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EVALUATION OF PATIENTS WITH CHRONIC COUGH IN SCHOOL AGE CHILDREN

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Abstract

Aim: Chronic cough is a common problem in childhood. Simple viral infections can cause chronic cough, as well as underlying progressive diseases. For this reason, guidelines that can be applied in clinical practice are very valuable. In the study, we aimed to evaluate our patients with chronic cough in the light of the literature.

Methods: The documents of patients over the age of 6 who applied to the pediatric allergy outpatient clinic due to cough that was ongoing for more than 4 weeks between January 2022 and June 2022 were evaluated retrospectively.

Results: 182 patients aged 6-17.9 years old were included in the study. There were 62.1% males. The mean age was 9.8± 3.8 years. 32.4% of our patients were diagnosed with asthma; 43.4% Upper Airway Cough Syndrome (20.9% sinusitis, 17.6% allergic rhinitis, 4.9% non-allergic rhinitis); 7.68% Protracted bacterial bronchitis, 6.59% postinfectious cough, 4.9% patients had psychogenic cough, 4 (2.2%) patients had Gastroesophageal reflux disease, 2 (1.1%) patients had bronchiectasis, 2 (1.1%) patients had Primary ciliary dyskinesia, 1 (0.55%) patient was diagnosed with eosinophilic esophagitis.

Conclusions: Many different diseases can cause chronic cough in childhood. It is observed that drugs such as antibiotics and symptomatic medicines are frequently used unnecessarily by the parents. Accurate evaluation of patients, especially taking a detailed history, is very important in the management of these patients. It is very important to evaluate each patient individually.

Keywords: *Asthma, childhood, chronic cough, etiological evaluation*

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Introduction

Cough is a reflex that cleans the respiratory system, defends and protects the respiratory mucosa[1]. Chronic cough is among the most common reasons for consulting a doctor in childhood. Normally, viral and/or bacterial upper respiratory tract infections often cause coughing. In addition, different etiological factors such as asthma, allergic rhinitis, sinusitis, pneumonia, specific lung infections, gastroesophageal reflux disease (GERD), foreign body aspiration, pneumonic infiltrations accompanying immune deficiencies

may cause cough. For this reason, it is appropriate to investigate the underlying etiology, especially when the cough becomes chronic[2]. Chronic cough is a finding that disturbs both the family and the physician and is frequently encountered in clinical practice. Algorithms on chronic cough are published from various centers in order to facilitate the clinician's work, speed up the diagnosis process, reduce repetitive doctor visits, and reduce unnecessary antibiotic use. In recent years, guides related to this subject have been issued. Guidelines are published by ERS (Europen Respiratory Society), ACCP (American College of Chest Physicians), BTS (British Thorasic Society)[3-5]. Basically, there are similar features between these guidelines. However, the duration of cough, the terminology used and the recommended treatment and duration vary in terms of definitions.

The aim of the study is to retrospectively review school-age patients followed up with chronic cough and to discuss the underlying etiology of this clinical definition in the light of the literature.

Materials and Methods

All patients between the ages of 6 and 18 years old with chronic cough who applied to Adana City Hospital pediatric allergy outpatient clinic between January 2022 and June 2022 were included in the study. Coughs lasting longer than 4 weeks were considered chronic.

The detailed history of the patients was taken and it was questioned whether the cough was productive, whether the complaints increased with exercise, whether there was a cough at night, whether there was a complaint of shortness of breath and wheezing, and whether allergic rhinitis was accompanied by complaints. Detailed physical examination was performed. Chest radiographs were taken at the first examination of all the patients. Pulmonary function test- (PFT) with spirometry was applied to each patient.

Blood eosinophil counts (BEC) were measured in all patients. When findings suggestive of atopy are found in the history and physical examination of the patients, skin prick test-(SPT) were performed to define the atopy status of the patients. (Dermatophagoides pteronyssinus, D.farinea, Cat-Dog danders, Alternaria alternata, Tree mix, Grass mix, Parietaria officinalis pollens) (Stallergenes S.A., Antony, France). When findings suggestive of reflüx are found in the history of the patients, anti-reflux therapy was given to the patients.in patients. Immune panel (level of serum IgG, IgA, IgM) and lymphocyte subgroups were studied from patients who were suggestive of immunodeficiency in the history and physical examination. First of all, if the patient had a productive cough, the patient was given antibiotic therapy for 2 weeks. Advanced imaging (thorax computer tomography) was applied to patients with productive cough who did not respond to antibiotic treatment. If the cough was accompanied by gastrointestinal findings (such as abdominal pain, burping, feeling of stuck in foods, long chewing of foods), an endoscopy of the patients was also planned by evaluating with the pediatric gastroenterology department.

Exclusion criteria: Patients with neuromotor development retardation, development-growth retardation, cardiac disease, any known chronic disease, those who could not cooperate in PFT, and patients who do not come to regular follow-up.

The patients were called for a monthly control, with the first control 15 days later. Patients were followed up for 3-6 months.

Definitions:

(i)Asthma: Patients with a forced expiratory volume in 1 s value under 85% at PFT and a recovery rate of ≥12% following bronchodilator responsiveness test [15 min after the administration of three puffs (100 mcg/puff) albuterol via mask] and whose cough resolves following with treatment of inhaled corticosteroid (ICS) such as budesonide 400 µg/day[6].

(ii)Upper airway cough syndrome-(UACS): This syndrome includes sinusitis, allergic

rhinitis, nonallergic rhinitis, and adenoidal hypertrophy[7].

(iii)Protracted bacterial bronchitis (PBB): These patients have chronic isolated wet cough after other underlying conditions excluded. No pathological finding is detected in thorax imaging. (Amoxicillin clavulanate, 40 mg/kg/day, 2 weeks)[8].

(iv)Postinfectious cough is a diagnosis that should be considered after other possible causes have been ruled out. Unless there is an active infection, follow-up without treatment is recommended. These patients are typically characterized by only a dry cough. Physical examination, chest X-ray and PFT are normal. These children are generally healthy [9].

(v)Psychogenic cough: A disruptive bizarre honking cough in a patient who exhibits 'la belle indifference' is suggestive of a psychogenic cough usually observed to cease when the patient sleeps or focuses attention somewhere else[10].

(vi)GERD: It occurs as a result of reflux of stomach contents into the esophagus causing various symptoms (heartburn, regurgitation, dysphagia, pulmonary and laryngo-pharyngeal symptoms) that resolves with treatment [lansoprazol (15 mg/day), domperidone (1 mg/kg/day)] and diet for 4 weeks[11].

(vii)Bronchiectasis: Chronic irreversible dilatation of the bronchi. These patients have productive cough. Diagnosis is made by thorax HRCT [12].

(viii)Primary ciliary dyskinesia (PCD): When PICADAR scoring is done for PCD in patients presenting with chronic and recurrent productive cough, if the patient's score is ≥ 10 patients, it is evaluated as PCD with 90% probability[13].

(ix)Eosinophilic esophagitis: In addition to clinical suspicion (Symptoms reflect esophageal dysfunction) endoscopic (typical endoscopic features include linear grooves, white plaques, and concentric rings) and microscopic findings (requires 15 or more eosinophils per field on the light microscope) are essential for diagnosis[14].

Statistical Analysis

First of all, the descriptive properties of the variables (mean, median, number and percentage) were found. It was checked whether the numerical variables fit the normal distribution. When comparing the two groups, the Student's t test was used for normally distributed numerical variables, and the Mann-Whitney U test was used for non-normally distributed numerical variables. In cases where more than two variables were compared, ANNOVA was used for those with normal distribution, and the Kruskall Walllis test for those who were not normally distributed. Chi-square was used when comparing categorical variables and Spearman correlation analysis method was used for correlation analysis. "Statistical Package for Social Sciences" SPSS 25 (IBM Corp., Armonk, NY, USA) program was used to evaluate the results. $P<0.05$ was considered significant.

Results

In the first stage of the study, 249 patients were included; during the follow-up of the patients, 67 patients were excluded from the study because they didn't come to regular follow-ups. Of 182 patients aged 6-17.9 years, there were 113 males (62.1%). The mean age was 9.8± 3.8 years (range 6-17.9 years). Demographic characteristics of the patients are shown in Table 1.

59 (32.4%) of our patients were diagnosed with asthma; 38 (20.9%) sinusitis, 32 (17.6%) allergic rhinitis, 9 (4.9%) non-allergic rhinitis, 14 (7.68%) PBB, 12 (6.59%) postinfectious cough, 9 (4.9%) psychogenic cough, 4 (2.2%) GERD, 2 (1.1%) idiopathic bronchiectasis, 2 (1.1%) PCD, 1 (0.55%) patients were diagnosed with eosinophilic esophagitis. Table 2. illustrates diagnostic

distribution of the patients in the final examination. Atopy evaluation was performed in 59 patients diagnosed with asthma. Atopy was detected in 71.2% (n=42) patients. In addition, these patients were questioned in terms of allergic rhinitis and allergic rhinitis was diagnosed in 37 (62.7%) of the asthma patients.

Table 1. Demographic characteristics of the patients

Characteristics	Values
Mean age (year)	9.8 ± 3.79 (6-17.9)
Female gender, n (%)	69 (37.9)
Mean length of cough (weeks)	6.2 ± 3.8 (range 4-20)
Cough type, n (%)	
• Dry	48 (26.37)
• Wet	54 (29.7)
• Dry + wet	80 (43.9)
Cough timing, n (%)	
• Night	64 (35.1)
• Daytime	68 (37.4)
• Night + daytime	50 (27.4)
Cough during or post exercise, n (%)	35 (19.2)
Presence atopy, n (%)	86/138 (62.3%)
Presence of family atopic disease, n (%)	127 (69.8%)
Blood Eosinophil Count n (%)	
>500-1000	54 (29.7)
>1000	35 (19.2)
Passive smoking, n (%)	61 (33.5)
Active smoking, n (%)	9(4.94%)

*atopy examination was applied to 138 patients

After all the evaluations, our patients who were diagnosed with asthma were questioned in detail whether they had shortness of breath and wheezing. 38 % of these patients did not have these complaints in their history. These patients had only a dry cough, especially exacerbated by exercise. In addition, 27 of the patients with dry cough were found to be positive in PFT reversibility.

All of our patients diagnosed with sinusitis were evaluated for atopy, and atopy was found in 31.6% (n=12) of the patients. It was thought that sinusitis developed on the basis of allergic rhinitis in these patients.

Atopy examination was performed in all 41 patients with chronic cough and rhinitis, and atopy was found in 78%. Non-allergic rhinitis was diagnosed in 22% of the patients whose atopy tests were negative.

Amoxicillin-clavulanate treatment was started in our patients diagnosed with PBB, as recommended in the literature. At the follow-up of the patients 15 days later, the complaints of the patients were gone.

Immune panel was evaluated in patients with productive cough that did not respond to antibiotic treatment. The results of the patients whose immune panel was studied were normal.

Table 2. Diagnostic distribution of the patients in the final examination

Diagnosis Values, n (%)	Values
Asthma	59 (32.4)
Upper airway cough syndrome	79 (43.4)
• Sinusitis	38 (20.9)
• Allergic rhinitis	32 (17.6)
• Nonallergic rhinitis	9 (4.9)
Protracted bacterial bronchitis	14 (7.68)
Postinfectious cough	12 (6.59)
Psychogenic cough	9 (4.9)
Gastroesophageal reflux disease	4 (2.2)
Isolated Bronchiectasis	2 (1.1)
Primary ciliary dyskinesia	2 (1.1)
Eosinophilic esophagitis	1 (0.55)

One of the patients with chronic cough and GER findings had an endoscopy by the pediatric gastroenterology department since food was found to be stuck in the anamnesis. Eosinophilic esophagitis was diagnosed as a result of endoscopy findings and pathology. This patient was examined for possible food allergy. No food allergy was detected.

Discussion

Chronic cough, which is frequently encountered in childhood, can be caused by many different etiological factors. In our study, we found that asthma was the most common cause of chronic cough. Asthma is one of the most common chronic diseases in childhood. Typical features are that it causes shortness

of breath, wheezing and chronic cough, shows reversibility in pulmonary function test with inhaled salbutamol, and the patient is well in the internal period. Asthma in childhood generally shows an intermittent course[15]. 38% of our patients diagnosed with asthma did not have shortness of breath and wheezing in the anamnesis. A diagnosis of cough variant asthma was considered in these patients. As reported in the literature, patients can be diagnosed by reversibility in spirometric findings, responding to inhaled steroid treatment, and resumption of symptoms when treatment is stopped[16].

We found atopy in most of our patients (71.2%) diagnosed with asthma. Studies have shown that 80% of asthma patients are associated with allergic rhinitis[17]. For this reason, we questioned our patients diagnosed with asthma in terms of allergic rhinitis. We found that 62.7% of our patients had allergic rhinitis.

43.4% of our patients had UACS. The definition of UACS includes the diagnoses of allergic rhinitis, non-allergic rhinitis, postnasal drip and acute chronic sinusitis, and adenoid hypertrophy[7,18]. In our UACS group, 17.6% of our patients were diagnosed with allergic rhinitis, 4.9% with non-allergic rhinitis and 20.9% with sinusitis. Atopy examination was performed in patients diagnosed with sinusitis in case of findings and complaints suggestive of allergic rhinitis in their histories and/or if there was a familial history of atopy. And 31.6% of 38 patients diagnosed with sinusitis were found to have atopy. Symptomatic treatment for allergic rhinitis was initiated in the controls of these patients.

We diagnosed PBB in accordance with the literature in our patients who did not have sinusitis and pneumonia, no inflammation was detected on direct chest X-ray, and no crackles or postnasal discharge was found on physical examination especially in patients with productive cough. These patients were given amoxicillin clavulanate treatment for 14 days[8]. It was observed that the complaints of the patients did not recur at the end of their treatment. Unlike us, Kompare M et al.[19] continued AB treatment for 4 weeks in 70 patients diagnosed with UBB. The 2008 BTS cough guidelines recommend that patients with PBB be given antibiotics for 4-6 weeks[5]. A recent study reported that patients with chronic wet cough who did not respond to 4 weeks of antibiotic therapy were more likely to have bronchiectasis on thorax CT scan[20].

Sensitivity to capsaicin increases for more than 1 month in viral upper respiratory tract infections. It causes cough that continues after infection. Impaired ciliary activity and mucus retention due to inflammation are other causes of coughing. It is known that as the affected airway level descends distally, the duration of coughing gets longer[9]. Cough lasts longer than 3 weeks in 57% of patients with Chlamydophila pneumoniae and 28% of patients with Mycoplasma pneumonia[21]. Bordetella pertusis is one of the most common microorganisms causing prolonged cough in children and adults. Cough in pertussis cases continues for an average of 4 to 6 weeks[22].

In our study, we followed up 6.59% of patients with the diagnosis of postinfectious chronic cough, all of our patients in this group had dry cough. Respiratory system findings, spirometric findings and imaging of these patients did not reveal any pathological condition. Postinfectious cough is a diagnosis that should be considered after other possible causes have been ruled out. Unless there is an active infection, follow-up without treatment is recommended[9].

Psychogenic cough is a diagnosis that should be considered in the differential diagnosis when other specific causes are excluded[10]. It is more common in children and adolescents than adults. It has been shown that 3-10% of children and adolescents with cough lasting longer than one month have psychogenic cough[23]. No difference was found between the genders in terms of incidence of psychogenic cough. It is characterized by a barking, loud, explosive, repetitive and dry cough in the patients with psychogenic cough. The severity of the cough is so loud that it can be heard from afar. Often there is no cough during sleep, it decreases during activities that the patient enjoys. When the pa-

tient is with parents, teachers, or doctors, the severity of cough increases. Physical examination is completely normal[23]. It is appropriate for these patients to be followed up by Child and Adolescent Psychiatry Clinic.

Although GERD is frequently detected among the etiological agents that cause chronic cough in adults, it is a rare condition in childhood[1]. As a matter of fact, Khoshoo et al.[24] reported that they found a significant relationship between cough and GERD in their study. On the other hand, Chang et al[25] reported that the evaluation of the cough—acid reflux relationship using esophageal pH monitoring and a cough logger did not detect any temporal association between the two conditions. We questioned in detail the complaints suggestive of reflux in the stories of our patients. We applied anti-reflux treatment and diet to the patients we thought had GERD. All patients responded to treatment. In addition to reflux complaint, only 1 patient had a feeling of being stuck in food. Due to the possible diagnosis of EoE, the patient was consulted with pediatric gastroenterology, and endoscopy was performed. As a matter of fact, widespread eosinophils were detected in the esophageal mucosa in the pathology report of the patient, and the patient's treatment was arranged together with pediatric gastroenterology. No case of EoE diagnosed with chronic cough was found in the literature. SPTs (both food and inhalant) of the same patient was performed and no atopy was found. Furthermore GERD was diagnosed by symptom and treatment response. Endoscopy and phmeter were not performed on these patients. The treatment response is obtained within weeks in reflux, this time may be sufficient for spontaneous coughing, which is a limitation.

Thoracic computer tomography was performed in two of the patients who had productive cough and did not respond to the antibiotic treatment. Bronchiectasis was detected in these patients. These patients should be questioned in detail in terms of underlying possible immunodeficiency or foreign body aspiration in the past[12]. These patients respond to antibiotic therapy, but the complaint of productive cough immediately recurs[20]. In our study, we detected bronchiectasis in 4 patients. It was determined that 2 of 4 patients had PCD in their etiology. Our patients were referred to Department of Pediatric Pulmonology for follow-up.

In our study, two female patients with productive cough were diagnosed with PCD. The PICADAR score of these two patients was above 10[13]. The mean age of these two diagnosed patients was 9.1±4 years. Both patients had productive cough. Recurrent otitis and recurrent pneumonia were found in the history of the patients. Moreover, it was learned that these two patients needed neonatal intensive care. Two patients had borderline growth retardation. No signs of hypoxia were found in our patients. Respiratory system examination of the patients at the time of first admission was evaluated as normal. On direct chest X-ray of the patients, atelectasis in the right middle lobe of one patient and bronchiectasis in the other patient were detected. Concomitant situs in versus anomaly was detected in two patients. The patients were followed up in Department of Pediatric Pulmonology with the diagnosis of PCD.

Chronic cough is a common condition in school-age children. It is observed that unnecessary antibiotics and medicines for symptomatic treatment are frequently used in these patients. In order to evaluate the patients correctly, it would be appropriate to follow the algorithms published by certain guidelines. While considering the recommendations of these guidelines, it should not be forgotten that each patient should be evaluated individually.

Conflict of interest
The authors declare that they have no conflict of interest.

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Ethical approval
This study was approved by the Local Ethics Committee of Adana City Hospital in order to conduct the study (decision no 2313/2022)

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