Case Report

A rare case of Kartagener's syndrome - A case report

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Abstract

Kartagener's syndrome is a rare disorder. The estimated prevalence of Kartagener's syndrome is about 1 in 30,000. It is autosomal recessive ciliary disorder comprising the triad of situs inversus totalis, chronic sinusitis, and bronchiectasis. There is a defective movement of cilia, which leads to recurrent respiratory infections, and ear/ nose/ throat infections, and infertility. We hereby report a rare case of Kartagener's syndrome, an infertile male with azoospermia. The clinician should have a high index of suspicion, so as to make an early diagnosis. An early diagnosis helps in such patients so that the options for timely treatment of infertility may be offered and unnecessary evaluation is avoided.

Key words

Kartagener's syndrome, Bronchiectasis, Sinusitis, Situs Inversus.

Introduction

Kartagener's syndrome (KS) is a subset of a large group of ciliary motility disorders called primary ciliary dyskinesias (PCDs). It is a genetic disorder with an autosomal recessive inheritance [1, 2] comprising a triad of situs inversus totalis, bronchiectasis and sinusitis [1, 2]. Although Siewart first described this condition in 1904, it was Kartagener who recognized the etiological correlation between the elements of the triad and reported four cases in 1933 [2]. The estimated prevalence of PCD is about 1 in 30,000 [3], though it may range from 1 in 12,500 to 1 in 50,000 [1]. In KS, the ultrastructural genetic defect leads to impaired ciliary motility which causes recurrent lung, ear/ nose/ throat (ENT), and sinus infections, and infertility. A high index of suspicion is needed to make an early diagnosis so that timely treatment

may be offered for infertility in the young patients, It seems likely that early diagnosis is important for the preservation of pulmonary function, quality of life and life expectancy in this disease [4, 5].

More than 200 proteins and polypeptides are involved in ciliary formation and structure [6] most of which can be visualized clearly by electron microscopic examination. Ultrastructurally, a normal cilium consists of an axoneme and a pair of central singlet microtubules surrounded by nine pairs of doublets (the '9 + 2' pattern) [6]. Other structures such as the bridge connecting central singlets, central sheath, radial spoke, outer and inner dynein arm, nexin link, and ciliary membrane are all crucial to maintain the normal integrity and function of the cilium.

Any abnormality involving these structures may impair ciliary function. Most of the disease causing mutations are said to involve two genes coding for the dynein axonemal heavy chain [7] (DNA H5) and dynein axonemal intermediate chain 1 (DNAI1) [7].

Case report

A 28 year old male patient, driver by occupation admitted to the hospital with complaints of fever with chills and rigors since 15 days, cough with purulent sputum since 10 days.

History of present illness: Patient was apparently asymptomatic 15 days ago, then he developed fever with chills and rigors, which was relieved on medication, no history of night sweats, no diurnal variation. He developed cough with purulent sputum since 10 days which was insidious in onset, gradually progressive, scanty in amount, yellow in color, thick tenacious in consistency, showing diurnal variation occurring more in the morning, no history of hemoptysis. No history of wheeze, orthopnea, PND, Chest pain, palpitations, and pedal edema, No history of decreased urinary output. No history of loss of consciousness. No history of weight loss. History of loss of appetite since 10 days was present. No history of rashes, joint pains, melena, epistaxis, bleeding gums. No history of loose stools or vomiting was present.

Past history: Not a known case of Hypertension/ Diabetes Mellitus/ Tuberculosis / epilepsy / CVA / CAD /thyroid disorders / asthma/ COPD. No history of similar complaints in the past. No history of drug allergies.

Family history: No history of similar complaints in parents and grandparents, Both father and mother are known case of NIDDM and HTN, He is married, 5 years ago, and no off springs.

General Examination

Patient was conscious, coherent, cooperative, answering to questions well. Patient was thin built, well nourished, comfortably seated on the bed. Wt – 45 kg, Ht – 5'5", BMI – 16.7, No pallor, No icterus, No cyanosis, no clubbing, No lymphadenopathy, No pedal edema.

Vital data: Pulse - 80/ mt, regular, normal volume, No radio radial delay, no radio femoral delay, all peripheral pulses felt. BP- 120/80 mm Hg, rt arm supine position, RR- 20/min.
Temp- 98.4^0 f, JVP - Not raised.

Systemic examination

Upper Respiratory Tract

Nose: No nasal flaring, nasal septum central in position, normal nasal cavities, no polyps, ulcerations. Oral Cavity: Teeth-normal, Gums-normal, tongue-normal, hard and soft palate-normal, uvula-central, Sinus tenderness present at frontal sinus.

Examination of Respiratory system

Inspection: Shape of Chest-normal. Trachea - central in position.
Movements of the chest: equal on both the sides, No usage of accessory muscles, No inter costal indrawing, no engorged veins, no sinuses, no inter costal scars or swellings.

Palpation: All inspectory findings were confirmed. No local rise of temperature and tenderness. No bony swelling or tenderness.

Measurements:
Circumeference: Right hemithorax- inspiration: 39.5cm, expiration: 37cms,:
Left hemithorax inspiration: 38.5cm, expiration: 36 cm
AP: Transverse Ratio – 5:7, Transverse diameter-30 cm, Antero-posterior diameter – 25 cm
Vocal fremitus: Increased in left supraclavicular, mammary and inframammary areas.
Percussion: Dull note on left supaclavicular, mammary and inframammary areas.
Ausculation: Bronchial breath sounds in left suprascapular, infrascapular and mammary areas are heard, Adventitious sounds: Rt. Side- coarse leathery crepitations heard at infra axillary, inter scapular and infra scapular, Lt. Side - coarse leathery crepitations heard at infraaxillary, interscapular and infrascapular. Vocal Resonance: Increased on left supraclavicular, mammary, inframammary areas.

Cardio vascular system: Apex not felt on left side, Heart sounds -S1, S2 heard distant in 5th left intercostal space,but better heard on Rt. side, no murmurs.

Investigations: Hb-12.4 g%, WBC count 12000 cells/cumm with Neutrophils - 77%, Lymphocytes - 20%, Eosinophils - 2%, Basophils - 1%, Monocytes - 0%, Platelet count – 1.2lakhs/cu mm. Blood picture- Howell jolly bodies- Absent, Normocytic normochromic. ESR 1st hr - 35 mm, Blood Urea 30 mg%, Serum Creatinine - 0.9 mg, Serum Electrolytes: Na – 140 m mol/L, K – 4 m mol/L, CL – 99 m mol/L. LFT – Total bilirubin-1 mg/dl, Direct bilirubin-0.8,Indiect bilirubin-0.2, AST- 80U/L, ALT-128/L, ALP- 155U/L, GLO-2.7G/dl, A/G-1, Sputum for AFB - Negative, Sputum c/s- No growth, Sputum G/S -Normal flora, TRU NAAT- Negative,. X-ray chest (**Figure - 1**): cardiac apex and aortic arch on the Rt side, bilateral lower lobe pneumonitis. X-ray - P N S (**Figure - 2**) shows agenesis of frontal sinus, ECG in left sided leads (**Figure - 3**): Normal sinus rhythm, Rate- 76 bpm, Lead 1 - inverted "P" wave, Negative QRS, Inverted "T" wave., Biphasic QRS in aVR with upright "P" and "T"waves, S/O Dextrocardia; ECG in right sided leads (**Figure - 4**): Normal 'R' wave progression in Right sided precordial leads, Semen analysis - Total sperm count-1 millions (Normal: 20-50 millions) 100% non motile, Shape - Normal 70%, Abnormal 30%, Impression -Severe Oligoasthenozoospermia.

Figure – 1: X-ray Chest PA view: Cardiac apex and aortic arch on the Rt side, bilateral lower lobe pneumonitis.

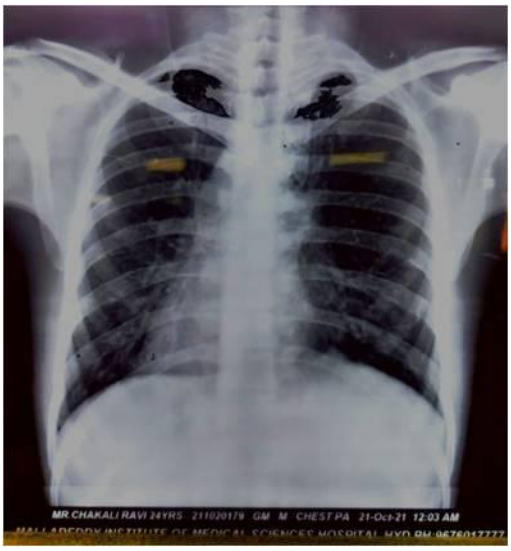


Figure – 2: X - ray - PNS shows agenesis of frontal sinus.

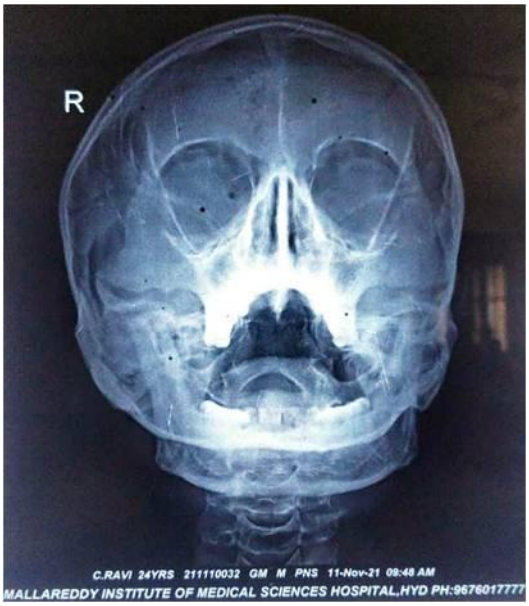


Figure - 3: ECG with normal lead positions: ECG in left sided leads: Normal sinus rhythm, Rate- 76bpm, Lead 1 - inverted "P" wave, Negative QRS, Inverted "T" wave., Biphasic QRS in aVR with upright "P" and "T" waves, S/O Dextrocardia.

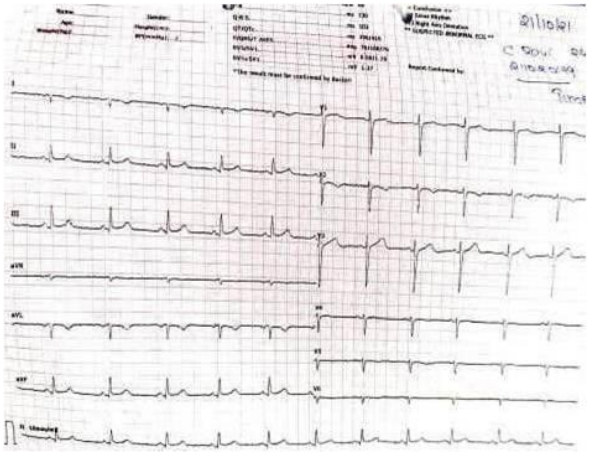


Figure - 4: ECG with Rt sided lead positions: Normal 'R' wave progression in Right sided precordial leads.

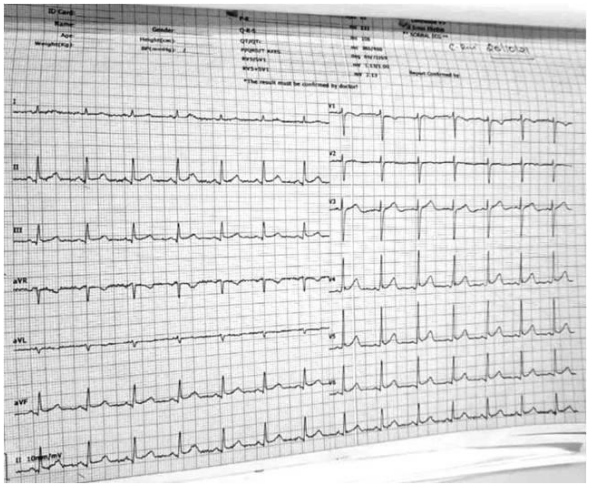


Figure – 5: Liver in left upper quadrant, Spleen in right upper quadrant, Aorta and I VC interchanged in position.

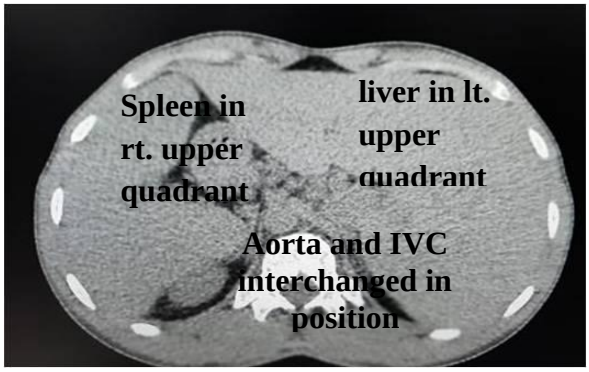


Figure – 6: Cardiac apex points towards right.

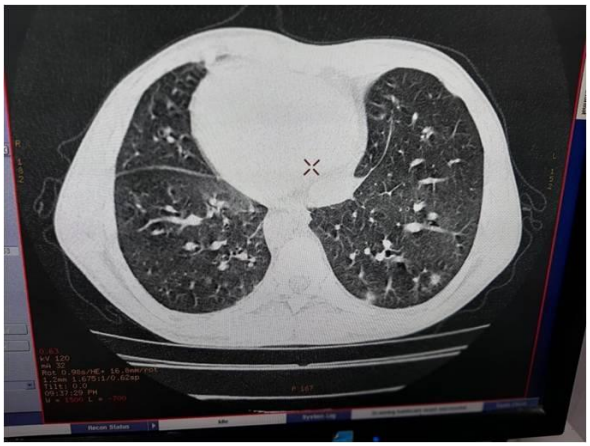


Figure – 7: Posterior segment of Right lower lobe, posterior segment of left lower lobe and left upper lobe patchy consolidation.

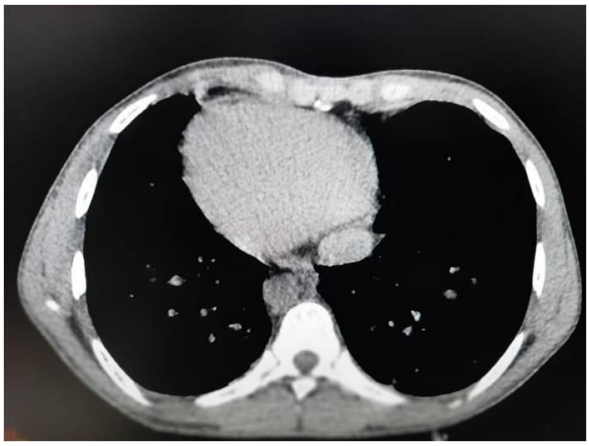
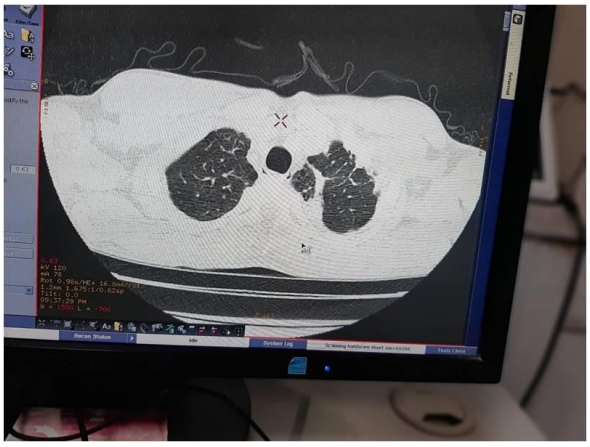


Figure – 8: Fibrosis with left upper lobe causing near collapse of left upper lobe.



CT Abdomen (**Figure - 5**). Liver in left upper quadrant, Spleen in right upper quadrant, Aorta and I VC interchanged in position. CT Scan Chest: Cardiac apex points towards right (**Figure**

- 6). Patchy consolidation with mild bronchiectatic changes in Posterior segment of Lt. Lower lobe, and Posterior segment of Lt. Upper lobe (**Figure - 7**). Fibrosis with Lt. Upper lobe causing collapse of Lt. Upper lobe (**Figure - 8**). Cystic bronchiectasis of left upper lobe. Emphysematous changes of left middle lobe (**Figure - 9**). Rt lung- 2 lobes, Lt lung- 3 lobes (**Figure - 10**). HRCT Chest **(Figure - 11):** Cystic and tubular broncheictasis along with fibrosis in left upper lobe and compensatory hyperinflation with emphysematous changes of left middle lobe segment. Patchy area of consolidation in lateral basal segments of right and left lower lobe. Few linear fibrotic strands in right lower lobe. Emphysematous changes in anterior segment of right upper lobe. **USG Abdomen:** Situs inversus, Mild hepatospleenomegaly, Both kidneys show mild increased parenchymal echotexture with preservation of CMD. Liver present in left hypochondriac region, 15.3 cm. Spleen present in right hypochondriac region, 13.7 cm. Portal vein measures 13 mm.

Figure – 9: Cystic bronchiectasis of left upper lobe.

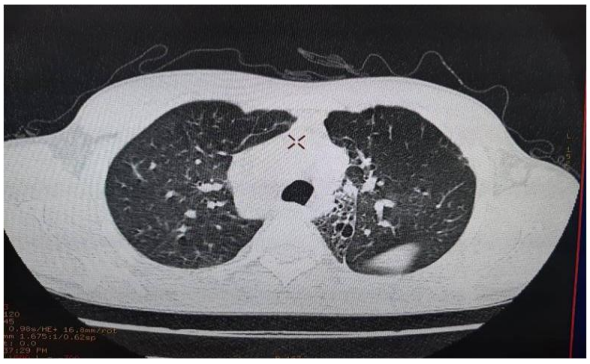


Figure – 10: Right lung has two lobes, and left lung three lobes.

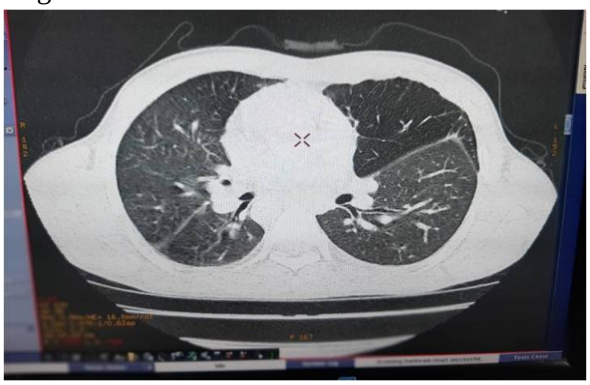
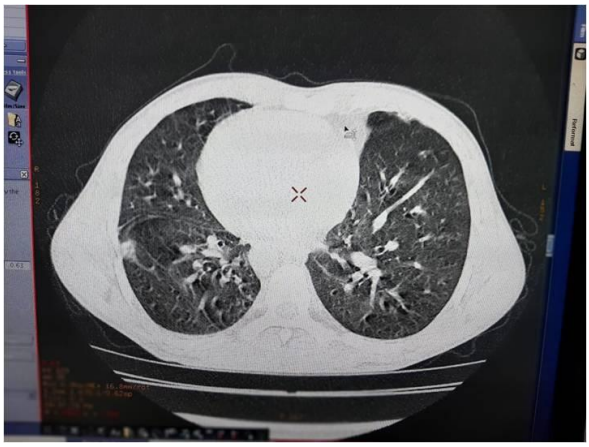


Figure – 11: Emphysematous changes of left middle lobe.



Diagnosis

Kartagener's syndrome

Treatment given:

Chest Physiotherapy,

Antibiotics and Mucolytics

Treatment suggested on follow up

A long-term prophylactic antibiotic is required in those with frequent exacerbation of bronchiectasis (≥3 times/year). Influenza and pneumococcal vaccination should be routinely given.

Discussion

Disorders of ciliary motility may be congenital or acquired. Congenital disorders are labeled as PCDs. Nearly 50% of PCD patients have situs inversus. PCD with situs inversus is known as Kartagener's syndrome [8]. PCD is a phenotypically and genetically Heterogeneous condition where the defect is in the ultrastructure or function of cilia [9, 10]. Such defects are identified in approximately 90% [11] of PCD patients. It involves the outer Dynein arms, inner Dynein arms, or both. 38%[11] of the PCD patients carry mutations of the Dynein genes DNAI [12] and DNAH5 [8].

Pathophysiologically, the ciliary motility disorder leads to accumulation of secretions and causes recurrent sinusitis, bronchiectasis, infertility. The severity of symptoms and the age at which the condition is diagnosed is quite variable, even though the symptoms are present

from birth [13, 14]. Occasionally, Kartagener's syndrome may be associated with reversible airflow obstruction [15]. Clinical progression of the disease is variable with lung transplantation required in severe cases.

Diagnostic criteria for this condition include [16] clinical picture suggestive of recurrent chest infections, bronchitis, and rhinitis since childhood, along with one or more of the following:
(1) Situs inversus in the patient/sibling;
(2) Alive but immotile spermatozoa;
(3) Reduced or absent transbronchial mucociliary clearance; and
(4) Cilia showing characteristic ultrastructural defect on electron microscopy.

Apart from fulfilling the criteria mentioned above, two types of tests are done for diagnosis of PCD – screening tests (exhaled nasal nitric oxide measurement which is usually low in PCD, and saccharin test to assess mucociliary function of nasal epithelium) and diagnostic tests (ciliary beat pattern and frequency analysis using video recording, and electron microscopic confirmation of the ultrastructural ciliary defect). The samples for these tests may be obtained by biopsy of nasal mucosa and laparoscopic biopsies of tubal mucosa in females, as was done by Halbert, et al. [17]. In some studies, they could not perform these tests and the diagnosis was essentially clinico-radiological, with variation in view of azoospermia and oligospermia [18-20]. Most infertile patients with KS have a normal spermatozoid count, but with a structural defect and a complete lack of motility [21].

Arge [22] first reported three male patients with this syndrome having immotile spermatozoa and sterility. Male patients with KS invariably present infertility, while women present reduced fertility [21]. 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 [22].

The development of assisted reproductive techniques has allowed rational treatment for these patients. Pregnancies were successful using subzonal insemination (SUZI) and intracytoplasmic sperm injection (ICSI) [23]. If there is no sperm motility, ICSI may be the most appropriate treatment and if sperm motility is present, a trial of in vitro fertilization (IVF) should be considered [23]. One concern regarding the fertility treatment of men with PCD is the possibility of resultant child has the risk of being affected by PCD. It is necessary to counsel couples regarding the possibility of genetic risks and to follow-up children fathered by men affected by PCD [23].

Normal ciliary beating is also necessary for visceral rotation and orientation during embryonic development. Patients with KS may have either situs solitus i.e., dextrocardia only or situs inversus totalis [24]. The cultures from lower respiratory tract most commonly yields Hemophilus influenzae, Staphylococcus aureus, streptococcus pneumoniae and rarely Pseudomonas aeruginosa [25]. Absence of nodal ciliary function leads to defects such as situs inversus or heterotaxy. Splenic abnormalities such as polysplenia, asplenia and complex congenital heart defects are more common in individuals with situs ambiguous and PCD.

Conclusion

Kartagener's syndrome is a rare autosomal recessive ciliary disorder comprising the triad of situs inversus totalis, chronic sinusitis, and bronchiectasis. There is a defective movement of cilia, which leads to recurrent respiratory infections, and infertility. KS patients are frequently troubled by repeated infection episodes for which they have to seek medical attention and this is largely the reason for their morbidity. But infertility is also an important aspect which needs to be addressed in evaluation so that they may beget children. An early diagnosis helps in such patients so that the options for timely treatment of infertility may be offered and unnecessary evaluation is avoided.

Now the development of assisted reproductive techniques has allowed rational treatment for these patients. Pregnancies were successful using subzonal insemination (SUZI) and intra cytoplasmic sperm injection (ICSI) [24].

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