

Underlying diseases of recurrent pneumonia in Turkish children*

Osman ÖZDEMİR¹, Sinan SARI², Arzu BAKIRTAŞ³, Pelin ZORLU⁴, Ülker ERTAN⁴

Aim: The aim of the present study was to determine the relative frequency of recurrent pneumonia in children and to describe its underlying illnesses.

Materials and methods: Children between 3 months and 16 years old who had a history of 2 or more episodes of pneumonia per year, or 3 or more episodes in a lifetime were investigated retrospectively at Doctor Sami Ulus Children's Training and Research Hospital between January 2002 and December 2004.

Results: Out of 595 children admitted for pneumonia, 62 (10.42%) met the criteria for recurrent pneumonia. An underlying illness was demonstrated in 56 patients (90.32%). In this study, the underlying illness was diagnosed during recurrence in all patients. The patients with persistent pneumonia were excluded from the study. Underlying diseases were bronchial asthma (30.64%), immune deficiency disorders (17.75%), aspiration syndromes (17.75%), and congenital anomalies (16.12%). No predisposing illness could be demonstrated in 6 patients (9.68%).

Conclusion: Approximately 1 in 10 children with pneumonia in our hospital had recurrent pneumonia. Most of these children had an underlying illness, which was demonstrated. Bronchial asthma was the most common underlying illnesses for undiagnosed recurrent pneumonia in children.

Key words: Aspiration syndromes, bronchial asthma, congenital anomalies, immune deficiency disorders, recurrent pneumonia

Türk çocuklarda tekrarlayan akciğer enfeksiyonuna neden olan hastalıklar

Amaç: Bu çalışmanın amacı çocuklarda tekrarlayan akciğer enfeksiyonuna neden olan hastalıkları tanımlamak ve göreceli sıklığını belirlemektir.

Yöntem ve gereç: Yılda iki veya daha fazla ya da hayatı boyunca üç veya daha fazla akciğer enfeksiyonu öyküsü olan, 3 ay ve 16 yaş arasındaki çocuklar, Ocak 2002 ve Aralık 2004 arasında, Doktor Sami Ulus Çocuk Eğitim ve Araştırma Hastanesi'nde geriye dönük olarak araştırılmıştır.

Bulgular: Akciğer enfeksiyonu kabul edilen 595 çocuktan 62'si (% 10.42) tekrarlayan akciğer enfeksiyonu kriterlerini karşıladı. Elli altı hastada (% 90.32) altta yatan hastalık gösterilmiştir. Bu çalışmada tüm hastaların altta yatan hastalığı akciğer enfeksiyonunun tekrarı sırasında tanı almıştır. Devamlı akciğer enfeksiyonu olan hastalar çalışmadan çıkarılmıştır. Altta yatan hastalıklar bronşiyal astım (% 30.64), immün yetmezlik bozuklukları (% 17.75), aspirasyon sendromları (% 17.75) ve doğumsal anomalilerdir (% 16.12). Altı hastada (% 9.68) altta yatan hastalık gösterilememiştir.

Sonuç: Hastanemizdeki akciğer enfeksiyonlu çocukların yaklaşık onda birinde tekrarlayan akciğer enfeksiyonu vardı. Bu çocukların çoğunda olan altta yatan hastalık gösterilmiştir. Daha önce tanı almamış tekrarlayan akciğer enfeksiyonu olan çocuklarda en sık altta yatan hastalık bronşiyal astımdır.

Anahtar sözcükler: Aspirasyon sendromları, bronşiyal astım, doğumsal anomaliler, immün yetmezlik hastalıkları, tekrarlayan akciğer enfeksiyonu

Received: 06.06.2009 – Accepted: 10.11.2009

¹ Department of Pediatric Cardiology, Keçiören Training and Research Hospital, Ankara - TURKEY

² Department of Pediatric Gastroenterology, School of Medicine, Gazi University, Ankara - TURKEY

³ Department of Pediatric Allergy, School of Medicine, Gazi University, Ankara - TURKEY

⁴ Department of Pediatrics, Doctor Sami Ulus Children's Training and Research Hospital, Ankara - TURKEY

Correspondence: Osman ÖZDEMİR, Sanatoryum Caddesi, Pınarbaşı Mahallesi, Ardahan Sokak, No:25, Keçiören Eğitim ve Araştırma Hastanesi, Ankara - TURKEY

E-mail: pedkard@gmail.com

* There is no financial support or relationship that may pose a conflict of interest.

Introduction

Recurrent pneumonia is defined as at least 2 pneumonia episodes in a 1-year period or more than 3 episodes at any time with radiographic clearing between episodes (1). By this definition, recurrent pneumonia occurs in 6.4%–9% of all children with pneumonia (2-5). Recurrent pneumonias usually result from deficiencies in the local pulmonary or systemic host defenses or from underlying disorders that modify the lung defense. Therefore, pediatricians should investigate these possible underlying causes (6,7). The factors associated with recurrent pneumonia in developed countries include asthma, immunodeficiency (e.g. human immunodeficiency virus infection, immunoglobulin deficiency), pulmonary anomalies, and foreign body aspiration (7,8). However, the factors associated with recurrent pneumonia have not been identified in developing countries. There are only a few studies of recurrent pneumonia in children (3,4). Especially in the developing countries, increasing studies of epidemiology to recurrent pneumonia will ease preventative and therapeutic approach (8). The purpose of this retrospective study is to determine the relative frequency of recurrent pneumonia in children in a tertiary care pediatric hospital and describe its underlying illnesses.

Materials and methods

In this study, children between 3 months and 16 years old who admitted to Doctor Sami Ulus Children's Training and Research Hospital between January 2002 and December 2004 with a hospital discharge diagnosis of pneumonia were identified. The hospital is a nation-wide center, located in the capital city of Turkey, Ankara.

The diagnosis of pneumonia was based on cough, chest indrawn and/or difficult breathing, tachypnea (≥ 50 respirations/minute in infants 3 to 12 months old; ≥ 40 respirations/min in children 12 to 60 months old; ≥ 30 respirations/min in children older than 60 months), fever (rectal temperature > 38.0 °C) and lobar or bronchopneumonic infiltration determined by X-ray (8). The patients who had a diagnosis of pneumonia without radiographic confirmations were excluded from the study. Patients were included in

this study if they had at least 2 pneumonia episodes per year or 3 or more episodes at any time with radiographic clearing between episodes (1). Patients were classified according to underlying illnesses that had previously been associated with pneumonia. These underlying conditions included bronchial asthma, immune deficiency disorders, congenital anomalies, aspiration syndromes, cystic fibrosis, primary ciliary dyskinesia, and pulmonary tuberculosis. Using a standardized data extraction form, information was obtained on patients' demographic characteristics, including sex and age of the child, dates of hospitalizations, clinical findings, and results of laboratory and radiographic investigations for underlying causes.

Confirmation of underlying pulmonary disorders were based on standardized laboratory tests including pulmonary function tests with methacholine challenge (for children older than 7 years old), X-ray and/or computerized tomography of the chest, laryngoscopy, flexible fibre-optic bronchoscopy, complete blood counts, quantitative immunoglobulins, the number of T and B lymphocytes, lymphoblastic transformation, specific immunoglobulins for various allergens (for infants younger than 3 years old), sweat chloride testing, Candida and tuberculin skin test. Congenital cardiac anomalies were demonstrated by echocardiography. Gastroesophageal reflux was demonstrated by barium swallow or 24 h pH monitoring. Human immunodeficiency virus antibody was assayed from serum samples. Primary ciliary dyskinesia was demonstrated by saccharine test and electron microscopy of nasal scrapings (6-8).

The patients with known chronic diseases, e.g. heart diseases, gastroesophageal reflux, immune deficiencies, neuromuscular diseases, bronchial asthma, or bronchopulmonary dysplasia were excluded from the study. In addition, the patients with persistent pneumonia, i.e. persistence of symptoms and radiographic abnormalities for more than 1 month, were also excluded (1).

Results

From January 2002 to December 2004, 595 patients admitted to the hospital were diagnosed with

pneumonia. Sixty-two of them (10.42%) met the definition of recurrent pneumonia with a mean age of 2.5 years (between 3 months and 16 years). There were 37 (60%) males and 25 (40%) females.

An underlying disease was demonstrated in 56 (90.32%) of the patients with recurrent pneumonia. Nineteen patients (30.64%) had bronchial asthma, 11 patients (17.75%) had immune deficiency disorders, 11 patients (17.75%) had aspiration syndromes, 10 patients (16.12%) had congenital anomalies, 4 patients (6.45%) had cystic fibrosis, and 1 patient (1.61%) had primary ciliary dyskinesia. No predisposing illness could be demonstrated in the remaining 6 patients (9.68%) (Table 1).

Discussion

The respiratory tract is protected by its local and general body defenses. Nevertheless, respiratory tract

infections constitute a major health problem all over the world (6,7). Pneumonia is an important cause of morbidity and mortality in children, especially those younger than 5 years of age in developing countries, accounting for 4 million deaths annually (8). In developed countries, the annual incidence of pneumonia ranges from 30 to 45 cases per 1000 children in those younger than 5 years to 16 to 22 cases per 1000 children in those aged 5 years and older (9). A subgroup of these children suffers from recurrent pneumonia, raising the question of whether there is an underlying illness predisposing them to such pneumonia recurrences. However, the lack of reports and epidemiological studies from developing countries where children suffer most from scarcity of resources make it difficult to plan worldwide strategies for prevention and treatment.

Although possible approaches to the investigation of recurrent pneumonia have been described, there

Table 1. Underlying causes of recurrent pneumonia in children.

Underlying illness	n	%	
Bronchial asthma	19	30.64	
Immune deficiency disorders	Common variable immunodeficiency	5	
	Combined immunodeficiency disease	3	17.75
	IgG ₂ and selective IgA deficiency	2	
	Ataxia-telangiectasia	1	
Aspiration syndromes	Gastroesophageal reflux	6	
	Other aspiration syndromes	3	17.75
	Respiratory foreign body	2	
Congenital anomalies	Ventricular septal defect	4	
	Patent ductus arteriosus	3	
	Congenital lobar emphysema	1	16.12
	Tracheomalacia with right bronchial anomaly	1	
Cystic fibrosis	Laryngomalacia with epiglottic insufficiency	1	
	Cystic fibrosis	4	6.45
Primary ciliary dyskinesia	1	1.61	
Unknown	6	9.68	
Total	62	100	

Ig: Immunoglobulin, n: Number of patients

are few studies of recurrent pneumonia (2-5) (Table 2). In our study 10.42% of admission to the hospital with a diagnosis of pneumonia met the definition of recurrent pneumonia. Similarly, 6.4%-9% of patients with pneumonia met the criteria for recurrent pneumonia in previous studies with large pediatric populations (2-5).

We demonstrated an underlying illness for recurrent pneumonia in 90.32% of our patients and no predisposing factors could be identified in the remaining 9.68%. Unknown etiology of patients with recurrent pneumonia was found 7.5%-15.7% in previous similar studies (2-5).

In our study, the most frequent underlying illness was bronchial asthma, followed by immune deficiency disorders, aspiration syndromes, and congenital anomalies. Cystic fibrosis and primary ciliary dyskinesia were relatively rare causes of recurrent pneumonia (Table 1). Bronchial asthma is an important underlying illness for recurrent pneumonia in children (1-9). Despite recent advances in health care, many children referred with recurrent pneumonia are shown to have undiagnosed asthma. There is no agreed clinical definition or pathognomic test for childhood asthma and making the diagnosis can be difficult, particularly in children younger than 3 years (10,11). These children were clinically

diagnosed as having asthma (multiple episodes of partially reversible airway obstruction).

Although most of our patients with immune deficiency disorders also had recurrent upper respiratory tract infections, similar to previous reports, we were able to demonstrate the immune defects (17.75%) only after pneumonia recurrences (2-5). Eleven of the patients were diagnosed with immune deficiency disorders, including common variable immunodeficiency, combined immunodeficiency disease, IgG₂ and selective IgA deficiency, and ataxia-telangiectasia. Immune deficiency should be suspected in children with infections that are especially severe and recurrent, that are caused by unusual organisms, or that involve multiple sites in addition to the lungs (6,7). Two of 5 patients with common variable immunodeficiency had spruelike syndrome and splenomegaly in the study. Three patients with combined immunodeficiency disease had recurrent pneumonia, cutaneous candidiasis, chronic diarrhea, and urinary tract infections. Serum concentrations of other immunoglobulins were normal in 2 patients with selective IgA deficiency and IgG₂ subclass deficiency in the study. A patient with ataxia-telangiectasia, 8 years old, had also progressive ataxia and oculocutaneous telangiectasias.

Table 2. Comprehensive etiologic studies of children with recurrent pneumonia.

Characteristics	Canada	India	Turkey	Spain	Turkey
Reference	2	3	4	5	Current study
Median age (year)	3.7	?	2	3	2.5
Male/Female	1.4	1.7	2.2	?	1.5
Patients with recurrent pneumonia (%)	238 (8)	70 (?)	71 (9)	106 (6.4)	62 (10.42)
Designated underlying illness (%)	220 (92.5)	59 (84.3)	60 (84.5)	92 (86.8)	56 (90.32)
Bronchial asthma (%)	19 (8)	9 (12.8)	23 (32.4)	28 (26.4)	19 (30.64)
Immune deficiency disorder (%)	24 (10.1)	11 (15.7)	7 (9.85)	9 (8.5)	11 (17.75)
Congenital heart disease (%)	22 (9.2)	6 (8.6)	6 (8.5)	27 (25.5)	7 (11.29)
Gastroesophageal reflux (%)	13 (5.5)	6 (8.6)	11 (15.5)	-	6 (9.68)
Other aspiration syndromes (%)	114 (47.9)	17 (24.3)	2 (2.8)	25 (23.6)	5 (8.06)
Anomalies of the respiratory system (%)	18 (7.6)	6 (8.6)	4 (5.6)	2 (1.9)	3 (4.84)
Other causes (%)	10 (4.2)	4 (5.7)	7 (9.85)	1 (0.9)	5 (8.06)
Unknown etiology (%)	18 (7.5)	11 (15.7)	11 (15.5)	14 (13.2)	6 (9.68)

Associated aspiration syndromes were found in 11 patients with recurrent pneumonia. In 6 patients with gastroesophageal reflux, there was a notable association between feeding and subsequent respiratory symptoms. Foreign body removed with the assistance of flexible fiber-optic bronchoscopy in the remaining 2 patients. All of these children were neurologically normal on physical examination. Oropharyngeal incoordination is an important cause of chronic aspiration and recurrent pneumonia. Cerebral palsy is the most common cause of oropharyngeal incoordination (2,3,5). Because patients with a known chronic disease such as cerebral palsy were excluded from our study, swallowing dysfunction associated with recurrent aspiration was found in only 3 patients. The 3 patients were diagnosed with mild cerebral palsy after pneumonia recurrences.

Congenital anomalies are an important underlying illness for recurrent pneumonia in children. The patients with congenital anomalies included 7 children with isolated left to right shunts, including ventricular septal defect and patent ductus arteriosus in our study. Three other patients had congenital anomaly of the respiratory system, including congenital lobar emphysema, tracheomalacia with right bronchial anomaly, and laryngomalacia with epiglottic insufficiency. Because of fetal echocardiography and cardiac murmur, all patients with congenital heart defect were diagnosed prior to the first episode of pneumonia. Thus, frequency of congenital heart defect was found lower in our study compared to a previous study (5).

Because consanguinity of parents is very common in our country, 4 patients with cystic fibrosis were not surprising in our study group. A patient with primary ciliary dyskinesia typically had chronic purulent

rhinitis and recurrent infection of middle ear. Tuberculosis is still an important problem in our country, and the diagnosis of this illness may be difficult (4). Tuberculosis generally causes persistent pneumonia without acquired immunodeficiency such as human immunodeficiency virus infection (6-8). Because patients with persistent pneumonia were excluded from the study, tuberculosis associated with recurrent pneumonia was not found in our patients.

Unfortunately, our study had several limitations. Some of our patients with a diagnosis of pneumonia at one time might be treated at another hospital later on for recurrences. Therefore, we may not know the true percentage of patients with recurrent pneumonia in our hospital. In addition, our study includes only hospitalized patients, we may be underestimating the true number of patients with this condition. Because of the retrospective nature of our study, we could not investigate the effect of passive smoking on recurrent pneumonia. Indeed, passive smoking is a well-described risk factor for many pulmonary diseases and is much more common than some of the rare illnesses encountered in our study group (12). In addition, we considered only one underlying illness as the cause of recurrent pneumonia. Therefore, we cannot know if 'underlying illness' was a direct effect of or the only reason for pneumonia recurrence.

Our study shows that approximately one-tenth of Turkish children with pneumonia admitted to our hospital had recurrent pneumonia. Most of these children had an underlying illness that could be demonstrated by intensive investigation. In undiagnosed recurrent pneumonia, bronchial asthma, immune deficiency disorders, congenital heart disease, and gastroesophageal reflux should be considered in the differential diagnosis.

References

1. Wald E. Recurrent and non-resolving pneumonia in children. *Semin Respir Infect* 1993; 8: 46-58.
2. Owayed AF, Campbell DM, Wang EEL. Underlying causes of recurrent pneumonia in children. *Arch Pediatr Adolesc Med* 2000; 154: 190-4.
3. Lodha R, Puranik M, Natchu UC, Kabra SK. Recurrent pneumonia in children: clinical profile and underlying causes. *Acta Paediatr* 2002; 91(11): 1170-3.
4. Çiftçi E, Güneş M, Köksal Y, İnce E, Doğru Ü. Underlying causes of recurrent pneumonia in Turkish children in a university hospital. *J Trop Pediatr* 2003; 49(4): 212-5.
5. Cabezuelo Huerta G, Vidal Micó S, Abeledo Gómez A, Frontera Izquierdo P. (Underlying causes of recurrent pneumonia). *An Pediatr (Barc)* 2005; 63(5): 409-12.
6. Sheares BJ. Recurrent pneumonia in children. *Pediatr Ann* 2002; 31(2): 109-14.

Recurrent pneumonia in children

7. Couriel J. Assessment of the child with recurrent chest infections. *Br Med Bull* 2002; 61: 115-32.
8. Heffelfinger JD, Davis TE, Gebrian B, Bordeau R, Schwartz B, Dowell SF. Evaluation of children with recurrent pneumonia diagnosed by World Health Organization criteria. *Pediatr Infect Dis J* 2002; 21: 108-12.
9. Panitch HB. Evaluation of recurrent pneumonia. *Pediatr Infect Dis J* 2005; 24: 265-6.
10. Eigen H, Laughlin JJ, Homrighausen RN. Recurrent pneumonia in children and its relationship to bronchial hyperreactivity. *Pediatrics* 1982; 70(5): 698-704.
11. Douglas T, Couriel JM. Differential diagnosis of asthma in children. *Asthma J* 2001; 6: 72-6.
12. Aligne CA, Stoddard JJ. Tobacco and children. An economic evaluation of the medical effects of parental smoking. *Arch Pediatr Adolesc Med* 1997; 151(7): 648-53.