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A Rare Case Report of Kartagener Syndrome

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Abstract

A 7-year-old girl presented with complaints of fever and cough since 4 days. Also she gave history of recurrent episodes of fever with cough and cold with difficulty in breathing since 1 year and she had visited local doctor 4 to 5 times in last 2 months. On respiratory examination, she had barrel shaped chest. Her apex beat was palpable in the right 4th intercostal space in the mid clavicualr line. Clinical examination revealed air entry equal bilaterally and crepitations in right infra axillary area. Investigation revealed dextrocardia, bronchiectasis Sinusitis, and ciliary dyskinesia. Considering all the findings, she was diagnosed as a case of Kartagener's syndrome. We are reporting this case because of its rarity and rare presence of genetically homozygous primary ciliary dyskinesia with uncertain significance in Kartagener's syndrome.

Keywords: Dextrocardia, Bronchiectasis, Ciliary dyskinesia, Kartagener's syndrome, Sinusitis

Introduction

Kartagener's syndrome is a rare hereditary disease and it can be cause by mutations in many different genes that are inherited in an autosomal recessive manner. Although scientists have identified many of the genes associated with Kartagener syndrome, the genetic cause of some cases is unknown [1, 2]. The signs and symptoms vary but may include neonatal respiratory distress; frequent lung, sinus and middle ear infections beginning in early childhood; and infertility [1, 3]. According to researchers in the Indian Journal of Human Genetics, anestimated 1 in 30,000 people are born with Kartagener's syndrome. Itcauses abnormalities in respiratory tract, it is known as primaryciliary dyskinesia (PCD). It also causes the positioning of some or all vitalorgans to be reversed or

mirrored compared to their normal positioning.This is known as situsinversus.PCD can cause a number of symptoms, including: frequent respiratory infections frequent sinus infections frequent ear infections chronic nasal congestion, infertility. There is no cure for Kartagener syndrome. Treatment varies based on sign and symptoms present in each person but may include airway clearance therapy and antibiotic [1, 3, and 4]. Highest care is needed during surgery in Kartagener's syndrome. Here, we are reporting a case of Kartagener's syndrome, who presented to us with recurrent episodes of fever with cough and cold with difficulty in breathing since 1 year.

Case Report

This was a 7-year-old girlof weight 13.5kg, height 109cm, born to non- consanguineous parents, 3rd by birth order.She was presented to the outpatient department of our hospital with complaints of fever and cough since 4 days.Cough was productive, wet sounding, white colour sputum, and copious amount withno diurnal and postural variation. She also gave history of recurrent episodes of fever with cough and cold with difficulty in breathing since 1 year and she had visited local doctor 4 to 5 times in last 2 months. There was no history of hemoptysis, any known heart disease, Kochs/koch's contact and any known allergy.

On physical examination, she was active, afebrile, heart rate (HR) was 116bpm, respiratory rate (RR) was 26/min, PP-wf, capillary refill time (CRT) <3secs, blood pressure (BP) was 104/64 mm Hg, grade 1 clubbing was present. There was no pallor, icterus, cyanosis, lymphadenopathy and edema was noted. A detailed systemic examination of respiratory system consists of inspection-barrel shaped chest, visible apical pulsations over right 4th intercostal space, bilateral chest movements' equal, no scars and sinuses. All inspectory findings confirmed. Her apex beat was palpable on the right 4th intercostal space in felt over right mid clavicualr line on palpation. Percussion notes were resonant bilaterally. Auscultation revealed air entry equal bilaterally and crepitations in right infra axillary area. Cardio-vascular examination revealed the normal heart sounds on right side include S1, S2 without any murmur. The abdomen was soft and nontender with no organomegaly. Neurological examination shows normal tone, power and reflexes.

Child was admitted in view of recurrent lower respiratory tract infection (LRTI). Chest x-ray and USG abdomen revealed **dextrocardia** with situsinvertus as shown in figure 1. 2D Echo showed visceraatrial situs inversus, ILI, right aortic arch. HRCT thorax was showing honeycomb appearance (Figure 2a), suggestive of **bronchiectasis**. CT scan PNS (Figure 2b) showed bilateral maxillary and ethmoidal sinusitis.

Figure 1: Chest x-ray revealed dextrocardia with situsinvertus

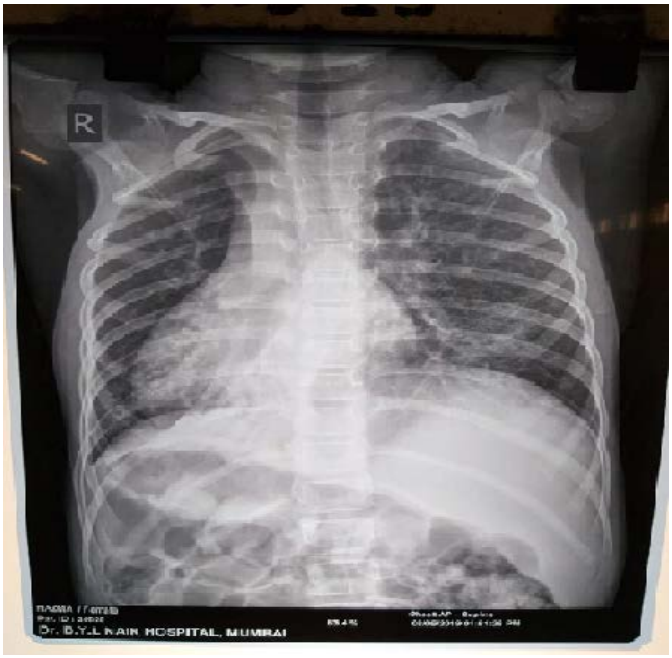
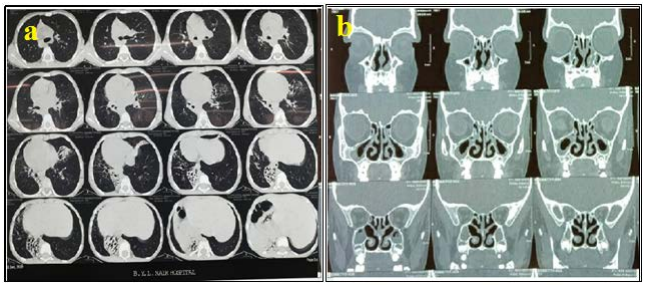


Figure 2: a) CT chest and b) CT of the Para Nasal Sinuses



The DNA test report revealed **primary ciliary dyskinesia-9** with or without situsinversus and it is genetically homozygous, a predominantly autosomal-recessive inherited disorder but classification showed uncertain significance, (Table 1).

Table 1: shows the DNA test report

Gene (Transcript)	DNA12(+) (ENSTOOOOO446837.2)
Location	Exon 10
Variant	c.1376G>A (p.Arg459GIn)
Zygosity	Homozygous
Disease(OMIM)	Primary ciliary dyskinesia-9 with or without situsinversus
Inheritance	Autosomal recessive
Classification	Uncertain significance

Discussion

Kartagener syndrome (KS) is a rare, autosomal recessive ciliary disorder characterized by the clinical triad of chronic sinusitis, bronchiectasis, and situsinvertus with incidence approximately 1 in 30,000 live births [5, 6]. It was first described in 1904 by Siewert and therefore some people call it Siewert syndromeas well [6].This was followed by another report by Oeri in1909 [7]. Kartagener reported four cases in 1933 [8], and sevenmore in 1935 [9].Since then, others have also reported cases of KS [10-12]. Recently, Ciancio et al have reviewed eight cases of Kartagener syndrome from 2006 to 2014. However, two patients with more severe clinical behavior died before 2014 [13]. Arunabha et al also reported a classical case of Kartagener syndrome [14].

We reported7-year-old girl presented with history of recurrent episodes of fever with cough and cold with difficulty in breathing since 1 year.Imaging findings revealed dextrocardia, bronchiectasis sinusitis, and ciliary dyskinesia, which metthe diagnostic criteria for KS. Theimportance of diagnosing this rare disorder lies in the fact that deterioration in lung functionoccurs early in childhood [6, 15].The diagnostic criteria recommended for this syndrome are history of chronic bronchial infection and rhinitis from early childhood, combined with one or more of following features: 1) Situsinvertus or dextrocardia in a patient or a sibling, 2) Alive but immotile spermatozoa, 3) Absent or impaired tracheobronchial clearance, 4) Cilia showing characteristic ultrastructural defect on electron microscopy [16].Our case had some of these features.

Normal ciliary function is critical for respiratory tract host defense, sperm motility, and normal visceral orientation during embryogenesis. Lack or dysfunction of dynein arms, radial spokes, and microtubules of cilia are recognized structural and functional abnormalities of ciliaryultrastructures, encoded by the mutated genes DNAI1 and DNAH5. These faulty genes cause the cilia to be the wrong size or shape or move in the wrong way, making ciliary motility defective. However, abnormal ciliary motility at sites leads to chronic recurrent sinopulmonary infections and infertility. Impaired ciliary motility during embryogenesis predisposes to left– right laterality defects like situssolitus (that is, dextrocardia only) or situsinversustotalis.Infertility in male KS patients is due to diminished sperm motility, while in females it is due to defective ovum transport because of dyskinetic

motion of oviductal cilia, suggesting that the ciliated endosalpinx is essential for human reproduction [17].

Primary Ciliary Dyskinesia (PCD) is a genetically and phenotypically heterogeneous hereditary disorder mainly transmitted by autosomal recessive inheritance. The genetic basis of the variety of defects affecting ciliary structure and function in PCD is not clear: to date, mutations in more than 30 different genes have been referred [18]. The disease occurs as a direct result of congenital defects in motile cilia covering the respiratory epithelia, leading to impairment of the mucociliary clearance. PCD is characterized by chronic upper and lower respiratory tract infections; the clinical phenotype is broad and overlaps with other chronic airways diseases; the incidence and the severity differ from one patient to another, even among siblings. The estimated prevalence of PCD is about 1 in 16,000, but this could be an underestimation due to missed diagnosis [19].

Labaratotoryscreening tests for PCD- exhaled nasal nitric oxide level determination and saccharin test for assessing nasal epithelial mucociliary function. Diagnostic tests were 1) high-speed video microscopy for assessing ciliary beat frequency and pattern transmission, 2) Electron microscopic for detecting ultrastructuralciliary defect and Genetic testing for DNAI1 and DNAH5 mutations were the confirmatory laboratory tests.The samples for these tests for examining motility and ultrastructure of cilia may be obtained by biopsy of nasal mucosa and laparoscopic biopsies of tubal mucosa in females. Abnormal laboratory findings in KS include- 1) Reduced nasal nitric oxide level (~10% of normal), 2) Prolonged saccharin clearance time (>1 hour), 3) Reduced ciliary beat frequency (<11Hz/second), 4) Absent ciliary ultrastructure (dynein arms), and 5) Mutated DNAI1 and DNAH5 genes. In this report, the DNA12 (+) (ENSTOOOOO446837.2) gene was identified as a causative gene for PCD using homozygosity mapping.This approach requires the analysis of a large affected inbred family and assumes that the recessive disorder is caused by a homozygous mutation that is inherited from the common ancestor.We are reporting this case because of its rarity and rare presence of genetically homozygous primary ciliary dyskinesia -9 with uncertain significance.

There are no specific guidelines for the treatment of Kartagener syndrome. Barbato et al compiled existing evidence to formulate general clinical recommendations which include at least biannual clinical visits with routine spirometry, sputum culture and if needed imaging studies [20]. Standard treatment for sinopulmonary problems in people with KS includes chest physiotherapy, mucolytic and antibiotics. A long-term low-dose prophylactic antibiotic is required in those with frequent exacerbation of bronchiectasis (≥3 times/year). Influenza and pneumococcal vaccination should be routinely given. Genetic counseling and fertility issues should be addressed once KS is diagnosed.

Conclusion

Kartagener`s syndrome is a rare condition, occasionally picked up by the physician. It is important to consider the diagnosis of Kartagener syndrome in a child or young adult who presents with a history of recurrent respiratory tract infections coupled with chronic sinusitis or bronchiectasis with dextrocardia. It may prove challenging if high index of suspicion is not made. Thorough clinical evaluation, adequate investigations, proper timely management, etc. go a long way in alleviating the patient`s symptoms, prevent

the deterioration of the lung function, reducing the morbidity and improving the quality of life.

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