Türk Pediatri Arşivi
Turkish Archives of Pediatrics

Original Article / Özgün Araştırma

Early diagnosis effects the prognosis in children with atypical wheeze

Atipik hışıltılı çocuklarda erken tanı prognozu etkilemektedir

Ezgi Ulusoy Severcan[1], Esen Demir[1], Figen Gülen[1], Raziye Burcu Güven Bilgin[2], Remziye Tanaç[1]

[1]Division of Pediatric Allergy and Immunology, Department of Pediatrics, Ege University Faculty of Medicine, İzmir, Turkey
[2]Department of Pediatrics, Ege University Faculty of Medicine, İzmir, Turkey

The known about this topic

Recurrent wheezing may occur due to various causes. Wheezing may be typical or atypical.

Contribution of the study

Early diagnosis of patients with atypical wheezing influences prognosis.

Abstract

Aim: Recurrent wheezing is a common problem in preschool children. It is classified into two groups because there can be many reasons for wheeze: typical and atypical. The aim of this study was to identify the general features of atypical wheezy children.

Material and Methods: Three hundred two children who presented to our clinic between 2000 and 2015 for three or more wheezing attacks and were diagnosed as having an underlying disease such as bronchiectasis, foreign body aspiration, recurrent aspiration pneumonia, cystic fibrosis, bronchopulmonary dysplasia, congenital anomalies, and tuberculosis, were included in the study.

Results: In this study, 127 (42.1%) girls and 175 (57.9%) boys were evaluated. The diagnostic distribution of the patients was as follows: bronchopulmonary dysplasia (21.9%), bronchiolitis obliterans (16.6%), bronchiectasis (14.5%), bronchiolitis obliterans + primary immunodeficiency (12.3%), cystic fibrosis (10.3%), bronchiectasis + primary immunodeficiency (7.9%), recurrent aspiration pneumonia (3.6%) and foreign body aspiration (3.3%), and other diseases (9.6%). Mosaic oligemia, bronchiectasis, atelectasis, bronchiolectasis, and small airway disease were the most distinct findings on high-resolution lung tomography. When the patients were evaluated clinically, radiologically, and according to pulmonary functions after an average period of 40 months, it was seen that 9.2% deteriorated, 33.9% regressed, and 56.7% remained stable. Presentation to hospital after the first attack occurred earlier in patients with bronchopulmonary dysplasia, bronchiolitis obliterans and bronchiolitis obliterans + primary immunodeficiency compared with

Öz

Amaç: Tekrarlayan hışıltı atakları çocuklarda okul öncesi dönemde en sık karşılaşılan durumlardan biridir. Hışıltı birçok neden sonucunda ortaya çıkabilecek bir durum olması nedeniyle tipik ve atipik hışıltı olmak üzere iki gruba ayrılmıştır. Çalışmamızda kliniğimiz tarafından izlenen atipik hışıltılı çocukların genel özelliklerinin ortaya konulması amaçlanmıştır.

Gereç ve Yöntemler: Alerji kliniğine 2000-2015 yılları arasında üç ve daha fazla hışıltı nedeniyle başvurup izleminde bronşektazi, yabancı cisim aspirasyonu, tekrarlayan aspirasyon pnömonisi, kistik fibrozis, bronkopulmoner displazi, doğuştan anomaliler, tüberküloz gibi altta yatan bir hastalık saptanmış olan 302 hasta çalışmaya alınarak değerlendirilmiştir.

Bulgular: Çalışmamızda hastaların 127'si (%42,1) kız, 175'i (%57,9) erkekti. Hastaların etiyolojik tanı dağılımını; bronkopulmoner displazi (%21,9), bronşiolitis obliterans (%16,6), bronşektazi (%14,5), bronşiolitis obliterans + primer immün yetmezlik (%12,3), kistik fibrozis (%10,3), bronşektazi + primer immün yetmezlik (%7,9), tekrarlayan aspirasyon pnömonisi (%3,6), yabancı cisim aspirasyonu (%3,3) ve diğer hastalıklar (%9,6) oluşturmaktaydı. Yüksek rezolüsyonlu akciğer tomografisinde mozaik oligemi, bronşektazi, atelektazi, bronşiolektazi ve küçük hava yolu hastalığı en belirgin bulgulardı. Hastaların ortalama 40 ay süreli izlemleri sonucunda klinik, radyolojik ve solunum işlevlerine göre %9,2'sinde kötüleşme, %33,9'unda gerileme olduğu %56,7'sinin stabil kaldığı gözlendi. Bronşiolitis obliterans, bronşiolitis obliterans + primer immün yetmezlik ve bronkopulmoner displazili hastalarda üçüncü hışıltıdan sonra

Cont. ➡

Cite this article as: Ulusoy Severcan E, Demir E, Gülen F, Güven Bilgin RB, Tanaç R. Early diagnosis effects the prognosis in children with atypical wheeze. Turk Pediatri Ars 2020; 55(3): 251–6.

Corresponding Author/Sorumlu Yazar: Ezgi Ulusoy Severcan E-mail/E-posta: ezgiulusoy13@hotmail.com
Received/Geliş Tarihi: 10.06.2019 **Accepted/Kabul Tarihi:** 13.12.2019

DOI: 10.14744/TurkPediatriArs.2019.35467

patients with bronchiectasis, bronchiectasis + primary immunodeficiency, and cystic fibrosis. When presentation time and outcomes were evaluated, it was found that 63.4% of patients who presented to hospital early (0–6 months) and 7.5% of patients who presented late (after 5 years) had regression.

Conclusion: Recurrent wheezy children must be promptly evaluated for an underlying disease. Early diagnosis and treatment influence the prognosis.

Keywords: Atypical wheeze, bronchiectasis; bronchopulmonary dysplasia, cystic fibrosis, wheezing

hastaneye başvuru bronşektazi, bronşektazi + primer immün yetmezlik ve kistik fibrozlu hastalara göre daha erkendi. Başvuru süreleriyle son izlem sonuçları karşılaştırıldığında 0–6 ayda başvuran hastalarda bulgularda gerileme %63,4 iken geç başvuranlarda (5 yıldan sonra) gerileme %7,5 olarak saptandı.

Çıkarımlar: Sonuç olarak tekrarlayan hışıltısı olan çocuklar atipik hışıltı nedenleri açısından araştırılmakta gecikilmemelidir. Erken tanı ve tedavi prognozda etkilidir.

Anahtar sözcükler: Atipik hışıltı, bronşektazi, bronkopulmoner displazi, kistik fibrozis, hışıltı

Introduction

Wheezing is a musical, high-pitched sound heard in expirium as a result of turbulent flow and vibrations caused by narrowing in the airway with conditions such as inflammation, mucosal edema, anatomic compression, and bronchospasm (1, 2). Recurrent wheezing episodes are one of the most common conditions observed in the preschool period in children. About one-half of children have a wheezing episode in the first year of life. Therefore, it is a public health problem in both social and economic aspects. As wheezing is a common condition that may result from a variety of different causes and it is divided into two groups as typical and atypical wheezing (3–5). Typical wheezing involves transient wheezing, persistent wheezing and late-onset wheezing, whereas atypical wheezing is defined as wheezing that occurs as a result of other underlying diseases including gastroesophageal reflux, foreign body aspiration, bronchopulmonary dysplasia (BPD), bronchiectasis, cystic fibrosis (CF), bronchiolitis obliterans (BO), primary ciliary dyskinesia (PSD), and primary immune deficiency (PID). Different symptoms may accompany wheezing according to the underlying disease. This may constitute a clue for physicians in terms of differentiating atypical wheezing from typical wheezing. For example, growth retardation and a history of death of a sibling in association with consanguineous marriage suggest cystic fibrosis, and presence of accompanying recurrent sinusitis findings suggests primary ciliary dyskinesia, both of which are autosomal recessive diseases in the differential diagnosis, and premature delivery primarily suggests bronchopulmonary dysplasia (6–10). Atopy findings mostly suggest typical wheezing.

In this study, it was aimed to demonstrate the general characteristics of children with atypical wheezing who were followed up by our clinic.

Material and Methods

Three hundred two patients who presented to the allergy clinic between 2000 and 2015 because of three or more episodes of wheezing and were found to have underlying morbidities such as primary immune deficiency [e.g. transient hypogammaglobulinemia of infancy (THI), selective and partial immunoglobulin (Ig)-A deficiency, combined immune deficiency, chronic granulomatous disease, hyper IgM syndrome, DiGeorge syndrome), bronchiectasis, bronchiolitis obliterans, foreign body aspiration, congenital anomalies, and tuberculosis, were included in the study and evaluated retrospectively.

The patients' demographic, clinical and laboratory characteristics were evaluated by completing questionnaire forms. The patients were also evaluated in terms of being in a progressive, regressive or stable state according to the clinical picture during the follow-up period (complete regression in wheezing episodes), radiologic changes [regression in findings compared with previous computed tomography (CT) in the patients in whom CT had been performed (82%)] and changes in pulmonary functions [normal pulmonary function test in the follow-up in patients in whom pulmonary function test could be performed (33.7%) and restrictive disorder was found]. Patients who had no differences in all three characteristics were considered stable, those who were observed to have an improvement in any of the characteristics were considered to have regression, and patients who were observed to have deterioration in any of the characteristics were considered to have progression.

Ethics committee approval was obtained from the non-pharmacologic research ethics committee (Approval date: 09.08.2016, Number: 16-6/7). The study was conducted in accordance with the principles of the Helsinki Declaration.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) Ver. 16.0 program. Percentages mean±standard deviation and median (min-max) values were calculated and the Chi-square test was used for comparisons of the groups.

Results

A total of 302 patients including 127 (42.1%) girls and 175 (57.9%) boys were evaluated, retrospectively. In patients whose wheezing started at a median age of 8 (range, 1–92)

months, the first episode occurred in the neonatal period with a rate of 12.2%, between 0 and 6 months with a rate of 55.9%, between 0 months and 1 year with a rate of 66.9%, and above the age of 5 years only with a rate of 12.2%. The median age at the first presentation was 24 (range, 3–324) months, and the current median age was 10±6.9 (range, 1–30) years. The mean follow-up period was 40±43 months.

A history of hospitalization was present in 96.7% of patients and the episodes occurred in the winter with a rate of 41% and throughout the year with a rate of 54.8%. Prematurity was observed with a rate of 25.2%, consanguineous marriage was present with a rate of 18.2%, and atopy in the family was present with a rate of 8.4%. The highest rates of consanguineous marriage were found in the patients who had primary ciliary dyskinesia (50%), primary immune deficiency (39%), bronchiectasis (33%), cystic fibrosis (37,9%) and bronchiolitis obliterans (26%). Passive smoking was found with a rate of 46.9% and stoves were used for indoor heating with a rate of 65.6%. Although no statistically significant correlation was found between the yearly number of episodes and passive smoking or the use of stoves, it was observed that patients who had passive smoking had more episodes. Irritant substances were specified as attack triggers with a rate of 10.7%. Infections were the most common attack trigger with a rate of 88.8%. Ninety percent of patients had a moderate and low average income, and university education was found with a rate of 18.2% in the mothers and with a rate of 29.5% in the fathers (Table 1).

Aeroallergen-spIgE was positive in 9.8% of the subjects. Reversibility was not observed in patients in whom PFT could be performed among these patients, and asthma was not considered clinically. Allergic rhinitis symptoms were observed in a portion of these patients.

The patients' etiologic diagnosis distribution was as follows: bronchopulmonary dysplasia (21.9%), bronchiolitis obliterans (16.6%), bronchiectasis (14.5%), bronchiolitis obliterans + primary immune deficiency (12.3%), cystic fibrosis (10.3%), bronchiectasis + primary immune deficiency (7.9%), recurrent aspiration pneumonia (3.6%), foreign body aspiration (3.3%), and other diseases (9.6%) (Fig. 1). It was observed that three cases of bronchiolitis obliterans developed following bone marrow transplantation.

In addition, THI or selective partial IgA deficiency accompanied in 6.6% of patients in whom a cause other than primary immune deficiency was found as the etiology of recurrent wheezing. No additional immunity disorder was observed in any of the patients with cystic fibrosis,

Table 1. The patients' demographic properties

Property	n/%
Sex	175 /57.9 male, 127/42, one female
Consanguineous marriage	55/18.2%
Place of living	176/58.3 provincial center, 113 /37.4 district, 13/4.3 village
Prematurity	76/25.2
Maternal education	Primary school: 76/25.2
	Secondary school: 138/45.7
	High school: 33/10.9
	University: 55 /18.2
Paternal education	Primary school: 53/17.5
	Secondary school: 128/42.4
	High school: 32/10.6
	University: 89/29.5
Family income	Low: 202/66.9
	Moderate: 74/24.5
	High: 26/8.6
The heating device used at home	Stove: 198/65.6
	Central heating: 98/32.4
	Air conditioner: 6/2
Passive smoking	142/46.9
Having a pet at home	5/1.6
One or more siblings	203/67.3

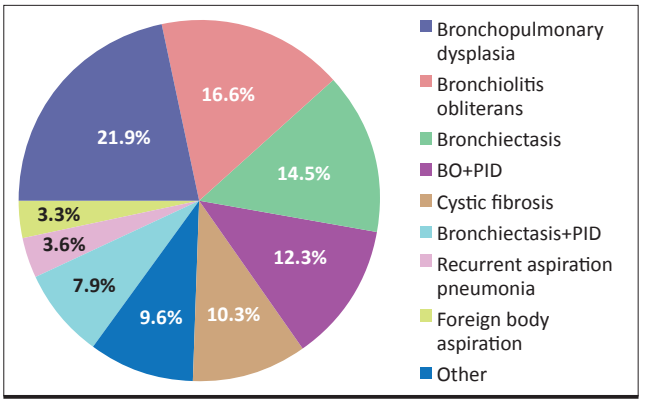

Figure 1. Distribution of patients with atypical wheezing

and no pulmonary disease other than bronchiolitis obliterans and bronchiectasis was noted in the patients who were found to have primary immune deficiency.

High-resolution lung tomography was performed in 82% of the patients, and mosaic oligemia, bronchiectasis, atelectasis, bronchiolectasis, and small airway disease were the most prominent findings.

Table 2. Prognosis by disease in patients with atypical wheezing

	Final status		
	Progression (%)	Regression (%)	Stable (%)
Bronchopulmonary dysplasia	0	65.1	34.9
Bronchiolitis obliterans	6	32	62
Bronchiectasis	5	17	78
Bronchiolitis obliterans+ primary immune deficiency	10.9	21.6	67.5
Cystic fibrosis	16.2	0	83.8
Bronchiectasis+primary immune deficiency	37.5	8.3	54.2
Recurrent aspiration	0	0	100

Pulmonary function tests could be performed in 33.7% of the patients at the initial presentation. At baseline, a FEV1 value below 80% was found with a rate of 56.7% and a FEV1 value below 60% was found with a rate of 23.1%, a FEV1/FVC value below 80% was found with a rate of 7.8%, and a FEV1/FVC value below 60% was found with a rate of 2%. A MEF25-75 value below 80% was found with a rate of 63.5% and a MEF25-75 value below 60% was found with a rate of 38.5%, a PEF value below 80% was found with a rate of 57.3% and a PEF value below 60% was found with a rate of 28.1%.

As a result of 40-month follow-up of the patients, clinical (attacks of all patients were evaluated), radiologic (evaluated in 82% of the patients whose CT was obtained at the time of diagnosis), and pulmonary function (evaluated in 33.7% of the patients in whom PFT could be performed at the time of diagnosis) evaluations revealed deterioration in 9.2% of the patients, regression in 33.9%, and stable disease in 56.7%. Presentation to hospital after the third wheezing attack occurred earlier in patients with bronchiolitis obliterans, bronchiolitis obliterans + primary immune deficiency, and BPD compared with the patients with bronchiectasis + primary immune deficiency and cystic fibrosis. Considering the presentation times after symptom onset as 0–6 months (n=84), 6–12 months (n=76), 13–60 months (n=70), and over 61 months (n=72), the final follow-up outcomes were compared by presentation times and regression was found with a rate of 63.4% in patients who presented in 0–6 months, whereas it was 7.5% in patients who presented later (after 5 years) ($p<0.05$). Table 2 shows the distribution of prognoses in patients with atypical wheeze by diseases.

Discussion

Recurrent wheezing is a common public health problem that frequently occurs in childhood. Although regression is observed in the majority of this group at advanced ages, atypical wheezing occurs in a small portion. In our study, the general characteristics of the children who presented to our clinic with recurrent wheezing and were found to have atypical wheezing were investigated. The rates of females and males were similar. Consanguineous marriage was found with a rate of 18.2% and the highest rates were found in patients with primary ciliary dyskinesia (50%), primary immune deficiency (39%), bronchiectasis (33%), cystic fibrosis (37.9%), and bronchiolitis obliterans (26%). A certain part of cases of primary ciliary dyskinesia, cystic fibrosis, and primary immune deficiency is autosomal recessive diseases. In countries where rates of consanguineous marriage are high such as Turkey, these conditions must be evaluated in the differential diagnosis, especially in patients whose lung tomography reveals bronchiectasis. The definite diagnosis of primary ciliary dyskinesia can be made by the genetic tests (11–13). In our country, a part of these patients is probably being followed up with a diagnosis of bronchiectasis because genetic tests for primary ciliary dyskinesia are insufficient.

The parents of more than half of the subjects had an education level of primary school or secondary school, and their family income levels were low. The majority (65%) heated their houses with stoves and the rate of passive smoking was high (46%), but these findings were not significantly correlated with attacks. However, it was observed that patients with passive smoking had more attacks, though the difference was insignificant.

Symptoms started in the previous 6 months and before in more than half of the patients and almost all patients had a history of hospitalization. The predominant trigger for attacks was infections. The rate of prematurity was found as 25% and patients with pulmonary dysplasia constituted the majority.

When the distribution of etiologic diagnoses was examined, it was observed that the most common underlying diseases included bronchopulmonary dysplasia (21.9%), bronchiolitis obliterans (16.6%), bronchiectasis (14.5%), bronchiolitis obliterans + primary immune deficiency

(12.3%), cystic fibrosis (10.3%), bronchiectasis + primary immune deficiency (7.9%), recurrent aspiration pneumonia (3.6%), and foreign body aspiration (3.3%).

Bronchiolitis obliterans is observed rarely in children, but its frequency is not known clearly (14, 15). It mostly develops as a result of infections caused by agents such as adenovirus, influenza, and mycoplasma pneumonia, but a certain part of the cases develop as a result of bone marrow transplantation (BMT), lung transplantation, toxic gas inhalation or gastroesophageal reflux (16). Bronchiolitis obliterans may also be observed because of frequent infections due to primary immune deficiency. A very small number of our cases developed as a result of BMT and the others were associated with previous infection and primary immune deficiency.

In the last 10 years, an increase has been observed in multiple pregnancies and premature deliveries due to the increased use of assistive reproductive techniques. In addition, increased rates of bronchopulmonary dysplasia due to improved care in neonatal intensive care units and decreased mortality in preterm babies may explain the fact that BPD was first in order in the study group.

Bronchiectasis is mostly associated with cystic fibrosis but many other underlying causes may be found (17). Although its frequency is not clearly known, it has been reported that the frequency is lower in developed countries and this is related to less crowded environments, better hygienic conditions, and nutrition (18–20). When the general characteristics of the study patients were examined, it was noted that the socioeconomic level was generally low. In primary immune deficiencies, respiratory tract problems constitute a significant cause of morbidity and mortality. Among the causes of bronchiectasis, immune deficiencies also have a significant place following cystic fibrosis, and a history of pneumonia (21, 22).

When the patients were evaluated clinically, radiologically, and according to pulmonary function tests in the follow-up, it was observed that 9.2% deteriorated, 33.9% regressed, and 56.7% remained stable. Regression was found with a rate of 32% in cases of bronchiolitis obliterans, with a rate of 21.6% in cases of bronchiolitis obliterans + primary immune deficiency, with a rate of 65% in cases of BPD, and with a rate of 17% in cases of bronchiectasis. Various publications have reported that pulmonary functions can remain stable and even improve with favorable control in cases of bronchiectasis (23–25). In bronchiolitis obliterans, improvement may be observed in the clinical picture and pulmonary functions after a 2–3-year follow-up (15, 26). In a study conducted by Zhang et al. (27), clinical improvement was observed with a rate of 22.6%. In patients with BPD, a rate of 65% is a high regression rate. It was thought that this could be associated with the treatment approaches used in NICUs and the use of prophylactic steroids. When the final follow-up outcomes were compared by presentation time, regression was found with a rate of 63.4% in patients who presented in 0–6 months, whereas it was 7.5% in patients who presented later (after 5 years). The presentation time affected prognosis.

The most important limitation of this study was that it was a retrospective study. Prospective studies are needed for more detailed evaluation.

To the best of the authors' knowledge, this study is the first in Turkey in which cases of atypical wheezing were evaluated generally.

In conclusion, the evaluation of children with recurrent wheezing in terms of causes of atypical wheezing should not be delayed. Early diagnosis and treatment influence the prognosis.

Ethics Committee Approval: The study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was obtained from Ege University Faculty of Medicine ethics committee (date: 09.08.2016, number: 16-6/7).

Informed Consent: Written consent was not obtained from the patients' parents because all patients included in the study were evaluated retrospectively.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - E.D.; Design - E.D., E.U.S.; R.B.G.B.; Supervision - E.D., F.G., R.T.; Funding - E.U.S., E.D.; Materials - E.U.S., E.D.; Data Collection and/or Processing - E.U.S., R.B.G.B.; Analysis and/or Interpretation - E.U.S., E.D.; Literature Review - E.U.S., E.D.; Writing - E.U.S.; Critical Review - E.D., F.G., R.T.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Kurul Onayı: Çalışma Helsinki deklarasyon prensiplerine uygun olarak gerçekleştirildi. Bu çalışma için etik kurul onayı Ege Üniversitesi Tıp Fakültesi Etik Kurulu'ndan alınmıştır (tarih: 09.08.2016, sayısı: 16-6/7).

Hasta Onamı: Çalışmaya alınan tüm hastalar geriye dönük olarak değerlendirildiğinden ebeveynlerden yazılı onam alınmamıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - E.D.; Tasarım - E.D., E.U.S.; R.B.G.B.; Denetleme - E.D., F.G., R.T.; Kaynaklar - E.U.S., E.D.; Malzemeler - E.U.S., E.D.; Veri Toplanması ve/veya İşlemesi - E.U.S., R.B.G.B.; Analiz ve/veya Yorum - E.U.S., E.D.; Literatür Taraması - E.U.S., E.D.; Yazıyı Yazan - E.U.S.; Eleştirel İnceleme - E.D., F.G., R.T.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

References

1. El-Gamal YM, El-Sayed SS. Wheezing in infancy. World Allergy Organ J 2011; 4: 85–90.
2. Brown MA, von Mutius E, Morgan WJ. Clinical assessment and diagnostic approach to common problems. In: Taussig, LM, Landau LI, Le Souef PM, Martinez FD, Morgan WJ, Sly PD, editors. Pediatric respiratory medicine. Vol. 2nd edition. Philadelphia: Mosby Elsevier; 2008.p.112–3.
3. Süleyman A, Güler N. Hışıltılı çocuğa güncel yaklaşım. J Turk Fam Physician 2011; 1: 4–10.
4. Alper Gürz A, Artıran İğde FA, Dikici MF, Yarış F. Approach to Wheezy Infant In Primary Care. Turk J Fam Med 2013; 7: 18–25.
5. Tanaç R. Hışıltılı çocukta tanı ve ayırıcı tanı (Hangisi Astım?). Güncel Pediatri 2005; 71: 12–4.
6. VanDevanter DR, Kahle JS, O'Sullivan AK, Sikirica S, Hodgkins PS. Cystic fibrosis in young children: A review of disease manifestation, progression, and response to early treatment. J Cyst Fibros 2016; 15: 147–57.
7. Fitzgerald DA, Shapiro AJ. When to suspect primary ciliary dyskinesia in children. Paediatr Respir Rev 2016; 18: 3–7.
8. Dehlink E, Hogg C, Carr SB, Bush A. Clinical phenotype and current diagnostic criteria for primary ciliary dyskinesia. Expert Rev Respir Med 2016; 10: 1163–75.
9. Dodge JA. A millennial view of cystic fibrosis. Dev Period Med 2015; 19: 9–13.
10. Davidson LM, Berkelhamer SK. Bronchopulmonary Dysplasia: Chronic Lung Disease of Infancy and Long-Term Pulmonary Outcomes. J Clin Med 2017; 6: 4.
11. Shapiro AJ, Zariwala MA, Ferkol T, Davis SD, Sagel SD, Dell SD, et al. Diagnosis, monitoring, and treatment of primary ciliary dyskinesia: PCD foundation consensus recommendations based on state of the art review. Pediatr Pulmonol 2016; 51: 115–32.
12. Lucas JS, Paff T, Goggin P, Haarman E. Diagnostic Methods in Primary Ciliary Dyskinesia. Paediatr Respir Rev 2016; 18: 8–17.
13. Fitzgerald DA, Shapiro AJ. When to suspect primary ciliary dyskinesia in children. Paediatr Respir Rev 2016; 18: 3–7.
14. Yu J. Postinfectious bronchiolitis obliterans in children: lessons from bronchiolitis obliterans after lung transplantation and hematopoietic stem cell transplantation. Korean J Pediatr 2015; 58: 459–65.
15. Tomikawa SO, Rodrigues JC. Current research on pediatric patients with bronchiolitis obliterans in Brazil. Intractable Rare Dis Res 2015; 4: 7–11.
16. Pekcan S, Özçelik U. Bronşiyolitis obliterans. Hacattepe Tıp Dergisi 2008; 39: 16–21.
17. Redding GJ. Bronchiectasis in children. Pediatr Clin North Am 2009; 56: 157–71.
18. Al Subie H, Fitzgerald DA. Non-cystic fibrosis bronchiectasis. J Paediatr Child Health 2012; 48: 382–8.
19. Chang AB, Redding GJ, Everard ML. Chronic wet cough: Protracted bronchitis, chronic suppurative lung disease and bronchiectasis. Pediatr Pulmonol 2008; 43: 519–31.
20. Twiss J, Metcalfe R, Edwards E, Byrnes C. New Zealand national incidence of bronchiectasis "too high" for a developed country. Arch Dis Child 2005; 90: 737–40.
21. Jesenak M, Banovcin P, Jesenakova B, Babusikova E. Pulmonary manifestations of primary immunodeficiency disorders in children. Front Pediatr 2014; 2: 77.
22. Haidopoulou K, Calder A, Jones A, Jaffe A, Sonnappa S. Bronchiectasis secondary to primary immunodeficiency in children: longitudinal changes in structure and function. Pediatr Pulmonol 2009; 44: 669–75.
23. Bastardo CM, Sonnappa S, Stanojevic S, et al. Non-cystic fibrosis bronchiectasis in childhood: longitudinal growth and lung function. Thorax 2009; 64: 246–51.
24. Kapur N, Masters IB, Chang AB. Longitudinal growth and lung function in pediatric non-cystic fibrosis bronchiectasis: what influences lung function stability? Chest 2010; 138: 158–64.
25. Goyal V, Grimwood K, Marchant J, Masters IB, Chang AB. Pediatric bronchiectasis: No longer an orphan disease. Pediatr Pulmonol 2016; 51: 450–69.
26. Cazzato S, Poletti V, Bernardi F, et al. Airway inflammation and lung function decline in childhood post-infectious bronchiolitis obliterans. Pediatr Pulmonol 2008; 43: 381–90.
27. Zhang L, Irion K, Kozakewich H, et al. Clinical course of postinfectious bronchiolitis obliterans. Pediatr Pulmonol 2000; 29: 341–50.