Complete Ciliary Aplasia; a Rare Form of Primary Ciliary Dyskinesia

Komplet Silier Aplazi; Primer Silier Diskinezinin Nadir Formu

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ABSTRACT

This report describes the ultrastructural alterations observed in the bronchial mucosa of a 29-year old male patient suffering from chronic upper and lower respiratory tract infections since his childhood and operated due to bronchiectasis and sinusitis.

Electron microscopic evaluation of the bronchial biopsy specimens revealed ciliated cells appeared to be replaced by columnar cells lacking cilia and basal bodies, and bearing on their surface cilium-like projections without any internal axonemal structure.

These ultrastructural features are consistent with complete ciliary aplasia which is a rare form of primary ciliary dyskinesia.

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Key words: Ciliary aplasia, dyskinesia, bronchiectasis

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ÖZET

Bu yazıda çocukluğunda bronşektazi ve sinüzit nedeniyle ameliyat olan, kronik üst ve alt solunum yollarında kronik infeksiyonu olan 29 yaşındaki erkek hastanın bronş mukozasının mikroskopik incelemesinde anormallik saptanmıştır.

Bronş biyopsisi örneklerinin elekron mikroskopik incelemesinde silialı hücrelerin olması gereken bölgelerde kübik hücrelerin olduğu, silialaın ve bazal cisimciklerin yok olduğu, içinde internal aksonal yapı olmayan siliaya benzer yapıların olduğu izlendi. Bu mikroskopik bulgular primer siliyer diskinezinin nadir bir formu olan komplet silier aplazi varlığını göstermektedir.

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Anahtar sözcükler: Siliyer aplazi, bronşektazi, diskinezi

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INTRODUCTION

Primary ciliary dyskinesia (PCD) is a term used to describe the conditions that result from primary defect in the structure or function of cilia [1].

It is an autosomal recessive disorder characterized by chronic upper and lower respiratory tract symptoms. Situs inversus occurs randomly in approximately 50% of subjects with PCD [1-3]. The prevalence is estimated at approximately 12000 to 17000, as extrapolated from radiographic studies [4,5]. PCD may be caused by one of a number of different ciliary ultrastructural defects, each of which results in ineffective ciliary function. These defects include lack of inner and/or outer dynein arms, defective radial spokes, ciliary disorientation, and ciliary transposition. The most common abnormality recorded was absence of the inner dynein arms [6].

In this article we report a case at the age of 29 and had operations due to bronchiectasis and sinusitis, now diagnosed as complete ciliary aplasia which is a rare form of PCD.

CASE

A 29-year old male patient was admitted to our hospital with the complaints of dyspnea, productive cough, and nasal obstruction. Though he has not any symptoms during his neonatal period, complains of bronchitis has begun at early childhood. He was a smoker (3 pack/year). In his past medical history it was learned that, he had operations due to bronchiectasis at the age of 12 and sinusitis when he was 25. Physical examination showed a blood pressure of 120/70 mmHg, heart rate of 102 bpm, temperature of 36.8°C and respiratory rate of 22/min. At respiratory system examination a thorocotomy scar was seen at the left hemithorax. Auscultation of the lungs revealed crackles over the right base, and bilaterally sonour ronchi. Cardiovascular and abdominal examinations were normal**.** Laboratory studies showed a WBC of 8x10^3/UL, ESR of 10 mm/hr.

Serum biochemical tests and urinary examination were in normal range. Pulmonary function tests revealed a mixed obstructive and restrictive pattern. Chest X-ray showed a volume loss in the left hemithorax, and bilateral bronchovascular signs became clear in lower zones especially at paracardiac localizations. (Figure 1). In his high resolution computerized tomography (HRCT), there were peribronchial thicknesses, bronchiectasis in the localization of medial and lateral segments of right middle lobe. (Figure 2). He was also examined for nasal obstruction and diagnosed as chronic sinusitis with nasal polyposis.

Our patient had recurrent cough, purulent sputum episodes since childhood and had operations due to

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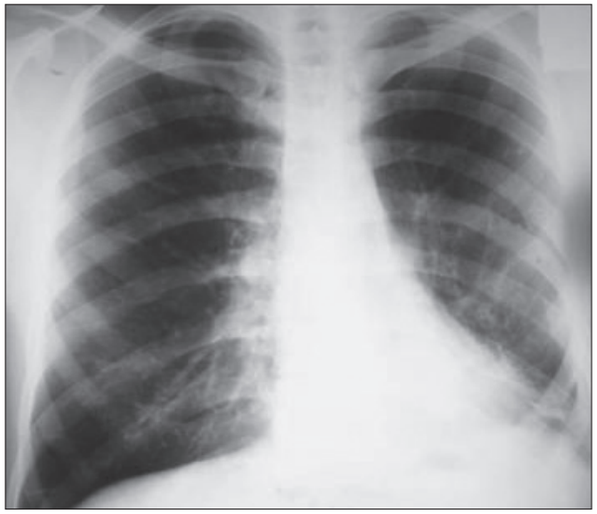

Figure 1. Chest X-ray showed a volume loss in the left hemithorax, and bilateral bronchovascular signs became clear in lower zones especially at paracardiac localizations

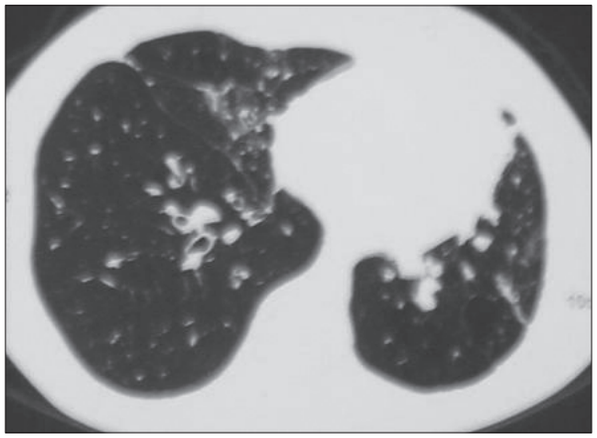

Figure 2. HRCT showed peribronchial thicknesses, bronchiectasis in the localization of medial and lateral segments of right middle lobe

bronchiectasis at an early age and sinusitis at a later term. And now his new HRCT revealed bronchiectasis at a different site. Investigations excluded an immunoglobulin deficiency, tuberculosis, and cystic fibrosis. Cystic fibrosis was excluded by the clinical picture and a normal sweat test. His α-1 antitrypsine level was found in the normal range.

According to ear, nose and throat consultation, it was concluded that the nasal mucosa is not preferred to obtain biopsies for the investigation of the ciliary morphology. So fiberoptic bronchoscopy was performed after the two weeks of antibioterapy. Mucosal biopsies were obtained from different sites and bronchial lavage fluid was also taken. With the direct light microscopic examination, inflammatory findings were seen. The ultrastructural analysis of the cilia with electronmicroscopy revealed ciliated cells appeared to be replaced by columnar cells lacking cilia and basal bodies, and bearing on their surface cilium-like projections without any internal axonemal structure. (Figure 3, 4). These morphological features of electron microscopy consistent with complete ciliary aplasia which is a rare form of primary ciliary dyskinesia.

DISCUSSION

Primary ciliary dyskinesia (PCD) is an inclusive term for diseases that occur as a direct result of congenital defects in cilia. It includes Kartegener syndrome, immotile cilia syndrome and ciliary orientation defects [1]. A large range of ultrastructural defects of the cilia may cause this syndrome and the most common pattern of inheritance is autosomal recessive disease [6]. A prevalence of 1 in 15000 has been estimated, but the number of actually identified cases is an order of magnitude lower because of unawareness of the condition and the complexity of the diagnostic tests [7]. Most patients with PCD have deficient dynein arms-inner, outer, or both. There is a wide spectrum of dynein arm defects, ranging from partial to complete absence. Defects of outer dynein arms have more effect on motility because there is a positive correlation of ciliary motility with the number of outer dynein arm numbers, seen by electron microscopy but not with numbers of iner dynein arms [8]. A number of other defects have been identified, such as radial spoke defects and microtubule translocations defects, in which a peripheral double passes to the center tubules [2,9]. The first ultrastructural primary defect of cilia described in humans was the absence of dynein arms. The most common ultrastructural defects are observed in the outer and inner dynein arms [5]. Also radial spoke defect, microtubule translocation defect, random ciliary orientation, abnormal long cilia, abnormal short cilia, abnormal basal bodies and ciliary aplasia have been identified [6]. Ultrastructural analysis of our patient's cilia revealed complete loss of 9+2 pattern of microtubular structure, instead microvillus-like structures were present. This structural abnormality was reported as complete ciliary aplasia. Complete ciliary aplasia is a rare form of PCD which is characterized by the absence of cilia in respiratory epithelium. The cause of this structural abnormality still remains obscure [7].

Abnormalities of ciliary ultrastructure can be divided into primary defects seen in PCD and secondary defects made by respiratory infections, physico-chemical injury of the mucosa, locally applied drugs and exacerbation of asthma. Secondary ciliary dyskinesia is a reversible ultrastructural ciliary abnormality [2,3].

Chronic rhinosinusitis is one of the most frequent clinical findings in PCD patients. Chronic and severe secretory otitis media is generally present in childhood. Significant hearing problems occur in approximately 50% of children. Up to 50% of patients with PCD have situs inversus. Secondary to a failure in mucociliary defense mechanisms, recurrent pulmonary infections often leads to bronchiectasis seen in PCD patients. Male patients may have reduced fertility due to sperm immotility or abnormalities of the vas deferens [4,8,9]. Coexisting of retinitis pigmentosa and PCD have been reported in same cases [10]. Our patient has recurrent sinopulmonary infections in his medical history. He was operated due to bronchiectasis and sinusitis.

The specific diagnosis relies on demonstration of ineffient ciliary function, by microscopy and photometric technics which is only available in very specialized centers. Transmission electron microscopy is an essential part of diagnostic testing, but the benefit of ultrastructural findings as criteria for the diagnosis of PCD is sometimes limited [11]. Normal ciliary ultrastructure has been

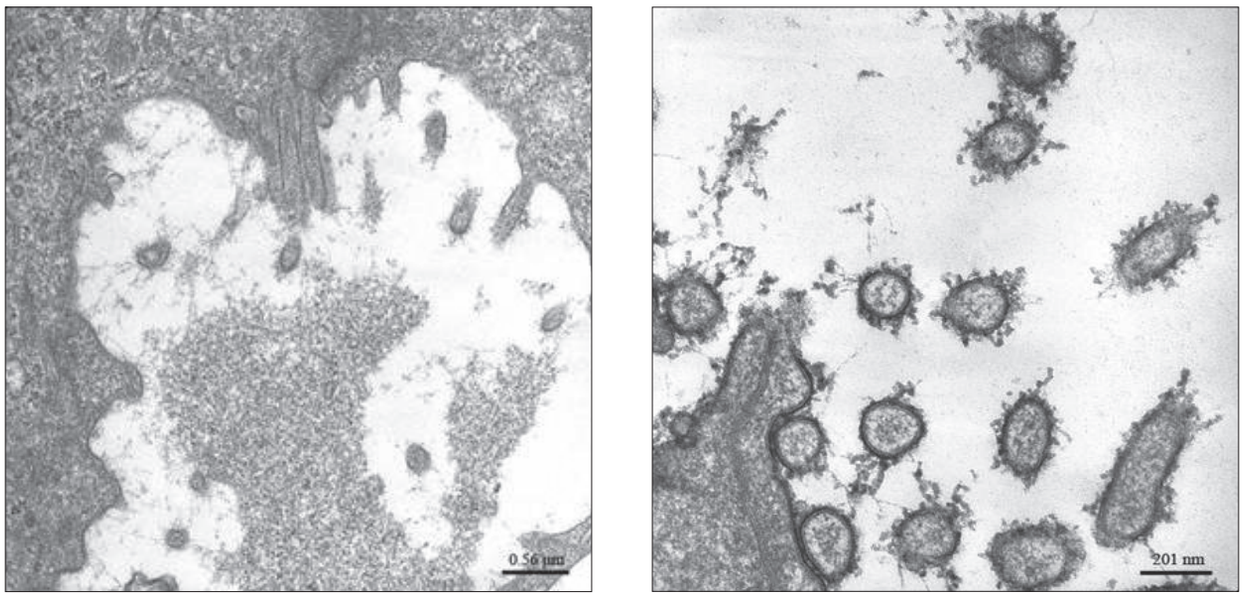

Figure 3-4. The ultrastructural analysis of the cilia with electronmicroscopy revealed ciliated cells appeared to be replaced by columnar cells lacking cilia and basal bodies, and bearing on their surface cilium-like projections without any internal axonemal structure

reported in few patients with immotile cilia. Measurement of abnormal ciliary beat frequency by photodiode or photomultiplier techniques can also be supportive for the diagnosis. To reduce possible misinterpretation, as a result of secondary ultrastructural defects, mucosal biopsy should be obtained at least 4-6 weeks after complete resolution of respiratory infection. And it is essential to obtain the mucosal biopsy in at least two different sites to avoid false diagnosis [2]. History and clinical findings of the patient support the diagnosis.

In differential diagnosis, PCD should be distinguished from cystic fibrosis, Young syndrome, immune deficiency and allergy [12]. Cystic fibrosis cannot be excluded by clinical picture since pancreatic sufficient cystic fibrosis patients can present with similar symptoms [13]. In our case it was excluded as sweat test result was in the normal range. Immunoglobulin subgroups, α1 antitrypsine levels were also normal. For the specific investigation of PCD mucosa biopsies were taken with fiberoptic bronchoscopy. The ultrastructural analysis of the cilia with electron microscopy was performed.

There is not an available therapy for the management of PCD described, it is essentially symptomatic. In acute infective exacerbations, antibiotics and physiotherapy can be useful. For patients who have progressed to bronchiectasis, postural drainage and the other physiotherapy is helpful. Early diagnosis and treatment of infections may slow progress to bronchiectasis. Treatment of the severe form of the disease should include regular lung function monitoring, sputum microbiology and aggressive airway clearance and antibiotics [6]. Cough has the potential for increasing mucus clearance rates towards normal in PCD with absent mucociliary transport. Because of this, self induced coughing every 2-3 hours during the day can be advice to PCD patients [14,15].

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