Primary ciliary dyskinesia due to DRC1/CCDC164 gene mutation

Sir,

Primary ciliary dyskinesia (PCD) is a rare autosomal recessive condition affecting the structure and function of motile cilia, thereby resulting in impairment of mucociliary clearance.[1] The common manifestations in children include neonatal respiratory distress, early-onset chronic wet cough, and recurrent respiratory infections, leading to bronchiectasis, recurrent rhinosinusitis, and middle ear infections.[1] Around one-half of PCD patients have dextrocardia and/or situs inversus totalis.[2] In the reproductive age group, PCD can be associated with male infertility and subfertility in females.[1] Diagnosis of PCD involves identification of the clinical phenotype and a combination of tests that require expertise to conduct and interpret the results.[3] The upfront screening tests are nasal nitric oxide measurement and high-speed video microscopy of nasal brushings for ciliary beat pattern and frequency [Figure 1].[3] Hallmark ciliary ultrastructure abnormalities and/or bi-allelic disease-causing mutations in known PCD genes would be diagnostic.[3] PCD can occur in the presence of normal ciliary ultrastructure, and at present, genetic testing can identify mutations in more than 80% of PCD patients.[4] Due to lack of awareness among clinicians and nonavailability of diagnostic tests, PCD is underdiagnosed and the exact frequency of PCD in India is still not known. We report a 14-year-old boy with PCD due to *DRC1*/*CCDC164* mutation for the first time from the Indian subcontinent.

A 14-years-old boy, born to nonconsanguineous parents, presented to us with purulent nasal discharge, persistent productive cough, and recurrent respiratory infections with wheeze since infancy. He was born at term and did not have respiratory distress in the neonatal period. His weight and height were on the third centile. He had purulent nasal discharge and auscultation of his chest revealed bilateral crackles and wheeze. High-resolution chest tomography revealed right upper lobe collapse and centrilobular opacities. Sweat chloride estimation and serum immunoglobulin profile were within normal limits. Primary ciliary dyskinesia rule,[5] a predictive score with seven simple questions to predict the likelihood of having PCD, was 4, i.e., the likelihood of PCD was not high. Nasal nitric oxide analysis using portable electrochemical device, NIOX VERO® (Circassia, Sweden), was very low at 11.6 ppb (3.5 nl/min). High-speed video microscopy analysis (HSVA) of nasal brushings revealed motile cilia with stiff motility (reducing bending capacity) and a ciliary beat frequency of 14 Hz. The HSVA videos were reviewed by PCD team, Southampton University Hospital, UK. EDTA peripheral blood sample was sent for targeted next-generation targeted sequencing of the genes known to be associated with PCD. A homozygous nonsense variation in exon 10 of the DRC1 gene (chr2:26667625G>A; depth: 70x) that results in a stop codon and premature truncation of the protein at codon 402 (p.Trp402Ter; ENST00000288710.2) was detected. He is being managed by a multidisciplinary team and is under follow-up.

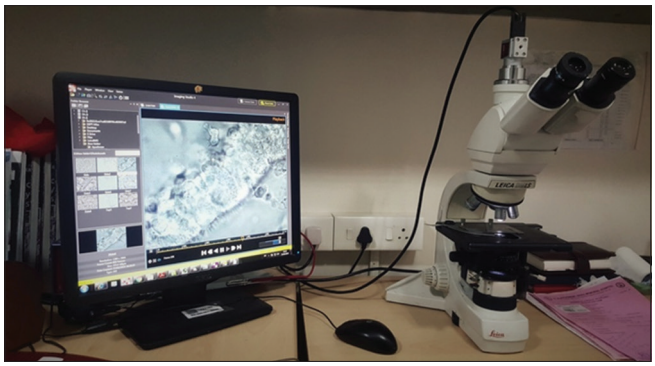

Figure 1: High-speed video microscopy

PCD can be caused by bi-allelic mutations in the *DRC1*/*CCDC164* gene.[6] This disorder characteristically starts in infancy with chronic sinopulmonary infections due to abnormal ciliary function.[6] The available literature shows that individuals with *DRC1*/*CCDC164* mutations do not have any abnormal left–right body symmetry.[6] Our patient did not have any left–right body asymmetry. HSVA from our patient showed uniformly stiff cilia. These findings are similar to previous reports in PCD with documented *DRC1*/*CCDC164* mutation.[6] We did not perform transmission electron microscopy due to lack of this facility at our center.

PCD with normal body symmetry makes diagnosis even more difficult and late. When there is a strong suspicion based on other clinical features, we should proceed with diagnostic testing for PCD. Early diagnosis of PCD and prompt intervention have the potential to stall the progression of disease.

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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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Conflicts of interest

There are no conflicts of interest.

Antony Terance Benjamin[1], Ram Ganesh[1], Jagdish Chinnappa[2], Ilin Kinimi[2], Jane Lucas[3]

[1]Paediatric Pulmonology, Primary Ciliary Dyskinesia Unit, G Kuppuswamy Naidu Memorial Hospital, Coimbatore, Tamil Nadu, India, [2]Department of Paediatrics, Manipal Hospitals, Bengaluru, Karnataka, India, [3]Primary Ciliary Dyskinesia Diagnostic Service, University Hospital Southampton NHS Foundation Trust, Southampton, UK.
E-mail: antonyterance@gmail.com

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