Primary Ciliary Dyskinesia - An Underdiagnosed Entity

Ajay Garg*, Raman Wadhera**, SP Gulati***, Naveen Sharma†, Sheetal Garg‡

Abstract
Primary ciliary dyskinesia (PCD) also known as immotile cilia syndrome is a genetic disorder characterised by chronic infections of the upper and lower respiratory tracts, male infertility and situs inversus totalis. Authors are presenting clinical details of a patient who was operated upon for recalcitrant rhinosinusitis. Investigations carried to find out the predisposing factors for such sinusitis, resulted in diagnosing the patient a case of PCD, a rare but well known cause of recalcitrant sinusitis.

Introduction
Primary ciliary dyskinesia is a genetic disorder causing dysfunctional motility of cilia and impaired mucociliary clearance, resulting in a myriad of clinical manifestations including recurrent sinopulmonary disease, laterality defects and infertility.1 Heterogenous clinical presentations of PCD and limitations of electron microscopy to assess ultrastructural defect of cillum pose a diagnostic challenge to clinicians. This article describes normal ciliary structure, pathophysiologic correlation, clinical characteristics, diagnostic and treatment modalities of PCD.

Case Report
An 18 years old male presented with clinical manifestations of chronic rhinosinusitis since childhood. He took treatment from general practitioners many a times but couldn’t be relieved of symptoms completely. Anterior rhinoscopy examination revealed purulent discharge in both nasal cavities while otological examination was unremarkable. Computed tomography scan of paranasal sinuses (PnS) observed mucosal hypertrophy of both maxillary sinuses (Fig. 1a) and bilateral frontal sinus aplasia (Fig. 1b). High resolution computed tomography of chest observed bronchiectatic changes in both the lung fields (Fig. 2a) with right sided heart shadow (Fig. 2b). CT scan of abdominal cavity showed all the viscera in alternate positions i.e. left sided liver and right sided spleen (Fig. 3). Keeping in view the diagnosis of PCD patient was advised to undergo his complete semen analysis, which reported all the parameters of sperms with in the normal limits except that all the sperms were immotile. None of his family members were found affected by this syndrome when examined. Patient was properly counselled about the disease and precautions to be taken in future. Functional endoscopic sinus surgery (FESS) guided inferior meatal antrostomy was done to allow gravity drainage of sinus mucus thus helping in relieving the symptoms of rhinosinusitis.

Discussion
PCD is described as autosomal recessive condition with estimated incidence of 0.5 – 1 in 30,000 live births. Numerous defects are encompassed under PCD including structural abnormalities of the dynein arms, radial spokes, nexin links, cilial length and orientation of the cilia. The most common abnormality is absence or reduced number of dynein arms which decreases the ciliary beat frequency. Approximately one half of the patients with PCD fall in to the subgroup of Kartagener Syndrome (KS) in which situs inversus accompanies bronchiectasis, and sinusitis.3

The motile cilia of upper and lower respiratory tract, the oviducts of the female reproductive system and flagellum of male reproductive system is characterised by ‘9+2’ arrangement of microtubules composed of various proteins. Coordinated action of these multiple proteins and sliding of the microtubules act to generate mucociliary transport, important for normal respiratory functions and resistance to respiratory infection.2 Clinical manifestations of PCD ascribed to primary ultrastructural defect in cillum, which lies in mutations in any of the 250 proteins that make up the complex structure of the cillum. Once cilia become dyskinetic their coordinated, propulsive action is diminished and bacterial clearance is impaired.

The majority of PCD patients present with significant respiratory distress in immediate new born period. Chronic rhinosinusitis, recurrent otitis media are common clinical presentations in upper airway. Nasal polyps are recognized in 30% of affected individuals. Impaired mucociliary clearance of the lower respiratory tract leads to recurrent episodes of pneumonia or bronchitis. Chronic lung involvement and inflammation may lead to bronchiectasis.2 Afzelius proposed that normal ciliary beating is necessary for visceral rotation during embryonic development. The cause of lateralisation of organs is answered by functional nodal cilia, without which thoracoabdominal orientation is random. In patients with PCD organ rotation occurs as a random event therefore, half the patients have situs inversus and the other half have normal situs. Male infertility attributes to impaired spermatozoa motility secondary to defective sperm flagella. Female infertility may also be an issue owing to ciliary dysfunction in the fallopian tubes.4

Diagnostic criteria of PCD includes the phenotypic presentation and ultrastructural defect of cillum. Patients of PCD sometimes may have normal ciliary ultrastructure with variable or subtle phenotypic presentation owing to its genetically mediated heterogeneity, thus making it a diagnostic challenge for the clinicians.5 Electron microscopy of nasal epithelium is gold standard to assess ultrastructural defects with in the cillum. Ciliary beat frequency, ciliary beat patterns and measurement of nasal nitric oxide (NO) are some diagnostic and screening tools for PCD.3 High resolution CT scan of chest is most sensitive modality for documenting early and subtle abnormalities of airway and pulmonary parenchyma. CT scan of sinonasal cavities may reveal mucosal thickening, opacified sinus cavities and hypoplastic frontal sinuses.6 Adenoid hyperplasia, cystic
Fig. 1: (a) CT PNS showing mucosal hypertrophy of bilateral maxillary sinuses (black arrow), (b) CT PNS coronal view showing bilateral aplastic frontal sinuses (black arrow).

Fig. 2: (a) CT chest showing bronchiectatic changes (white arrow) in both the lung fields, (b) CT scan showing heart shadow on the right side (white arrow) [dextrocardia].

Fig. 3: CT abdomen showing all the viscera in alternate positions i.e. left sided liver (big arrow) & right sided spleen (small arrow) [situs inversus].

fibrosis, allergic bronchopulmonary aspergillosis, Samter’s triad, congenital cartilage deficiency are some of the differential diagnosis.

Airway disease develops early in childhood with increasing airway obstruction, infection and inflammation that eventually results in development of bronchiectasis, but the progression and extent of the lung disease can be slowed with early diagnosis and therapy. Strategies to augment mucociliary clearance include postural drainage, percussion vests, and positive expiratory pressure devices. Cough should not be suppressed as it is the only mechanism left for mucus clearance. Antimicrobial therapy must be instituted as early as possible whenever signs and symptoms of respiratory infections are present. *H. influenza*, *S. aureus* and *S. pneumoniae* are commonly isolated from airway culture of patients of PCD. Use of arginine which augments production of airway NO and enhances ciliary beat frequency and Uridine-5’-triphosphate which stimulates chloride ion secretion and mucin release in goblet cells resulting in increased airway hydration and enhanced cough clearance are other novel approaches advocated in treatment of PCD. Chronic otitis media with effusion (OME) warrants tympanostomy tube insertion.
Recalcitrant sinusitis needs FESS guided inferior meatal antrostomy, relies on gravitational drainage rather than ciliary clearance of mucus.  

PCD is a genetic disorder that results in dysfunction of motile cilia resulting in chronic infections of the upper and lower respiratory tracts, male infertility and situs inversus totalis. Subtle clinical presentation and variable ultrastructural defects are limiting factors in the diagnosis of PCD. Comprehensive genetic testing may serve a diagnostic tool to identify PCD in infancy so that early and prompt treatment could be instituted, thus lowering morbidity and progression of lung disease.

References