A 6-month-old boy was referred to the Royal Brompton PCD diagnostic service with a history of levocardia, abdominal situs inversus, left atrial isomerism and functional hyposplenism. In the neonatal period he developed seizures and was admitted to the neonatal unit for treatment with phenobarbitone. MRI showed multiple brain lesions consistent with intrauterine infection. He was subsequently weaned from anti-epileptic drugs and has remained seizure free. At 11 months he has no respiratory symptoms or rhinitis and has passed two hearing examinations. There is no family history of respiratory problems, however, there is unexplained infertility in a paternal uncle and cousin.

Genetic testing identified one paternally inherited, previously described, pathogenic mutation in DNAH11 (DNAH11:c.4333C>T;p.(Arg1445Ter)) and one maternally derived missense variant of unknown significance (DNAH11:c.10472G>A;p.(Arg3491His)). High speed video microscopy showed a borderline beat pattern, not entirely consistent with the findings normally associated with DNAH11; some cilia were stiff at the base but not consistently throughout. The ciliary beat frequency was within normal limits at 13.45Hz. Transmission electron microscopy (TEM) was normal, however, this is to be expected if his condition was related to the DNAH11 mutation.

30% of patients with PCD have a ciliary ultrastructure that appears normal with standard TEM and whilst genetic analysis supports the diagnosis in many circumstances, it may not identify definitive bi-allelic pathogenic mutations in every case. We used existing diagnostic samples to undertake electron tomography and were able to successfully visualise ultrastructural volume loss in the outer dynein arm in the proximal part of the axoneme, in keeping with a DNAH11 defect. The outer dynein arm to microtubular doublet volume ratio was 10.24 (median (IQR) is 10.3% (9.3–10.5%) in DNAH11 subjects compared to 13.8% (12.9–14.4%) in controls.

It is likely that DNAH11:c.10472G>A;p.(Arg3491His) is a novel pathogenic mutation associated with PCD.