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Case Report

Kartagener's Syndrome with Focal Bronchiectasis! Masquerading with Pneumonia, Bronchial Asthma and Cardiac Issues: A Unique Case

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Abstract

This report addresses how an inherited disease masquerades with infective, cardiac or immunity related disorders and provides the precedent of a rare generalized disease in the disguise of a focal phenomenon. Kartagener's syndrome is an uncommon genetic disorder, inherited as autosomal recessive entity and affects the function of cilia anywhere in body. It involves and produces symptoms in upper and lower respiratory tracts including paranasal sinuses, middle ear, eustachian tube, fallopian tube and spermatozoa. Bronchiectasis is usually diffuse and advanced at the time of diagnosis. Herein, we describe a unique case with focal bronchiectasis and primary infertility in female. Patient presented with fever, cough, shortness of breath and left sided chest pain masquerading with acute chest infection, exacerbation of bronchial asthma and mimicking with cardiac issues. Clinical, radiological and laboratory work-up disclosed the diagnosis of Kartagener's syndrome. Negative saccharin test concluded Primary Ciliary Dyskinesia.

Keywords: *Cilia; Dyskinesia; Female; Infertility; Focal Bronchiectasis; Kartagener's Syndrome*

Abbreviations

OPD: Out-Patient Department; MRC: Medical Research Council; ECG: Electrocardiography; BP: Blood Pressure; JVP: Jugular Venous Pressure; GIT: Gastrointestinal Tract; CNS: Central Nervous System; HIV: Human Immunodeficiency Virus; IgG: Immunoglobulin-G; IgE : Immunoglobulin E; HRCT: High Resolution CT; FSH: Follicle Stimulating Hormone; LH: Luteinizing Hormone; IVF: *Invitro* Fertilization; ICSI: Intracytoplasmic Sperm Injection; FVC: Forced Vital Capacity; FEV1: Forced Expiratory Volume in First Second

Introduction

Kartagener's syndrome is a rare genetic disorder associated with the triad of bronchiectasis, dextrocardia and sinusitis. It belongs to the group of primary ciliary dyskinesia, characterized by ciliary motility dysfunction [1]. It is inherited as an autosomal recessive trait with substantial heterogeneity. Any defect in the morphology or function of cilia gives rise to the issues of organ laterality, sinusitis, bronchiectasis and infertility [2]. About 50% cases of primary ciliary dyskinesia fall in to this category [3]. In 1904, Siewert noticed the association of situs inversus, chronic sinusitis, and bronchiectasis [4]. Manes Kartagener recognized this as a congenital clinical syndrome in 1933 [5]. It is a rare syndrome with an incidence of approximately 1 in 30,000 live births [6]. No distinct predilection for gender is recognized but it is fairly common in male [7]. Normal cilia perform vital functions of respiratory host defense, ensure exact visceral orientation, perfect motility of sperm and transport of egg in fallopian tube [8]. Any mutation at *DNAI1* and *DNAH5* results in impaired ciliary

motility and predispose to recurrent sinopulmonary infections, abnormal situs and infertility. This report describes the case of a 29 years old female having Kartagener's syndrome with focal bronchiectasis and infertility and is presented here owing to its rarity.

Case Report

A young female patient reported in OPD with productive cough (2 ½ Year), dyspnea (02-years), left sided chest pain (07 months), mild hemoptysis (06 months), epigastric burning relieved temporarily by antacids (06 months), frequent episodes of sneezing (03 months) and fever (10 days). Patient described repeated events of nasal blockage, ear-ache and noticed whistling sounds in chest usually at night. Cough was mild, productive and intermittent, more on lying flat or on the right side, relieved by cough expectorant. Cough was infrequently associated with blood-stained sputum off and on and frequently precipitated shortness of breath and wheeze. Patient narrated repeated nasal blockade and post nasal drip usually at night accompanied with frontal headache.

Patient was MRC-1 short of breath in the beginning and progressed to MRC-III during the last six months (stated by the patient). Shortness of breath was aggravated by exertion and settled temporarily by medications from local physicians. Patient noticed wheezing sounds in chest but there was no history of episodic attacks of dyspnea, tachycardia, palpitation, syncope, orthopnea and swelling of feet. Patient stated left sided chest pain off and on for the last three months which was intermittent, mild and subsided by pain killer medicine while exaggerated with cough, usually on the front and lower aspect of the chest, radiating to neck region. ECG was negative many times for any ischemia or infarction. She also pointed out about bilateral earache time and again.

Patient developed high grade fever with rigors ten days back associated with generalized body aches and settled with medications from local practitioners but re-occurred. Patient also proclaimed about frequent low grade evening rise in temperature and night sweats.

Previously she was treated for pulmonary tuberculosis three years back with a full course of anti-TB medicines. Patient had laparoscopy done in 2017 for pelvic issues.

Parents are alive and has three siblings, two sisters and one brother. Her sister has repeated respiratory tract issues. Mother is known diabetic and hypertensive while father is a chain smoker and had brain hemorrhage two years back. Patient belongs to middle class and lives in joint-family system. She is non-smoker and not involved in any kind of drug abuse. She has irregular menstrual cycles and described frequent yellow and foul-smelling vaginal discharge. She married seven years back, kept healthy better-half but no child and was divorced after five years for the same issue.

Physical examination divulged Pulse: 113/min, BP: 130/80 mmHg, Temp: 99.4°F, R/R: 26/min, weight; 54 Kg and patient was 05 feet and 02 inch tall. Oxygen saturation was 91% but without cyanosis, clubbing or raised JVP. Respiratory system exhibited elliptical chest, thoraco-abdominal respiration and equal chest movements, expansions and vocal fremitus with resonant percussion on both sides. On auscultation mild to moderate wheeze and coarse crackles noted at mid and lower parts of chest bilaterally. No pleural rub appreciated. Cardiovascular system examination conveyed only apex beat in 5th intercostal space at mid-clavicular line on the right side with normal cardiac auscultation. GIT, skin, CNS and musculoskeletal systems were unremarkable. Differential diagnosis of acute lower respiratory tract infection, reactivation tuberculosis, bronchiectasis, exacerbation of bronchial Asthma and Cardiac issues were considered.

X-ray chest PA view displayed subtle, ill-defined opacification in left lower lung fields, bilateral hilar calcification and normal sized heart shadow with cardiac apex pointing towards right, suggesting left lower lobe acute infection and dextrocardia. Patient was treated empirically with Ampicillin, bronchodilators, antipyretics and cough mixtures. Fever subsided, shortness of breath improved, sputum volume reduced but cough was not resolved. Patient was subjected to further investigations. Three early morning sputum samples tested for Acid Fast Bacilli by fluorescent microscopy for three consecutive days, were reported negative. Sputum Gene-X-pert and culture for *Mycobacterium tuberculosis* was negative while *Pseudomonas aeruginosa* was isolated on pyogenic culture.

Routine hematological tests performed (Table 1 and 2). Screening results for Hepatitis-B, Hepatitis-C and HIV were negative. Serum IgG level was 14.3 g/L (Ref. value: 5.40--18.22), Serum IgE level was 127 IU/ml (Atopy > 100). Serum Alpha-1 anti-trypsin level was 166.1 mg/dl (Ref. value: 90 - 200).

Test	Result	Reference Values
Hemoglobin	12.28	13 - 18 g/dl
ESR	55	1 - 15 mm1st Hour
WBC	12.700	4 - 11 X 10^3 /uL
RBC	4.1	4.5 - 6.5
HCT	32	40 - 54%
MCV	78	76 - 96
MCH	28	27 - 32 pg
MCHC	35	30 - 35 g/dl
Platelets	238	150 - 450 X 10^3 /uL
Polys	79%	40 - 75%
Lymphos	19%	20 - 45%
Monos	1%	2 - 10%
Eosinophils	1%	1 - 6%

Table 1: *CBC and ESR values.*
CBC: Complete Blood Count; ESR: Erythrocyte Sedimentation Rate; g/dl: Gram Per Desi-Liter; /uL: Per Micro-Liter; pg: Pico-Gram.

Test	Result	Reference Value
Serum Bilirubin	1.0	0.2 - 1.1 mg/dl
SGOT (AST)	38	5 - 45 u/dl
SGPT(ALT)	41	5 - 42 u/dl
Alkaline phosphatase	180	100 - 270 u/dl
Serum Protein	6.9	6 - 8 g/dl
Urea	20.0	10 - 50 mg /dl
Serum Creatinine	0.8	0.5 - 1.4 mg /dl
Serum Sodium	136	135 - 155 mmol/L
Serum Potassium	4.0	3.4 - 5.5 mmol/L
Blood Sugar Fasting	90	80 - 160 mg/dl
Serum Calcium level	10.2	9 - 11 mg/dl

Table 2: *Biochemistry and special tests.*

Radiological work-up communicated middle lobe bronchiectasis on the left side and dextrocardia (Figure 1A-1C). Paranasal sinus radiograph displayed hazy maxillary sinuses on both sides, absent frontal sinuses and fullness in nasal cavity (Figure 1H).

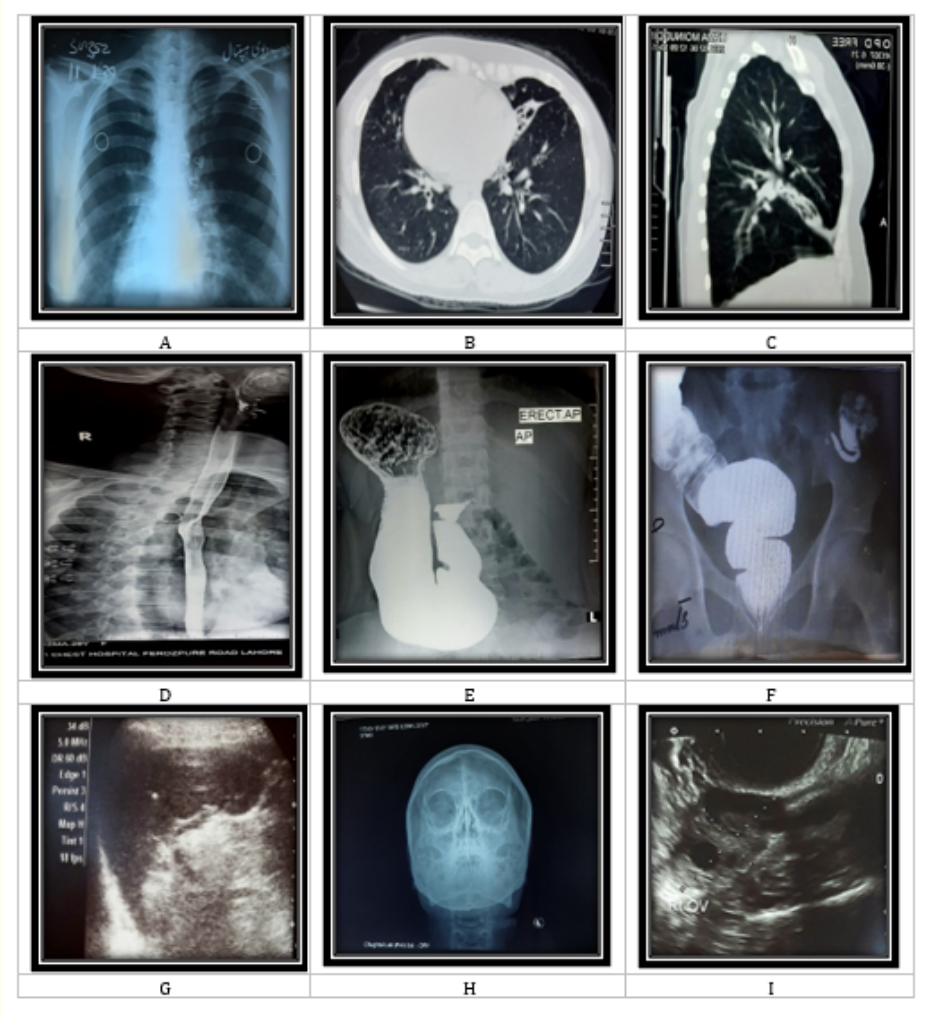

Figure 1: *Radiological investigations.*

A: X-Ray chest-PA view showing suspicion of lower zone infection on left side and dextrocardia. B: HRCT-axial view: Middle lobe bronchiectasis on left side. C: HRCT-Sagittal view: Middle lobe bronchiectasis. D: Normal Barium Swallow, E: Stomach position on the right side, F (Barium Enema): Cecum and appendix on the left side while recto-sigmoid and descending colon on the right side. G (Sonogram): Right sided Spleen, H: X-ray PNS: Bilateral Maxillary Sinusitis, I: Sonogram showing a mature follicle in right ovary.

Pulmonary function tests manifested decreased FEV1, FVC and reduced FEVI/FVC ratio. Bronchoscopy ruled out any obstructing etiology and described inflamed, dilated and full of pus middle lobe bronchus. Delta F508 mutation test was negative. Sweat test results were equivocal. Ultrasound abdomen was negative for any sign of cystic fibrosis, rather it babbled about the presence of liver and gall bladder on the left side and spleen on the right side. Barium series declared stomach on the right side, duodenal cap pointing towards left, cecum and appendix on the left side while sigmoid and descending colon on the right side. Electrocardiography intimated, heart rate: 118/min,

sinus rhythm and right axis deviation. Positive QRS complexes with upright P and T waves in AVR, inverted P wave, negative QRS, inverted T-wave in lead-1. Absent R-wave progression in the chest leads. On echocardiography, normal chambers, good biventricular function, ejection fraction 68% and dextrocardia were proclaimed. Bronchiectasis severity index by online tool was 3, communicating mild bronchiectasis. Audiometry showed mild to moderate hearing loss on left side. Transvaginal pelvic ultrasound reported a mature follicle in right ovary (Figure 1I). Hysterosalpingography revealed free peritoneal spill of contrast on both sides. Semen analysis of husband announced 75 million count and 85% motility with 4% abnormal heads. FSH, LH and Prolactin levels were within normal range. Saccharin test of the patient was negative for three times.

Discussion

Kartagener's syndrome is associated with the triad of bronchiectasis, dextrocardia and sinusitis. Being a genetic ciliopathy disorder, symptoms are produced in all cilia containing organs due to dysfunction of cilia. Because all cilia are affected that is why it is designated as diffuse disorder. In most of the cases patient show diffuse and advanced bronchiectasis at the time of diagnosis.

This patient, presenting with productive cough, fever, MRS-III SOB, left sided chest pain, missed apex beat on the left side and with risk factor of diabetes and hypertension in family raised the suspicion of cardiac issues but multiple ECG tracings and Echocardiography ruled-out ischemia, infarction or any other cardiac problem except dextrocardia. Clinical features also impersonated with acute pneumonitis and exacerbation of bronchial asthma making the case atypical. In the scenario of fever, TLC: 13,700, polys: 79%, ESR = 55 mm 1st hour, subtle ill-defined left para-cardiac shadows and dextrocardia, an acute pulmonary infection with isolated dextrocardia was considered and patient was treated empirically with amoxicillin, antipyretics, bronchodilators and cough mixtures for 10 days. Fever subsided, dyspnea improved, sputum volume reduced but cough did not resolve. Patient was subjected to further investigations to determine the precise etiology. HRCT-Thorax confirmed middle lobe bronchiectasis (Figure 1B and 1C). Negative delta-F 508 test, sweat test and ultrasound findings ruled-out cystic fibrosis bronchiectasis. A normal Alpha-1 antitrypsin level excluded this etiology.

Shortness of breath with lower and mid chest rhonchi on both sides and elevated level of IgE fabricated the impression of bronchial asthma. But dyspnea was not episodic, having no relation with season or other triggering factor except cough as precipitating factor. Pulmonary function tests displayed obstructive pattern but Bronchoscopy was negative for any obstructive lesion. Isolate of *Pseudomonas aeruginosa* in sputum and bronchoalveolar lavage and repeated exacerbations provided the clue for *Pseudomonas* colonization. Chest pain can be explained by inflammation of lung parenchyma and pleura due to exacerbation. She often complained about central chest pain and burning, when interpreted in the presence of lower zone ill-defined shadows, pointed towards the possibility of gastroesophageal reflux disease or tracheo-esophageal fistula but a normal barium swallow eliminated this possibility. Depiction of spleen on the right side (Figure 1G) while liver and gall bladder on the left side abdominal ultrasound gave rise to situs inversus partials but barium series announcing stomach, recto-sigmoid and descending colon on the right side and cecum and appendix on the left side (Figure 1D-1F), confirmed situs inversus totals. Sinus involvement was confirmed by paranasal sinus radiograph (Figure 1H). This patient with a triad of bronchiectasis, sinusitis and situs inversus totals qualified for the diagnosis of Kartagener's syndrome. Repeated upper and lower respiratory infections in this syndrome can be explained by modification in structure or function of cilia, disturbing normal muco-ciliary escalator *Pseudomonas* colonization. Ciliary abnormalities also lead to the malposition of organs during embryogenesis [9].

The patient was married seven years back and in-spite of having healthy better half had no baby. She was divorced after five years for the same reason. She married again two years back and is still to conceive. This phenomenon can be due to any defect in fallopian tube, hormonal imbalance, oogenesis or alteration in cilia. Hysterosalpingography showed patent fallopian tubes bilaterally. A normal serum FSH, LH and Prolactin levels and demonstration of mature follicle in right ovary by transvaginal pelvic ultrasound scan ruled-out these possibilities. A normal semen analysis of the husband determined the fitness of the husband. Because after maturation, egg is taken up by the fimbria and cilia in lining- epithelium of fallopian tubes are responsible for transporting the egg to the meeting place with sperm

by coordinated beatings. In failure of conception, possibly defect may be in cilia [9]. Saccharin test was performed which was negative three times indicating ciliary dyskinesia as the cause of infertility. Ultimately the diagnosis of Kartagener's syndrome with primary ciliary dyskinesia was made.

The patient was managed by multi-disciplinary approach. Surgeon advised conservative medical treatment. Patient is immunized and on anti-pseudomonal antibiotics. She is advised IVF/ICSI for pregnancy and is build up psychosocially.

A female patient with focal bronchiectasis in Kartagener's syndrome with primary ciliary dyskinesia which is a generalized disorder is quite unexpected feature. Similarly, involvement of left ear only is also a focal phenomenon. Furthermore, infertility in this syndrome is seen mostly in male. The finding of infertility is reasonably unanticipated. No doubt, this case is a good precedent of a diffuse congenital disorder with focal presentation and masquerading with general medical issues makes the case unique. As her younger sister is also having bronchiectasis in both lungs and still to have pregnancy, this fact further strengthens its genetic and diffuse nature.

This case is reported because of its unique features of focal bronchiectasis with Kartagener's syndrome and female infertility mimicking with pneumonia, bronchial asthma and cardiac issues.

Conclusion

- Repeated respiratory infections with Kartagener's syndrome may mimic with pneumonia, bronchial asthma and cardiac issues. A high index of suspicion is essential to clench the diagnosis.
- Early diagnosis of the condition can decelerate the progression of bronchiectasis which otherwise will appear in later life with extensive morbidity. This step may help in preserving pulmonary functions and improving quality of life.
- The issue of infertility can be addressed to have children if they desire.

Patient Consent

A written informed consent was obtained from the patient for the publication of this report.

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