Primary Ciliary Dyskinesia-Kartagener’s Syndrome: A Case Report & Review of the Subject

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ABSTRACT

Primary ciliary dyskinesia (PCD) is a heterogeneous group of inherited disorders in which cilia in the body are dysmotile/immotile due to their structural defects. Fifty percent of patients with PCD who have situs inversus have Kartagener’s syndrome. Our patient had history of recurrent upper & lower respiratory tract infections and infertility. He was admitted this time with features of hepatitis related to congestive hepatomegaly. He was diagnosed as a case of Kartagener’s syndrome when on further work up, he was found to have situs inversus along with immotile cilia & spermatozoa.

INTRODUCTION

Kartagener’s syndrome, a variant of PCD, is a rare genetic birth defect resulting in chronic sinus and lung disease because of immotility of cilia in respiratory passages. Sperm immotility results in infertility in males. Lack of Dynein arms remains the most common ciliary ultrastructural defect. In the presence of situs inversus & abnormal mucociliary clearance, the diagnosis can be confirmed by the biopsy of respiratory mucosa or microscopic examination of the sperm. Treatment is symptomatic including courses of antibiotics during infective episodes, bronchial hygiene therapy (postural drainage & physiotherapy), and avoidance of smoking & regular exercises to prevent sickness.

CASE REPORT

A 47 Year old male, married but issueless, cigarette smoker, shopkeeper, with positive family history of IHD & DM, was hospitalized with long standing complaints that included cough with mucopurulent sputum production and history of recurrent chest & ENT infections. He was taking treatment from GPs but was unhappy about his health. This time he presented with worsening of respiratory symptoms along with epigastric & left hypochondrial pain, recurrent vomiting & jaundice of one-week duration. On evaluation, he had a Pulse of 100/m, BP 110/70 mmHg and Temperature 38.5 C with a respiratory rate of 22 cpm. He was found to be clubbed, had slight pallor, jaundice and positive signs of dehydration. Positive findings on systemic examination included apex beat in 6th intercostal space on right mid-clavicular line & absent cardiac dullness on left side and bilateral vesicular breathing with basilar coarse crackles more on right side. There was tenderness in left hypochondrium & absent liver dullness on right. SpO2 was 94% on room air. His provisional diagnosis was ‘Acute hepatitis in the presence of chronic respiratory ailment-Bronchiectasis. With acute exacerbation & suspicion of situs inversus. Treatment on the lines of acute hepatitis & chest infection was started and investigations were undertaken that included: Hb: 11.4 G/dl, TLC: 7100 /µl, Platelets: 210,000/µl, PT: 12/12 s, aPTT: 32/30 s. LFTs: ALT: 1651u/l, AST: 396u/l, Alk.Phos: 200u/l, Total Bil: 3.5mg/dl, Direct Bil: 3.0mg/dl, S.Albumin: 3.0 g/dl; Viral serology for hepatitis A, B, C & E was negative. Renal profile: BUN: 12mg/dl & Cr:0. 8mg/dl, Serum electrolytes were within the normal range. Chest Radiograph showed reverse position of heart & aortic knuckle (Dextrocardia), prominent broncho-vascular markings & perihilar cystic changes (Fig.1)
ECG showing sinus tachycardia; right axis deviation; positive QRS in aVR & bifid P wave & R in V1 along with poor R wave progression V1-V6 (Fig. 2). ABG Analysis: pH 7.36; PO2 85mmHg; PCO2 33mmHg; HCO3 23mmol/L Urine CE: Unremarkable.

USG Abdomen: Liver (span 15.2cm) placed in left hypochondrium shows rather decreased parenchymal echogenicity with periportal accentuation & smooth surface reflecting acute diffuse parenchymal disease. Spleen being on right hypochondrial space. Accessory spleen is also noted. All other organs normal (Fig. 3).

There was symptomatic improvement in cough & sputum production after antibiotics & expectorants. His hepatitis features & LFTs settled over 7-10 days.

On the basis of long standing sinus & respiratory symptoms, situs inversus & infertility, a provisional diagnosis of Kartagener’s syndrome was considered accompanied by acute exacerbation of bronchiectasis and deranged liver functions due to acute hepatitis-probably drug induced (history of recent use of multiple medications from indigenous sources) or due to congestive hepatomegaly.

Further investigations were continued that included a repeat ECG with right-sided leads showing normal R wave progression from rV1 to rV6 (Fig. 4).

HRCT Chest which showed bronchiectatic changes with evidence of bronchocele & signet ring sign noted in superior lingual on left & lower lobe on right side with evidence of dextrocardia & few
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sub-diaphragmatic sections showed situs inversus (Figs. 5 and 6). CT Scan Para Nasal Sinuses revealed mucosal thickening involving left ethmoidal, sphenoidal, right maxillary and frontal sinuses with air fluid levels. Echocardiography confirmed dextrocardia & further revealed global hypokinesia with poor LV systolic function (EF 48%) and dilated LA, RA, RV with moderate RV systolic function & mild pulmonary hypertension.

Many ciliated respiratory epithelial cells were seen with no ciliary movement identified.

Saccharin Test employed a small drop of saccharin solution that was placed in posterior aspect of nose, while the patient in sitting position. No taste appreciated for 2½ hrs. (Control=45 minutes). Normal time=Up to 01 hour. Semen analysis showed many spermatozoa (Count=40 million/ml) appearing morphologically (70%) normal but no motile spermatozoa were identified.

Final Diagnosis on the basis of above features was Kartagener’s syndrome.

Patient was counseled for smoking cessation strategies & regarding disease management aspects. He was advised for regular chest physiotherapy & postural drainage of secretions & early introduction of antibiotics in case of infections. He received a shot of Pneumococcal vaccine during his stay in the hospital & was advised Influenza vaccination yearly & to have regular OPD follow ups in pulmonary, cardiac & ENT departments.

DISCUSSION

Kartagener Syndrome is a genetic disorder combining three major symptoms that include bronchiectasis, sinusitis and situs inversus1. Synonyms for Kartagener’s syndrome include: Chronic Sino-bronchial Disease and Dextrocardia, Bronchiectasis and Sinusitis, Kartagener Triad, Primary Ciliary Dyskinesia-Kartagener Type, Siewert Syndrome, Situs Inversus, Bronchiectasis and Sinusitis2. The genetic heterogeneity of the syndrome reflects the likelihood that many genes, and their proteins, participate in the construction of normal cillum and genetic mutation affecting any of them may impair ciliary function. The axoneme of cillum contains 200 different proteins, and defects in genes coding for any one of these products could conceivably be responsible for PCD. Ciliary motility is directed by a peptide whose gene expression was recently identified. Mutations in the sequence of DNA encoding a dynein axon are...
unique to patients with primary ciliary dyskinesia. Mapping of homozygosity in a consanguineous family with primary ciliary dyskinesia resulted in the identification of chromosome 5p15–p14 as a locus for a gene of interest in this region, DNA H5 that code for the heavy chain in a dynein arm. Olbrich et al. (2002) found 7 individuals from 6 families with Kartagener syndrome who had mutations in the DNAH5 gene. Primary ciliary dyskinesia is a heterogeneous group of inherited disorders characterized by a structural and generalized abnormality of cilia which renders them immotile or dysmotile. Approximately half of patients with PCD have Kartagener’s syndrome (bronchiectasis, sinusitis & situs inversus or partial lateralizing abnormalities). Propulsion of sperm (infertility) and mucus clearance from the respiratory tract (bronchiectasis & sinusitis) and middle ear are impaired. Ciliary ultrastructural abnormalities include: Absent/defective dynein arms (Commonest). Other abnormalities include overly long and overly short cilia, congenitally absent cilia, and cilia that are normal in appearance but randomly oriented & absent/abnormal radial spokes. Prevalence of PCD is 1 in 16,000 live births while that of Kartagener’s syndrome is 1 in 32,000 births. There is no geographic, racial, or sexual predilection and the disease is inherited as an autosomal recessive trait. Clinical Profile includes respiratory tract disease that starts from the very early childhood. There is chronic cough with mucoid sputum along with history of atelectasis and pneumonia. Bronchiectasis in dependent parts is an acquired sequel. Rhinitis, accompanied by nasal polyposis is seen in 30%. Other manifestations include chronic secretory otitis media with conductive hearing loss, chronic ethmoid and maxillary sinusitis & hypoplastic frontal sinuses. Male infertility is the rule when females may have normal fertility. There may be defective leukocyte migration due to their cytoplasmic microtubule defects. Hydrocephalus is caused by impaired ependymal ciliary motion.

The diagnosis of the condition has a menu of investigations that includes measurements of airway mucociliary clearance that employs Saccharin Test, which is non specific & non quantitative, but highly sensitive. Absence of sweet taste for greater than 60 minutes after particle placement is consistent with PCD. Airway mucociliary clearance can also be demonstrated via inhalation and tracking of radiolabelled particles, insoluble dyes and small particles in the nose, which can later be visualized in the oropharynx. Ciliary motility studies are undertaken by nasal mucosal biopsy/brushings or by biopsy of respiratory mucosa. More than one fresh specimen should be examined for demonstration of ciliary motion within 30 minutes. Semen analysis shows normal sperm count but abnormal motility. Ciliary motility studies includes: Oscillometry, Phase contrast photometry, computerized micro photometry and Electron microscopy which is not technically necessary from a clinical standpoint as the diagnosis can be finalized on light microscopic examination of cilia in the presence of appropriate clinical setting. Radiological investigations that can aid in the diagnosis are: X-Ray & CT Para Nasal Sinuses that shows changes consistent with chronic sinusitis, Plain chest radiograph and HRCT Chest to show situs inversus, dextrocardia & bronchiectasis.

Medical management is for symptomatic relief that includes regular chest physiotherapy and postural drainage, antimicrobials for recurrent infections & bronchodilators with or without inhaled corticosteroids in curbing airway reactivity. Situs inversus needs no treatment. Genetic counseling can be provided & at-risk siblings be identified. infertility counseling is provided to male patients & other methods such as in vitro fertilization can be offered. Surgical management options include resection of ectatic pulmonary segments, tympanostomy, and in some endoscopic sinus surgery may be repeatedly necessary. Other options include heart-lung transplantation or en bloc double lung transplantation with bilateral bronchial anastomoses.

With proper medical care and abstinence from smoking, the prognosis for primary ciliary dyskinesia is quite good. Most PCD patients seem to lead an active life & their life expectancy is close to or within the normal range.

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