

## CASE REPORT

# Novel homozygous mutations of DNAH5 in Kartagener syndrome

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## Learning points for clinicians

The diagnosis of Kartagener syndrome (KS) is usually delayed because the clinical symptoms are easily mistaken as common respiratory tract infections. Early diagnosis and treatment of KS are critical to prevent progressive lung damage and improve the quality of life. For suspected cases of KS, genetic testing should always be considered in the diagnosis.

## Case presentation

A 29-year-old man presented with productive cough and dyspnea for 1 month, who had a previous medical history of recurrent respiratory tract infections since childhood. He had a body temperature of 36.0°C, a blood pressure of 110/78 mmHg, a respiratory rate of 24 breaths per minute and a heart rate of 122 beats per minute. Physical examination revealed wet rales and wheezes at the bilateral lungs. Heart sounds were more pronounced at the right sternal border with no cardiac murmur or rub. Laboratory tests revealed an elevated blood neutrophil count and C-reactive protein level. Blood gas analysis revealed hypoxemia and mild hypercapnia. No sperm was found in a routine semen analysis. Chest radiograph revealed dextrocardia and bronchiectatic areas at the bilateral lungs (Figure 1A), and chest computed tomography (CT) also showed bronchiectasis with secondary infection of bilateral lungs (Figure 1D) and situs

inversus totalis (Figure 1B). Doppler echocardiography and Doppler ultrasound of abdominal organs confirmed the congenital mirror-image dextrocardia and situs inversus totalis. Paranasal sinus CT showed pansinusitis with effusion and bilateral mucosal thickening, especially in ethmoid sinus (Figure 1C). Pulmonary function tests demonstrated obstructive impairment (FEV1/FVC 54%) without obvious improvement after bronchodilator use and restrictive ventilation dysfunction (FVC, 32% of predicted). Because of excessive sputum, Bronchoscopy was performed. Bronchoalveolar lavage fluid culture revealed positive results for *Pseudomonas aeruginosa*. Genetic testing of his peripheral blood using whole exome sequencing showed mutations in DNAH5 gene. He had homozygous mutations in exon 49 of DNAH5 (NM\_001369.2; c.8030G>A; p.Arg2677Gln) (Figure 1E) and in exon 79E of DNAH5 (NM\_001369.2; c.13778C>T; p.Thr4593Met) (Figure 1F). These two mutations were confirmed by Sanger sequencing. We also obtained blood for a gene analysis from his brother who had no clinical findings suggestive of primary ciliary dyskinesia (PCD), and found no gene mutation. Based on these findings, he was diagnosed with Kartagener syndrome (KS). After 18 days treatment of antibiotics, bronchodilators and expectorant drugs, the patient was discharged with the resolution of symptoms.

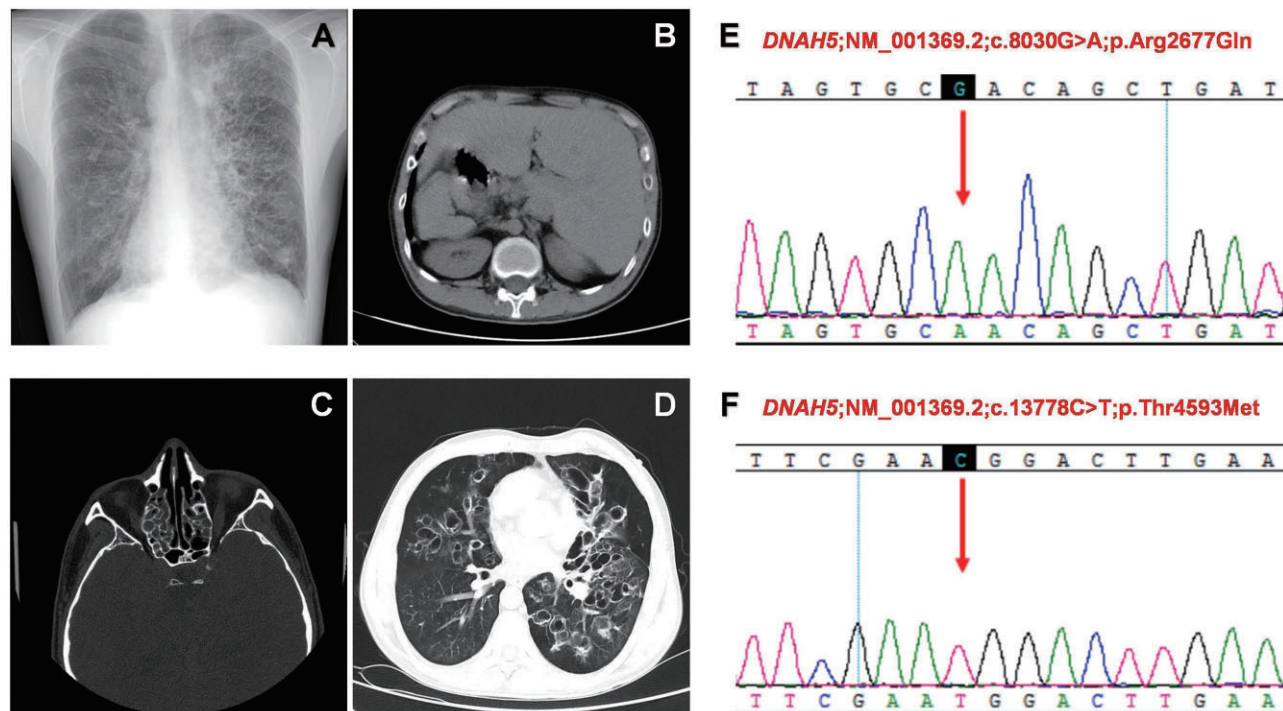
## Discussion

KS is one subtype of PCD, which is a genetically heterogeneous, autosomal recessive disorder and characterized by defective

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**Figure 1.** (A) Chest radiograph showed reticular shadows, honeycomb shadows, scattered opacities in bilateral lung fields especially in left lung and dextrocardia. (B) CT scan of chest revealed situs inversus totalis with stomach and spleen on the right, liver on the left side and dextrocardia. (C) CT scan of sinus showed pansinusitis with effusion and mucosal thickening. (D) CT scan of chest revealed the presence of bronchiectasis in bilateral lung fields. (E) Sanger sequencing of DNAH5 confirmed a homozygous G > A mutation (NM\_001369.2; c.8030G>A; p.Arg2677Gln). (F) Sanger sequencing of DNAH5 confirmed a homozygous C > T mutation (NM\_001369.2; c.13778C>T; p.Thr4593Met).

ciliary structure and motile cilia dysfunction. KS can be diagnosed by the presence of the clinical triad of situs inversus, chronic sinusitis and bronchiectasis or a PCD diagnosis combined with additional situs inversus, which accounts for approximately half of the subjects with PCD. Other important clinical features of KS include congenital heart disease, hydrocephalus and subfertility. In this case, situs inversus, chronic sinusitis and bronchiectasis occurred concurrently in the patient and no sperm was found in a routine semen analysis, which indicates infertility.

According to certain clinical guidelines, PCD was defined by typical clinical manifestations and some PCD diagnostic tests including nasal nitric oxide (nNO) measurement, high-speed video microscopy analysis (HSVMA), ultrastructural analysis by transmission electron microscopy (TEM), genetic testing and immunofluorescence [1, 2]. Genetic testing is becoming more common and feasible in the diagnosis of KS due to recent advances in next-generation sequencing. DNAH5 is reportedly the most frequently mutated gene in patients with PCD [3, 4]. It encodes the dynein axonemal heavy chain 5 protein, which is a component of the outer dynein arm (ODA). Homozygous or compound heterozygous mutations in DNAH5 result in ODA defects and cilia mobility dysfunction. In this case, we had no access to nNO testing and whole-exome sequencing was performed to confirm the diagnosis of KS. Two homozygous mutations in DNAH5 were identified in the patient. Both mutations had not been reported before and the homozygous mutation in exon 49 of DNAH5 was predicted to be pathogenic. With the application of whole-genome sequencing, genetic tests are

expected to become the preferred diagnosis approach for PCD in the future.

### Ethical approval

This study was approved and supervised by the ethics committee of the Central Hospital of Wuhan and informed consent was obtained from the patient for the publication of this article.

*Conflict of interest.* None declared.

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