Primary Ciliary Dyskinesia and Situs Ambiguus: A Rare Association

Abstract

Primary ciliary dyskinesia (PCD) is a rare disorder with impaired ciliary function resulting in a spectrum of clinical manifestations of varying severity. PCD affects approximately one in every 20,000 individuals with a reported prevalence between 1:4000 and 1:50,000. Due to its nonspecific clinical features, the condition is usually diagnosed late in its course, unless situs inversus (SI) or organ laterality defects are discovered at imaging. A small subset of patients with PCD display associated organ laterality defects, different from the classical SI totalis. We present here, the clinical and imaging findings in a young female with PCD along with left-sided isomerism, a variant of heterotaxy syndromes.

Keywords: *Bronchiectasis, left isomerism, organ laterality defects, primary ciliary dyskinesia, situs ambiguus, situs inversus*

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Introduction

Primary ciliary dyskinesia (PCD) is a rare autosomal recessive disease with impaired ciliary function that results in varied clinical manifestations from neonatal respiratory distress, chronic rhinorrhea, sinusitis, recurrent otitis media, chronic bronchitis, bronchiectasis, and infertility. PCD affects approximately one in every 20,000 individuals with a reported prevalence between 1:4000 and 1:50,000.[1] PCD is an underdiagnosed entity due to its common and nonspecific clinical manifestations. It usually remains unsuspected unless situs inversus (SI) or organ laterality defects are discovered at imaging. Although SI is classically described as an association of PCD, a subset of these patients have organ laterality defects different from classic SI totalis.[2] SI implies a mirror image or reverse arrangement of normal organs. Any laterality defect other than SI is termed as situs ambiguus (SA) and is included under heterotaxy syndromes. Heterotaxy is a group of congenital malformations resulting from failure to establish normal left–right (L–R) asymmetry during early embryogenesis.[3] Left isomerism is a variant of heterotaxy with complete left sidedness in the organ distribution as seen in our case.[4] Although a rare congenital disorder, the knowledge of association of PCD with organ laterality defects helps in early identification of this condition and the complications caused by existing anatomical alterations.

Case Report

A 17-year-old female presented with recurrent abdominal pain and vomiting over 1-month duration. She had frequent episodes of rhinosinusitis and recurrent respiratory tract infections since childhood for which she was treated symptomatically by local general practitioners. Her general physical examination was unremarkable. The examination of her respiratory system revealed bilateral rhonchi and bibasilar lung crepitations on auscultation. Her chest radiograph showed bilateral basal bronchiectasis [Figure 1a]. CT chest performed later revealed two lobes with a single fissure in both lungs and hyparterial location of both right and left bronchi representing "left" lung like morphology on both sides. The cardiac situs was normal, but an aberrant origin of the right subclavian artery from the aorta (distal to the left subclavian artery origin) was identified [Figures 1b, c and 2]. CT also confirmed the presence of bilateral bronchiectasis [Figure 1b and c].

CT also revealed a midline position of the liver and stomach lying on the right side of the abdomen. In addition, multiple small spleens (polysplenia), left-sided inferior vena cava, and midline location of aorta

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were also detected. CT also showed malrotation of the small bowel with evidence of midgut volvulus [Figure 3]. All these features were suggestive of left isomerism, variant of heterotaxy, or SA.

The patient underwent bronchoscopy which confirmed the absence of bronchus intermedius on the right side with bilateral bilobed lungs. The basal segmental bronchi were dilated with plenty of mucoid secretions within the lumen. The bronchial washings were negative for acid fast bacilli (AFB) and fungal elements with a negative BACTEC culture for AFB. Her pulmonary function tests showed moderate airway obstruction with significant response to bronchodilators.

A diagnosis of PCD with left isomerism was made, and the patient was treated with antibiotics, inhaled bronchodilators, chest physiotherapy, and postural drainage. The symptoms of abdominal pain and vomiting subsided with conservative management, and she was not subjected to surgery for midgut volvulus at this point. She improved clinically with medical management and is under regular follow-up.

Discussion

Normal ciliary motility plays an important role in clearance of mucus from the tracheobronchial airway. Patients with PCD have impaired mucociliary function leading to recurrent sinopulmonary infections and bronchiectasis.[5] Laterality anomalies result from a defect in embryonal nodal cilia which have 9 + 0 ciliary arrangement lacking central pair of microtubules.[6] These motile cilia in the embryonic node also play a critical role in generating nodal flow which is the central process in symmetry break down on the L–R axis.[7] SA results from failure to establish normal L–R asymmetry during early embryogenesis.[3] As motile cilia are responsible for mucociliary clearance as well as L–R patterning during embryogenesis, it is not uncommon to see coexistence of PCD with organ laterality defects.

In a study by Shapiro *et al*.,[2] 41% of patients with PCD had the classic SI and 12.1% of patients had SA with associated simple or complex cardiac defects in 4.9% of the patients. The rest (46.7%) had normal arrangement of organs (situs solitus). Our patient had PCD with SA and left isomerism but without any associated cardiac defects.

The estimated prevalence of PCD has doubled in recent years[6] probably due to increased awareness and recognition of association between SA and PCD. Although cases of SA have associated complex cardiac issues, the noncardiac issues in SA heterotaxy have also received significant attention in the recent years.[4] The absence of cardiac defects is probably the reason why these cases first present to the respiratory physician and not to the cardiologist.

Left isomerism is a variant of heterotaxy which includes two hyparterial bronchi, two bilobed lungs, polysplenia, and intestinal malrotation with less complex congenital heart diseases.[3] Other noncardiac issues in heterotaxy include duodenal and biliary atresia, midgut volvulus, sinopulmonary infections, bronchiectasis, genitourinary abnormalities, thromboembolism, and venous anomalies.[4] Our patient had intestinal malrotation with midgut volvulus which was managed conservatively. Prophylactic surgery for malrotation is not beneficial in asymptomatic patients, and this is well described in existing literature.[8]

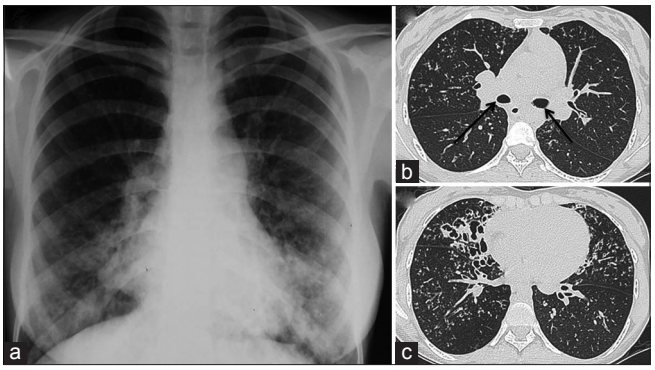

Figure 1: (a) Chest radiograph and (b and c) axial computed tomography images in lung window settings depicting bronchiectasis in both lungs with superadded infection. Also note the origin of both the right and left main bronchi at the same level (arrows). Both bronchi were hyparterial in origin

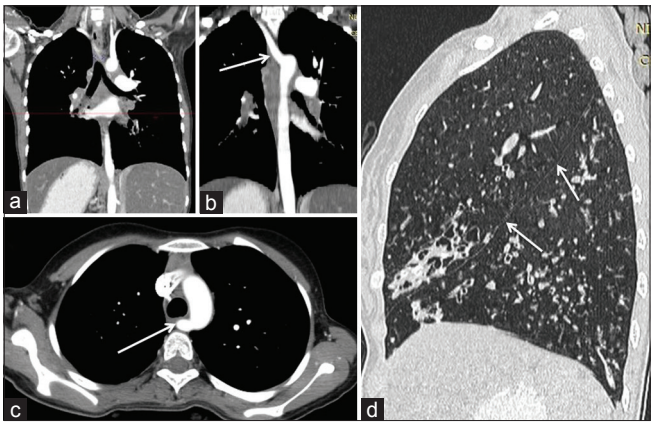

Figure 2: (a-c) Coronal and axial contrast-enhanced computed tomography images of the chest revealed an aberrant origin of the right subclavian artery from the aorta, distal to the left subclavian artery (arrows) and (d) sagittal reformatted image of the right lung reveals only a single major fissure dividing the lung into two lobes suggestive of left isomerism (arrows)

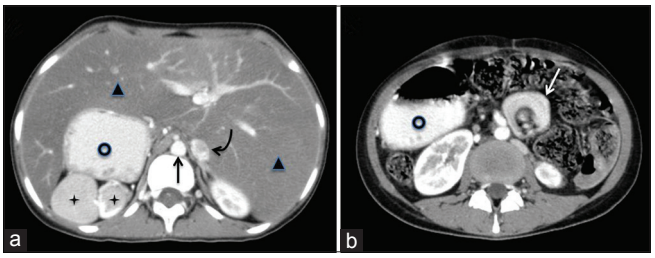

Figure 3: (a and b) Contrast-enhanced axial computed tomography image through the upper abdomen. There is evidence of polysplenia (+) with the stomach lying on the right side (O) and the liver lying in the midline (▲). The inferior vena cava (curved arrow) is lying to the left of the aorta (arrow) which is midline in location. There is malrotation of bowel with whirling of the mesenteric vessels suggesting midgut volvulus (white arrow)

The diagnostic workup of cases with suspected PCD requires a thorough clinical and physical examination along with assessment of ciliary beat frequency (CBF) and ciliary beat pattern (CBP) by high-speed video-microscopy analysis as a first-line diagnostic tool to confirm the ciliary dysfunction.[9] If CBF and CBP are normal, electron microscopic analysis of ciliary ultrastructure may not be required in most of the cases as it is time-consuming and costly and requires specialist expertise. High degree of clinical suspicion with a positive family history warrants full diagnostic evaluation including electron microscopy.[10] The mainstay of treatment in patients with respiratory manifestations is to improve mucous clearance by chest physiotherapy along with aggressive treatment of respiratory tract infections to prevent long-term complications and deterioration in lung function.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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