Case Report

Allergic Bronchopulmonary Aspergillosis in a Patient with Kartagener's Disease: An Unusual Association

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Abstract

Primary ciliary dyskinesia (PCD) is a congenital disorder characterized by abnormal ciliary motility with associated impaired mucociliary clearance. When PCD has associated situs inversus, it is known as Kartagener's disease. Due to recurrent sinopulmonary infections, patients of Kartagener's disease develop bronchiectasis. Allergic bronchopulmonary aspergillosis (ABPA) is an allergic disorder characterized by exaggerated immune response to the fungus *Aspergillus*. Patients with ABPA also develop bronchiectasis in advanced stages. Here, we report a patient of Kartagener's disease who also had coexisting ABPA. We believe such an association has been reported in just a handful of cases. As Kartagener's disease can be easily diagnosed radiologically and bronchiectasis is a feature of Kartagener's disease, many of these patients do not undergo further evaluation. In reporting this rare occurrence, we believe many such associations will be revealed in future.

Keywords: Allergic bronchopulmonary aspergillosis, primary ciliary dyskinesia, situs inversus

Introduction

Primary ciliary dyskinesia (PCD) is an autosomal recessive disease characterized by abnormal ciliary motility with associated impaired mucociliary clearance. Kartagener's disease is a part of disorders with impaired ciliary motility. Patients with Kartagener's disease have bronchiectasis, dextrocardia, situs inversus, and recurrent sinusitis. About 50% of patients with PCD have Kartagener's disease. We present a rare incident where a patient with Kartagener's disease also had allergic bronchopulmonary aspergillosis (ABPA).

Case Report

A 22-year-old-college student presented with recurrent episodes of chest tightness, wheezing, and cough since 15 years of age with symptoms aggravated for the past 6 months. She also complained of recurrent headaches and running nose. She had been diagnosed clinically as bronchial asthma and was on irregular treatment with inhaled bronchodilators and antihistamines. There was no family history of allergy or asthma. She denied previous treatment for tuberculosis. She was unmarried and her menstrual cycles were normal. On examination, the patient was stable and maintained normal saturation at room air. She had bilateral maxillary and frontal sinus tenderness with turbinate hypertrophy in both nostrils. Respiratory examination revealed bilateral expiratory wheeze and occasional coarse crackles. She was initially evaluated as a case of allergic asthma.

A chest X-ray and X-ray of paranasal sinuses were performed. Chest X-ray showed dextrocardia with situs inversus. There was also ring shadows in both the lung fields suggestive of bronchiectasis [Figure 1]. Paranasal sinus X-ray revealed haziness of maxillary sinus [Figure 2]. A possibility of Kartagener's disease was considered. Her blood total eosinophil count was elevated (880 cells/mm^3). Electrocardiogram showed mirror-image dextrocardia which was confirmed by echocardiography. In view of elevated eosinophils, she was also evaluated for the possibility of ABPA. Skin prick test for *Aspergillus* was positive. Serum total immunoglobulin E (IgE) was 1400 IU/L. Serum-specific IgE for *Aspergillus* was positive (via Radioimmunoassay - phadia ImmunoCAP). Serum

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precipitins immunoglobulin G (IgG) against *Aspergillus* was elevated. High-resolution computed tomography of the chest showed the presence of bilateral central bronchiectasis with dextrocardia and situs inversus [Figure 3]. Spirometry showed an obstructive pattern with significant reversibility. The patient was diagnosed to have ABPA along with Kartagener's disease. As the patient was unmarried, infertility could not be ascertained. Since the electron microscope was not available at our institute, ciliary dysmotility could not be demonstrated. However, given the clinical and radiological evidence, Kartagener's disease was considered. Applying the Rosenberg– Patterson criteria, she was diagnosed to have ABPA.

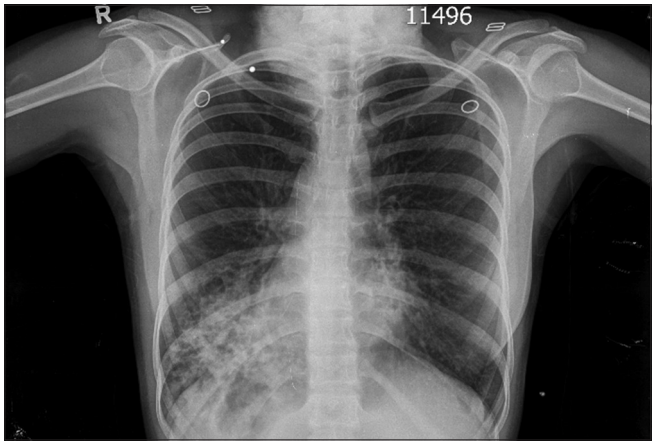

Figure 1: Chest X-ray showing dextrocardia with situs inversus. There are also ring shadows in both the lungs suggestive of bronchiectasis

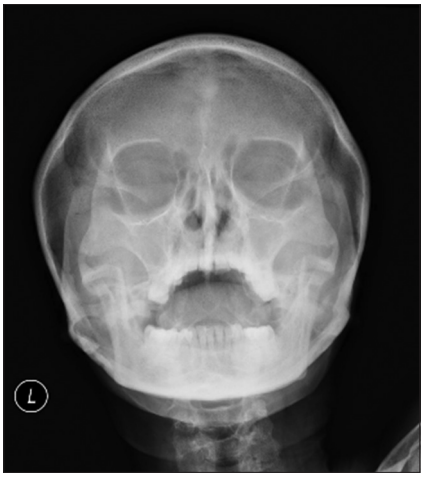

Figure 2: X-ray paranasal sinuses open mouth view showing haziness of bilateral maxillary sinuses with aplasia of frontal sinuses

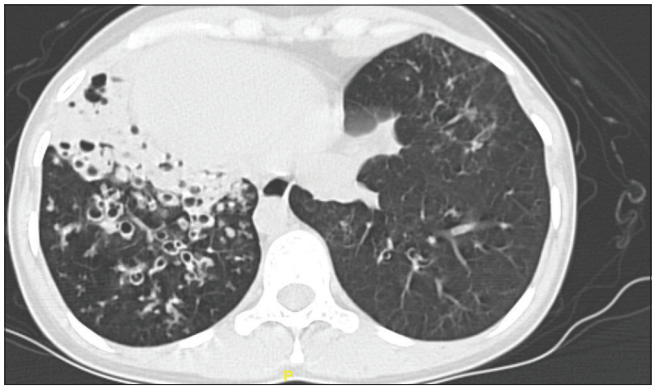

Figure 3: High-resolution computed tomography of the chest showing the presence of bilateral central bronchiectasis with dextrocardia and situs inversus

Oral prednisolone at 0.5 mg/kg/day was prescribed for 2 weeks and then slowly tapered. As spirometry showed an obstructive pattern with significant reversibility, she was also started on inhaled bronchodilators. She had good clinical improvement with the treatment. Her total IgE reduced. The sinusitis was managed as per otorhinologist's advice. There was a marked improvement in the general condition of the patient. She is on regular follow-up for 6 months.

Discussion

PCD was initially known as immotile cilia syndrome.[1] However, it is now suggested that disorganized motion, rather than immotile cilia result in incoordination and ineffective ciliary beat causing impaired mucociliary clearance. Hence, the term has been modified to PCD.[2] Ciliary dyskinesia can also occur transiently following epithelial injury from viral infections and is referred to as secondary ciliary dyskinesia. Ineffective ciliary motility leads to recurrent or persistent respiratory tract infections, sinusitis, otitis media, and infertility. Situs inversus wherein the position of visceral organs are reversed is seen in about 50% of the patients of PCD.[3]

Siewert first described the combination of situs inversus, chronic sinusitis, and bronchiectasis in 1904. However, Manes Kartagener first recognized this triad as a feature of a separate congenital syndrome in 1933, and the syndrome bears his name.[4] The incidence of Kartagener's syndrome is between 1 in 15,000 and 1 in 30,000 live births. There is no race or gender predisposition.[5]

Cilia are hair-like projections that line the superior surface of the epithelial cells of the upper and lower respiratory tract, middle ear, fallopian tube, spermatozoa, and ependyma of the brain. During the embryonic period, ciliary motility plays an important role in the development of organs in their normal positions. The loss of normal ciliary function results in diseases of the upper and lower respiratory tract and defects in organ position.[6]

PCD can be diagnosed based on clinical and radiological features, and by the demonstration of ciliary dysmotility. PCD can present as neonatal respiratory distress. However, most often, the diagnosis is not made until adult age. Recurrent respiratory tract infections are the most common clinical presentation.[7,8] The loss of normal ciliary function in Kartagener's syndrome results in ineffective clearance of airway mucus secretions predisposing to recurrent bacterial infections resulting in the development of bronchiectasis.

The diagnosis of PCD is made on the basis of recurrent respiratory tract infections, otitis media, radiological evidence

of dextrocardia, situs inversus, bronchiectasis, sinusitis, and demonstration of ciliary dysmotility, preferably by electron microscopy. Owing to sperm dysmotility, about half of the males with PCD are infertile.[3] Our patient had sinusitis and bronchiectasis with situs inversus.

ABPA is a hypersensitive reaction to the fungus *Aspergillus* that usually affects patients with bronchial asthma and cystic fibrosis. In normal persons, spores of inhaled *Aspergillus fumigatus* germinate in the airways and trigger an immune response which, in turn, is able to clear the fungus. In predisposed persons with underlying structural lung diseases, there is colonization of *A. fumigatus* in the airway mucus. Once germinated, the fungal hyphae release immunologically active substances which recruit CD4+ T-helper 2 cells and further activates the immune response leading to influx of neutrophils, eosinophils, and IgE cells into the airways.[9]

Several criteria have been put forth for the diagnosis of ABPA.[10] Rosenberg–Patterson criteria for the diagnosis of ABPA include the presence of asthma, fleeting pulmonary infiltrates, peripheral blood eosinophilia, immediate Type I skin reactivity to *Aspergillus* antigen, serum precipitin antibodies to *A. fumigatus*, elevated serum total IgE, increased levels of *Aspergillus*-specific IgE and IgG, and central bronchiectasis.[11]

The patient had positive skin prick test to *Aspergillus*, elevated serum total IgE, serum-specific IgE to *A. fumigatus*, peripheral eosinophilia, and positive serum precipitins to *A. fumigatus* confirming the diagnosis of ABPA.

Kartagener's disease associated with pulmonary aspergilloma has been described in the literature.[12,13] However, there are only a few case reports mentioning the occurrence of ABPA in patients with Kartagener's disease.[4,14] Available literature suggests a possibility of entrapment of spores of *Aspergillus* in the bronchial secretions of persons with Kartagener's disease. The viscid nature of sputum and bronchial secretions permits the colonization of the airways by this fungus. Furthermore, the impaired mucociliary clearance in these patients due to ciliary dysmotility results in ineffective mucus transport and clearing of these spores. Once colonized, these spores release proteolytic enzymes that injure the bronchial epithelium and permit absorption of the *A. fumigatus* antigens resulting in an exaggerated hypersensitive reaction, a feature of ABPA.[4]

Conclusion

Although bronchiectasis may be seen in Kartagener's disease, in a high prevalence setting, evaluation for ABPA should be carried out. The presence of bronchiectasis in Kartagener's disease as well as in advanced stages of ABPA may be a confounding factor in making a diagnosis. As the disease process in ABPA can be controlled with effective drugs, the early diagnosis and management of ABPA even in the background of a congenital disease such as Kartagener's disease can definitely improve the quality of life in these patients.

Declaration of patient consent

The authors certify that they have obtained appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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