cyst).

3-Cardiovascular: CHD especially Lt to Rt shunts ,Vascular ring.

E) Recurrent aspirations: Gastro-esophageal reflux , Swallowing abnormalities , Foreign body aspiration , Anomalies of the upper airways

F) Defects in the clearance of airway secretions especially cystic fibrosis and ciliary dyskinesias.

G) Disorders of systemic or local immunity: either primary or acquired immune deficiencies .

Approach to a Child with Persistent Pneumonia

The challenge for the pulmonologist approaching NRP is to discriminate between children with self-limiting or minor problems, who do not require more diagnostic work-up, and those with an underlying disease, for whom further investigation is required .Before proceeding to the investigations, a good history taking and physical examination are mandatory. There are several features that may help in reaching a diagnosis [8].

1.Age of onset

Onset of symptoms soon after birth increase the possibility of presence of hereditary/congenital disorder. Congenital malformations such as tracheoesophageal fistula, cystic adenomatoid malformation and congenital lobar emphysema present early in life. Disorders of humoral immunity usually present in later infancy.

2.Details of the pneumonia episode

A detailed account of the first episode of pneumonia and subsequent episodes should be obtained: onset, nature and duration of cough, occurrence of fever, documentation of signs of LRTI by a physician, radiographic evaluation. type and duration of antimicrobial therapy (adequate/appropriate), response to therapy and need for hospitalization. It is important to differentiate these episodes from recurrent wheezing episodes.

The parents should be asked about the timing of the symptoms in relation to feedings and the change in position, vomiting, irritability, and nocturnal symptoms of coughing and wheezing. In a child with depressed cough reflex, coughing or gagging may be minimal or absent. Sleep disturbances may be seen in gastro-esophageal reflux, and obstructive lesions, especially of upper respiratory tract.

3.Past history and other complaints

Occurrence of repeated infections at other sites should be asked for; a positive history may suggest systemic immunodeficiency. The type of infections may give a clue to the type of immunodeficiency. History of foreign body inhalation should be elicited. Diagnosis of tuberculosis in the past should not be ignored. Symptoms suggestive of malabsorption may be present in cystic fibrosis [50].

4.Perinatal history

Prematurity, history of bronchopulmonary dysplasia or prolonged exposure to oxygen, maternal infections, and blood transfusions should be looked for. Occurrence of meconium ileus or delayed passage of meconium should increase suspicion of cystic fibrosis.

5.Family history

It is important to ask about family history of atopic disorders, contact to TB cases, cystic fibrosis, and congenital anomalies. Recurrent severe infections in other family members may suggest immunologic disorder.

6.Environmental exposure

Sources of exposure to respiratory infection should be evaluated. Exposure to inhaled pollutants, irritants and passive tobacco smoking should be carefully assessed.

7.Physical Examination

The aim of the physical examination is to document presence of respiratory disease, localize the site of infection, and to detect any underlying etiologic factor.

General and systemic examination should be done including evaluation of growth and development and inspection for clubbing. Clubbing may be present in chronic lung disorders as bronchiectasis, cystic fibrosis, and bronchiolitis obliterans. Careful examination may reveal abnormalities of upper respiratory tract. Certain morphologic features may point towards specific disorders like the presence of cleft palate with hypertelorism in DiGeorge's syndrome, telangiectasia of eyes/ears in ataxia telangiectasia. Skin should be examined for evidence of infective foci or any skin rash [51].

Chest examination includes assessment of the evidence of distress, thoracic deformities, wheezing, stridor, the dimensions of the chest and auscultation of the chest to localize the affected lobe. Evaluation of the nose, paranasal sinuses and ears is mandatory. Nasal polyposis may be an important clue to CF. Recurrent middle ear infection may occur in immune deficiency syndromes and ciliary dyskinesia. As left to right shunts predispose to recurrent or persistent pneumonia, these should always be early detected. Dextrocardia may offer a clue to immotile cilia syndrome. Whenever the diagnosis of aspiration is considered, observation of the infant during feeding is essential. The palate, tongue,

and oropharynx should be examined for any anomalies. Based on history and physical examination, the severity of the primary disorder can be assessed [49].

The following findings indicate severity of the underlying cause of non resolving pneumonia (NRP):

• Failure to thrive

• Limitation of activity

• Persistent fever

• Persistent tachypnea and respiratory distress

• Persistent hyperinflation

• Significant sustained hypoxemia

• Persistent radiographic/PFT abnormalities.

• Presence of clubbing, growth retardation, increased A-P diameter of the chest indicate chronicity of the disease/infection.

Investigations to a child with persistent pneumonia

Investigations should be planned after careful history taking and clinical examination. As the causes of persistent pneumonias are so many, the child should be investigated judiciously. It is absolutely necessary to rule out tuberculosis and underlying congenital cardiovascular disease before proceeding to the further investigations [29].

A) Laboratory investigations

In child with non resolving pneumonia, microbiological examinations are mandatory to confirm the diagnosis of pneumonia because many microorganisms are known for delayed resolution [52].

When leukocytosis and CRP decrease , this strongly supports response to antibiotic therapy & no further investigation is necessary for NRP even if chest opacity persists. Useful laboratory investigations are:

• Sputum analysis for cell count & type

• Sputum Culture and Sensitivity , AFB if tuberculosis is suspected.

B) Imaging

Radiographic evaluation of chest is essential for localization of infiltrates, their extent and resolution over time, in any child having recurrent or persistent pneumonia.

Computed tomography of the chest, magnetic resonance imaging and bronchography may be required for detailed evaluation of the lungs and the airways. Chest CT is the most helpful in assessing NRP, which can detect pleural diseases, empyema or abscess or mediastinal masses [53]. High resolution CT is a more advanced modality for imaging of the lungs and the airways.

Follow up Chest X-Ray is an important investigation which confirms the persistence of radiological opacity.

C) Bronchoscopy

Fiberoptic bronchoscopy (FOB) is a very useful diagnostic tool after laboratory and radiological evaluation if the diagnosis of NRP is still not diagnosed as it allows direct visualization of affected areas and obtaining of samples (BAL).

Finally , if FOB is not successful or doesn't yield a definitive diagnosis, a transthoracic needle aspiration or open lung biopsy may be done in elected cases. ANA & ANCA should also be ordered to exclude connective tissue disorders. Serum angiotensin converting enzyme (SACE) also help in the diagnosis of sarcoidosis [40].

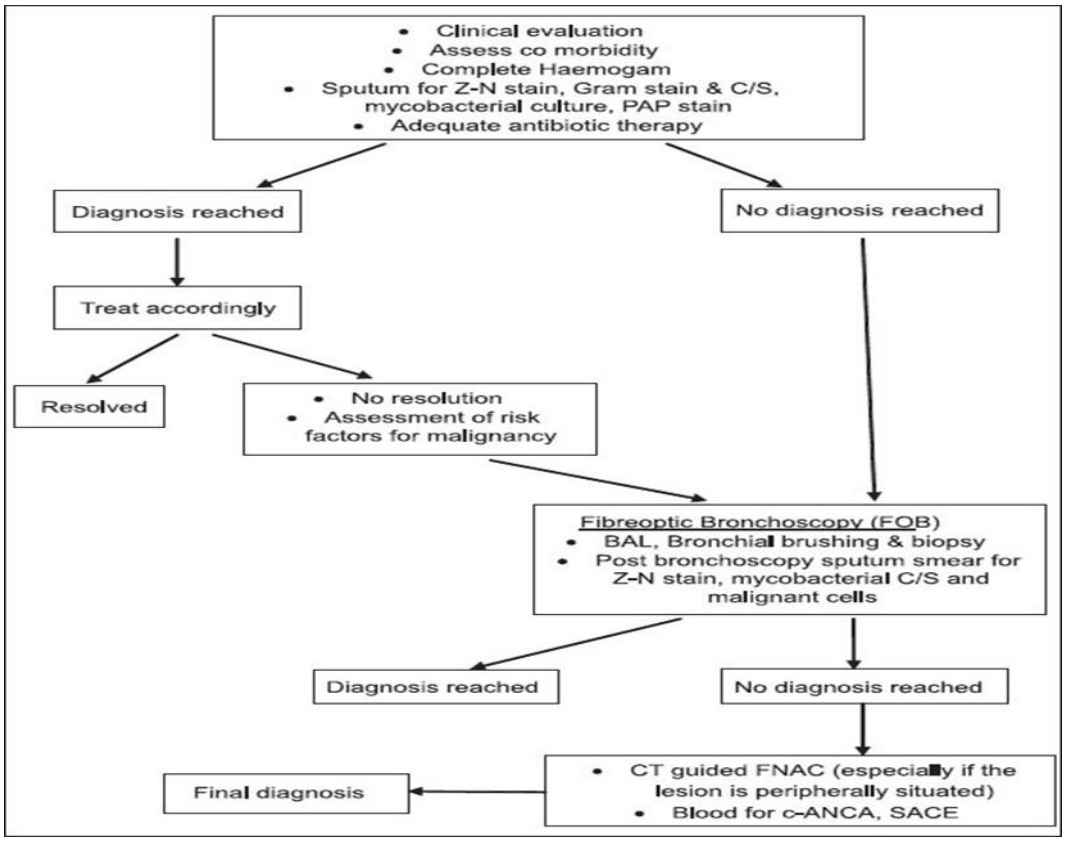


Figure (4): Approach to a child with non-resolving pneumonia[40].

No Conflict of interest.

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