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Research Article

AMELIORATION OF KARTAGENER SYNDROME BY HOMOEOPATHIC THERAPEUTIC AID

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ABSTRACT

Background and Objective :Kartagener Syndrome (KS) is a rare autosomal genetic disorder which cause a defect in the action of 'cilia', Swiss Physician Maneskartagener identified a cluster of symptoms in 1933 that include sinusitis, bronchiectasis, otitis etc. as well as situsinvertus.
A patient, Mr. K. Paul, aged 40 years of Howrah, W.B., was suffering from KS with symptoms of breathlessness and productive cough for last few years. He was treated by different generations of antibiotics and inhalation of steroid with minimal improvement. With the recurrence of the above symptoms complexes, he switched over to Homoeopathic treatment on 04/10/2010 seeking better aid.
Methods
Confirmation of diagnosis : By HRCT Scan of Lung shows bilateral lower and middle lobe bronchiectasis, USG of abdomen and CXR show situsinvertus of the organ and azospermia connotes the final diagnosis.
Proper case taking and repertorization were done as per homoeopathy.
Tuberculinum was the similimum of the case, and administered in 50 millisemal scale.
Pre and post-lung function test by spirometry to assess progress of the disease and response to treatment.
Result & Interpretation:
Clinically the condition of the patient is greatly improved by treatment
Lung function test by spirometry (Before treatment) – restrictive pulmonary dysfunction, FEV1 : FVC (decrease)
Lung function test (After treatment) – FEV1 : FVC (increase); pulmonary function improved with comparison to earlier report.
Conclusion :Nanoparticle laden homoeopathic medicine is capable enough to alleviate such rare disease without producing iatrogenic effect.

Keywords: Kartagener syndrome, situsinvertus, Bronchiectasis, Homoeopathic treatment, Spirometric response.

INTRODUCTION

107 years ago ,on 8th feb ,1904 the Berliner kinische wochen-schrift published a description, by Dr A.k.siewert ,of the patient" A.W",who since birth had the unusual combination of symptoms of bronchicectasis and situs invertus totalis. This was the first description of what since becomes known as Kartagener syndrome(KS).

This case study is an effort to combat against KS and its complications by homoeopathic therapeutic aid.

LITERATURE REVIEW

Kartagener Syndrome (KS) is a type of primary Ciliary dyskinesia associated with situsinvertus (mirror-image reversal of internal organs). KS is inherited in an autosomal recessive fashion and characterized by the triad (incidence 1:30000) situsinvertus, bronchicetasis and sinusitis.

Historical Data (from discovery till date

Although isolated cases had been reported by Siewert (Zivert) (1904), Oeri (1909), Guenther (1923). ManesKartagener (, 1933; Zurich Pulmonary Physician) was the first to call attention to the association of bronchicetasis and sinus maldevelopment with transposition of the viscera. KS is also known as immotile cilia syndrome or seiwart syndrome, Afzelius syndrome, Zivert KS triad. Camner and co-workers first suggested ciliary dyskinesia as the cause of KS in 1975. They describe 2 patients with KS who had immotile cilia and immotile spermatozoa. Later, Afzelius discovered that bronchial mucosal biopsy from patients with similar respiratory complaints showed cilia that appeared abnormal, were poorly mobile and were missing dynein arms. In 1977, Eliasson and co-workers used that descriptive phrase immotile cilia syndrome to characterize male patients with sterility and chronic respiratory infections.

In 1987 Rossmam and co-workers coined the term primary ciliary dyskinesia (PCD) because some patient with KS had cilia that were not immotile but exhibit uncoordinated and inefficient pattern. Current nomenclature KS includes big era of PCD.

Approximately one half of the patients with PCD have situsinvertus and thus as classified as having KS. Afzelius proposed that normal ciliary beating is necessary for visceral rotation during embryonic development. In patients with PCD, organ rotation occurs as a random event, therefore, half the patients have situsinvertus and the other half have normal situs.

Strugess etal described how the radial spoke which serves to translate outer microtubular sliding into cilia bending, was absent in some patients with PCD.

Seqence analysis of 21 genes located in the KS LINKAGE REGION ON CHROMOSOME 15q.

Pathophysiology and Genetics and Molecular Biology

KS is rare ciliopathic genetic disorder that causes a defect in the action of cilia lining the respiratory tract and fallopian tube, spermatozoa. Respiratory epithelial motile cilia, which resemble microscopic hair structure (unrelated to hair) are complex organelles that beat synchronously in the respiratory tract. Normally cilia beat of 7-22 times per second, any impairment can result in poor mucociliary clearance with upper and lower respiratory tract infection. Cilia also involved in other biological processes (such as nitric oxide production) which are currently the subject of research.

Motile cilia are made up of approximately 250 proteins. KS have ultrastructural defects affecting protein in the outer and/or inner dynein arm which give cilia their motility caused by mutation on two

genes DNA I¬1 and DNA H5 both of which code for protein found in the ciliary outer dynein arm.

CLINICAL PRESENTATION

History

Patients present with chronic upper and lower respiratory tract disease resulting from ineffective mucociliary clearance. A typical presentation of rhinorrhoea and/or mucopurulent discharge since birth. Immotile spermatozoa result in male sterility.

Physical

KS is usually present with triology of chronic sinusitis, bronchiectasis and situs invertus. But otitis media, infertility may be the common associate symptoms.

Upper Respiratory Tract

Patient may exhibit chronic, thick mucoid rhinorrhoea from early in childhood. Examination usually reveals pale and swollen nasal mucosa. Nasal polyps are recognized in 30% of affected individual. Recurrent otitis media is a common manifestation of PCD.

Lower Respiratory Tract

Chronic bronchitis and pneumonia are common condition with PCD then physical examination of the patient's chest, increased tactile fremitus, rhonchi, crackles and occasional wheeze may be present. Obstructive lung disease may another component of KS symptomatology. Bronchiectasis is the hallmark of KS.

Other Features

Cardiovascular examination of a patient with KS demonstrate a point of maximal impulse and the heart sounds are heard beat on the right side of the chest.

Rheumatoid arthritis, Renal abnormalities, cardiac defects, clubbing of fingers, conductive hearing loss are uncommon presentations.

TREATMENT AND MANAGEMENT

Medical Care (according to Modern Medicine)

Antibiotics, intravenous or oral and continuous or intermittent are used to treat upper and lower airway infection. Prophylactic antibiotics should be used with great caution in this era of emerging antibiotic resistance. Obstructive lung disease, if present should be treated by with inhaled bronchodilators. Inhaled corticosteroids are being used but no large studies support the use of these agents.

Laboratory Diagnosis

- Seminal analysis reveals abnormal sperm motility and ultrastructure, occasionally azospermic. (Afzelius, B.A. et al., 1976).
- Imaging Study – CXR or chest skiagram may illustrate bronchial wall thickening as an early manifestation of chronic infection, hyperinflation, bronchiectasis and situs invertus. The situsinvertus strongly suggest Kartagener Syndrome (KS).
- HRCT (High Resolution CT Scan) of the chest is the most sensitive modality for documenting early and subtle abnormality within airways and pulmonary parenchyma specially to detect bronchcetatic changes.
- ECG (12lead) – shows dextrocardia with tall R waves in V1 and absent R in V6.
- Ultrasonography of abdomen shows situsinvertus with spleen on the right side and liver on the left.

Other Tests

- Saccharin clearance test and nitric oxide (NO) test.
- Pulmonary function test (PFT) – spirometry often reveals an obstructive ventilatary defect with decreases in the ratio of Forced Expiratory Volume (FEV) in 1 sec to Forced Vital Capacity (FVC), reduced forced expired volume in 1 sec and reduced forced expiratory flow 25 - 75%
- Recent advances in genetic research have confirmed mutation of DNA H5 and DNA I1 (Geremeket al., 2004).
- Genetic testing is useful for counseling and has the potential for developing gene therapy for the management of PCD in the future.
- Primary cell epithelial cell culture can be done both gene testing and electron microscopy (EM) (Jorissenet al., 2000) in cases where the tissue and brush biopsy specimens are inadequate.
- Transmission electron microscope remains the most definitive method of establishing the diagnosis of PCD as the exact structural changes can be visualized.
- Ciliary beat frequency (Afzelius, 2004), ciliary beat pattern analysis by high speed video photography (Standard et al., 2004), and EM of ciliary ultrastructure (Teknoset al., 1997) and measurement of ciliary disorientation (Standard et al., 2004) are recommended wherever facilities exist.
- At present gene testing and EM are out of reach for many patients of PCD.

METHODS AND MATERIALS

This report is the review of the diagnosis and management of KS from the field of homoeopathic therapeutic perspective.

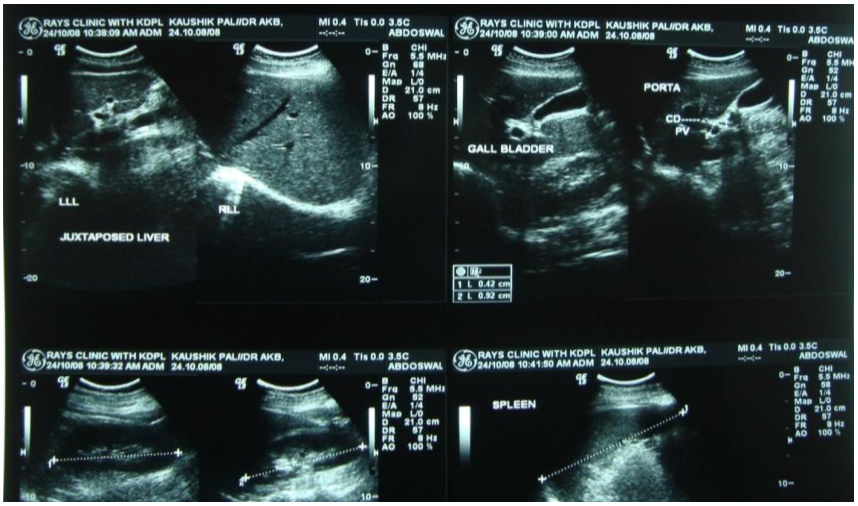
CASE STUDY

Mr. K. Paul, aged 40 yrs of Howrah District, W.B. came with productive cough, dyspnoea for last few years and had history of recurrent bouts of catarrhal inflammation since childhood. The patient was continuing his inhaler for bronchodilatation and he expressed his vexation for regular use of different degeneration of antibiotic prescribed by pulmonary specialist. He wanted to switch over to homoeopathic medicine avoiding those drugs. The pulmonary specialist diagnosed the case as COPD and treated accordingly.

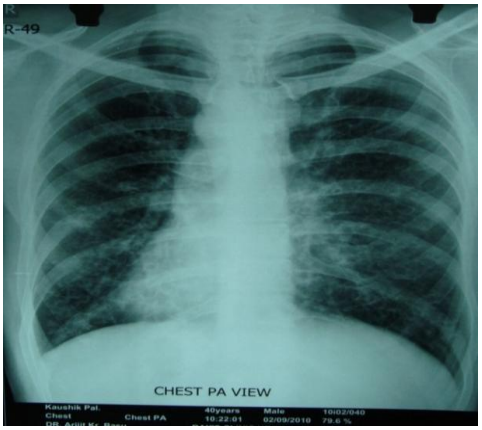
On clinical examination the positive findings of KS were detected

- Apex beat was heard over the right side of chest due to dextrocardia, S1S2 audible but no murmur.Vesicular normal breath sound, wheeze and crackles were found as added sound.
- Maxillary sinuses were tender.
- Patient was married for last 5 years but no children.
- Investigation had been done with the points keeping in the mind such as dextrocardia cough, cold, infertility and added breath sound.
- Ultrasonography of abdomen shows – situsinvertus of the organ specially liver (the left side) and spleen (on the right side).
- Seminal analysis shows azospermia.
- Skiagram of maxillary sinus – shows haziness of the sinus indicative sinusitis.

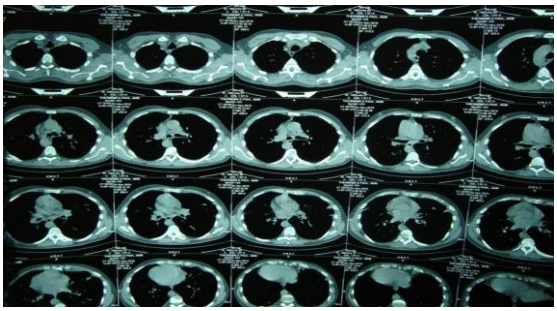
Clinical presentation along with laboratory investigations connotes the final diagnosis of Kartagener syndrome. Homoeopathic case taking were done on strict principle as per guideline of Organon of Medicine and Philosophy of Homoeopathy.



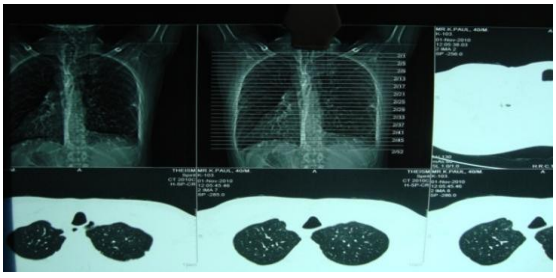
USG showing situs invertus, liver on the left and spleen on the right



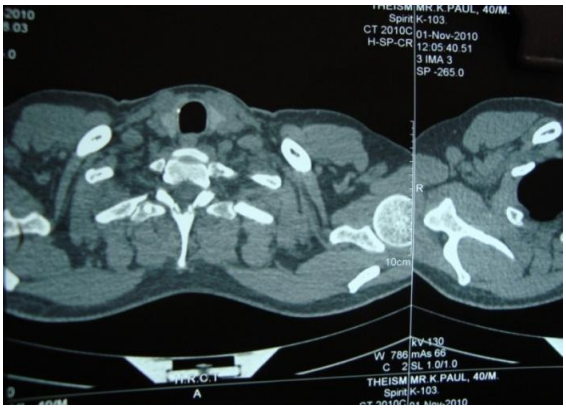
Chest X-ray showing dextrocardia and bronchiectatic changes



HRCT (High Resolution Computerized Tomographic Scan) – shows multiple small cystic lesion in lower zone of both lungs with bilateral lower and right middle lobe bronchiectasis.



HRCT scan of lungs shows bronchiectasis changes.



HRCT scan of lungs shows bronchiectasis changes.

Totality of Characteristic Symptoms is as follows

- The patient desires to travel different places and he changes his profession very frequently.
- The patient's tendency to take cold easily.
- Desire for smoked meat, fat, salty food, ice creams, aversion to bitter things.
- Fear of dogs and especially cats are marked.
- Strong sexual desire (though he is azospermic).
- The patient is chilly in thermal reaction.
- Intelligent, sensitive, irritable over daily circumstances.
- Cough, cold are aggravated by the least changes of weather.
- Rattling of chest.
- Dyspnoea with cough while lying down.

Constitution of the Patient

Lean, thin, emaciated (but he craves fat) fatty food and meat.

Personal History of Tuberculosis

At the age of 35 years old, this was treated by ATD (Anti Tubercular Drug).

Miasmatic Background

Predominantly psora mixed with syphilis.

Appropriate evaluation of symptoms is done on the basis of Kent's Philosophy.

Repertorisation had been done by consulting Kent's Repertory (Repertory of the Homoeopathic MateriaMedica).

Rubric chosen from the repertory are as follows

Rubric	Chapter
• Cosmopolitan (see travel)	Mind
• Fear of Dog	Mind
• Sensitive – oversensitive; external impression toal	Mind
• Industrious	Mind
• Mood – Changeable variable	Mind
• Desire for smoked meat	Stomach
• Desire for fat	Stomach
• Desire for ice creams	Stomach
• Desire for salty thing	Stomach
• Cold tendency to take	Generalities
• Heat, vital, lack of	Generalities
• Sexual passion increased	Genital
• Cough, weather change of	Cough
• Rattling	Respiration
• Respiration difficult lying while	Respiration

After critical analysis of the repertorial result and consultation with the source book of MateriaMedica we prescribed Tuberculinum, O/1, 14 doses in 4 ounce of Distilled Water for consecutive days , Considering the constitution of the patient, personal history of TB, after matching with the miasmatic as well as disease pathology.

KS scoring scale has been created for clinical evaluation (Table 1)

Ks scoring scale for clinical evaluation

Table 1

Dyspnoea	No dyspnoea 0	Severe exertion 1	Moderate exertion 2	Mild exertion 3	Rest 4
Cough	No Cough 0	Occasional paroxysm two to three /day 1	Few paroxysm 10-20/ day 2	Many paroxysm 20-30 /day 3	Constant Cough 4
Rattling or wheezing of the chest	No rattling 0	Intermittent 1	During day 2	During night 3	Always 4
Sputum Production	No Sputum 0	Thin sputum 1	Thick sputum 2	Stringy and Colourful 3	Mixed with blood 4
Pain in maxillary sinus	No pain 0	Mild pain 1	Moderate pain 2	Severe pain with nasal block 3	Severe pain with nasal block &swelling of the sinus 4
Sneezing and discharge per nose	Nil 0	Occasional attack (1-2 times) month 1	Infrequent attack (1-2 times in a week) 2	Frequent attack (10 -20 times in a week) 3	Regular attack 4

Interpretation Severe KS: 20-24, Moderate KS: 10-19, Mild KS :05-9

Table 2: Result of the case study

Date of Visit of the patient in OPD	Clinical Condition	Medicine prescribed or advice	Results
4.10.10	Dyspnoea=4,cough=4,Rattling of chest=4,Sputum production=3,pain in maxillary sinus=3,sneezing and discharge per nose=4	Tuberculinum O/1 (14 Doses in 4 Oz of aqua dist. and advised to come after 2 weeks. Advice : Spirometry for lung function	-
10.10.10	Dyspnoea=3 , cough=2 de, no rattling=0 sputum production=1,pain in maxillary sinus=2,sneezing and discharge per nose=2,	Placebo was prescribed	Clinically improved, no use of antibiotics and inhaler but spirometry shows severe obstructive pulmonary disease with no significant reversibility FEV_1 : FVC =48.57
01.11.10	Dyspnoea=2 , cough=2,Rattling=0, sputum production=1,pain in maxillary sinus=1,sneezing and discharge per nose=1,	Placebo was prescribed	Improved clinically
22.11.10	Dyspnoea=2 , cough=1 de, no rattling=0 sputum production=1,pain in maxillary sinus=1,sneezing and discharge per nose=1,no further improvement.	Tuberculinum O/2 (14 doses in 4 Oz of aqua dist)	Clinical improvement static
27.12.10	Dyspnoea=2 , cough=1 de, no rattling=1 sputum production=1,pain in maxillary sinus=1,sneezing and discharge per nose=1,	Placebo was prescribed	Clinically improvement persists
31.01.11	Dyspnoea=1 , cough=1 de, no rattling=1 sputum production=1,pain in maxillary sinus=2,sneezing and discharge per nose=1,	Placebo was prescribed	Do

07.03.11	No use of antibiotics till date, no use of inhaler, Dyspnoea =1,cough=1,rattling=1,sputurm production=1,pain in maxillary sinus=1,sneezing and discharge per nose=1,	Placebo was prescribed	Do
06.05.11	patient feels better No use of antibiotics till date, no use of inhaler, Dyspnoea =1,cough=0,rattling=0,sputurm production=0,pain in maxillary sinus=1,sneezing and discharge per nose=1,	Spirometry done to assess improvement	FEV_1 : FVC =64.78 & reversible in nature
17.06.11	patient feels better No use of antibiotics till date, no use of inhaler, Dyspnoea =1,cough=1,rattling=0,sputurm production=1,pain in maxillary sinus=1,sneezing and discharge per nose=1,	No new attack of lung infection	Clinical improvement progressive. No use of antibiotics and inhaler

Final result from Table 2:

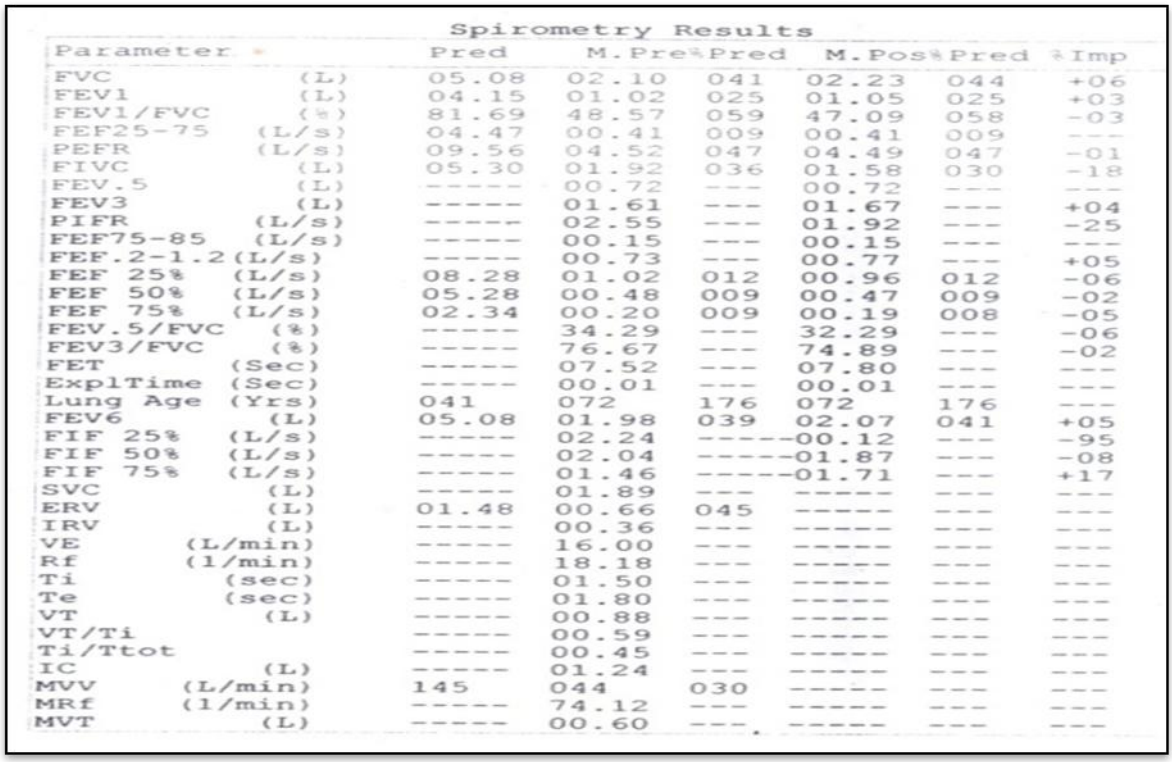
Prompt detection and treatment of PCD (Primary Ciliary Dyskinesia) can present its various complications (Bush *et al.,* 2007).

Pre treatment clinical KS scoring was = 22 that means severe ks.
Post treatment KS scoring is= 05 that means mild KS..

Homoeopathic medicine Tuberculinum which is nosode in origin is capable enough to alleviate the symptoms related to Kartagener Syndrome. This result shows the symptoms of KS patient are ameliorated clinically.

Spirometric assessment are used usually for corroborative or research purpose (Bush *et al.,* 2007). Spirometric investigation (pulmonary function test) was used as pre and post monitoring tool as a disease modality indicator. This study shows a significant change in pre and post spirometric assessment.

Before TreatmentFEV_1: FVC = 48.6 and show severe obstructive defect with no significant reversibility of lung.

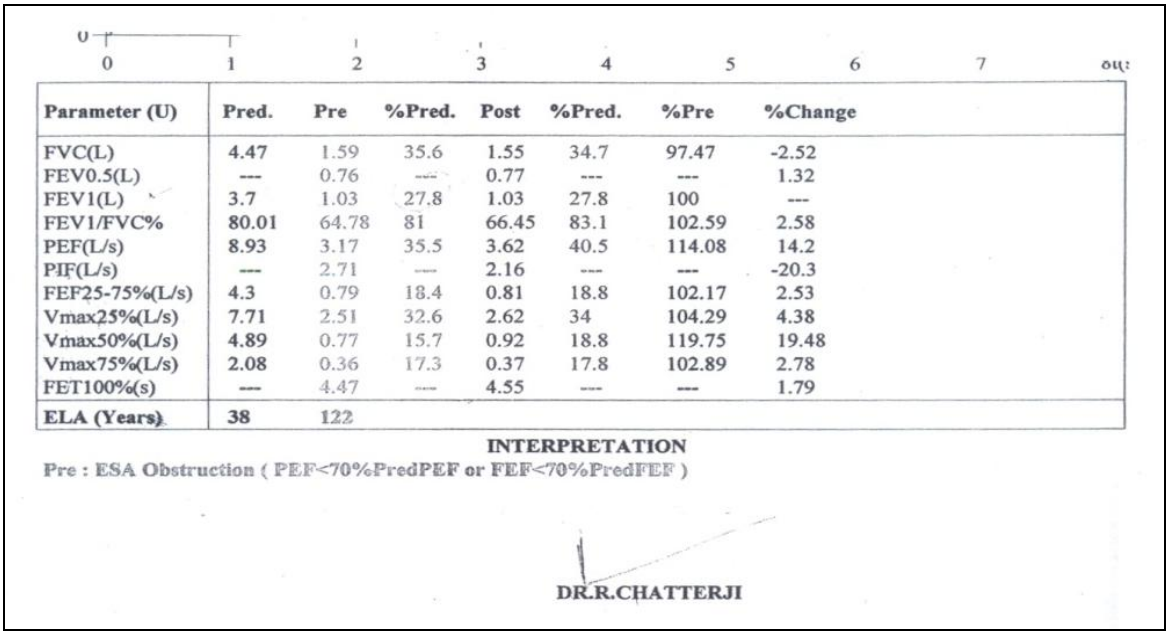


Spirometry Results

Parameter		Pred	M.Pre	%Pred	M.Pos	%Pred	%Imp
FVC	(L)	05.08	02.10	041	02.23	044	+06
FEV1	(L)	04.15	01.02	025	01.05	025	+03
FEV1/FVC	(%)	81.69	48.57	059	47.09	058	-03
FEF25-75	(L/s)	04.47	00.41	009	00.41	009	---
PEFR	(L/s)	09.56	04.52	047	04.49	047	-01
FIVC	(L)	05.30	01.92	036	01.58	030	-18
FEV.5	(L)	-----	00.72	---	00.72	---	---
FEV3	(L)	-----	01.61	---	01.67	---	+04
PIFR	(L/s)	-----	02.55	---	01.92	---	-25
FEF75-85	(L/s)	-----	00.15	---	00.15	---	---
FEF.2-1.2	(L/s)	-----	00.73	---	00.77	---	+05
FEF 25%	(L/s)	08.28	01.02	012	00.96	012	-06
FEF 50%	(L/s)	05.28	00.48	009	00.47	009	-02
FEF 75%	(L/s)	02.34	00.20	009	00.19	008	-05
FEV.5/FVC	(%)	-----	34.29	---	32.29	---	-06
FEV3/FVC	(%)	-----	76.67	---	74.89	---	-02
FET	(Sec)	-----	07.52	---	07.80	---	---
ExplTime	(Sec)	-----	00.01	---	00.01	---	---
Lung Age	(Yrs)	041	072	176	072	176	---
FEV6	(L)	05.08	01.98	039	02.07	041	+05
FIF 25%	(L/s)	-----	02.24	-----	00.12	---	-95
FIF 50%	(L/s)	-----	02.04	-----	01.87	---	-08
FIF 75%	(L/s)	-----	01.46	-----	01.71	---	+17
SVC	(L)	-----	01.89	---	-----	---	---
ERV	(L)	01.48	00.66	045	-----	---	---
IRV	(L)	-----	00.36	---	-----	---	---
VE	(L/min)	-----	16.00	---	-----	---	---
Rf	(1/min)	-----	18.18	---	-----	---	---
Ti	(sec)	-----	01.50	---	-----	---	---
Te	(sec)	-----	01.80	---	-----	---	---
VT	(L)	-----	00.88	---	-----	---	---
VT/Ti		-----	00.59	---	-----	---	---
Ti/Ttot		-----	00.45	---	-----	---	---
IC	(L)	-----	01.24	---	-----	---	---
MVV	(L/min)	145	044	030	-----	---	---
MRf	(1/min)	-----	74.12	---	-----	---	---
MVT	(L)	-----	00.60	---	-----	---	---

Pre-treatment spirometry: FEV1/FVC 48.57

After Treatment FEV_1: FVC = 64.78 and show obstructive defect with reversibility of lung.



0 1 2 3 4 5 6 7

Parameter (U)	Pred.	Pre	%Pred.	Post	%Pred.	%Pre	%Change
FVC(L)	4.47	1.59	35.6	1.55	34.7	97.47	-2.52
FEV0.5(L)	---	0.76	---	0.77	---	---	1.32
FEV1(L)	3.7	1.03	27.8	1.03	27.8	100	---
FEV1/FVC%	80.01	64.78	81	66.45	83.1	102.59	2.58
PEF(L/s)	8.93	3.17	35.5	3.62	40.5	114.08	14.2
PIF(L/s)	---	2.71	---	2.16	---	---	-20.3
FEF25-75%(L/s)	4.3	0.79	18.4	0.81	18.8	102.17	2.53
Vmax25%(L/s)	7.71	2.51	32.6	2.62	34	104.29	4.38
Vmax50%(L/s)	4.89	0.77	15.7	0.92	18.8	119.75	19.48
Vmax75%(L/s)	2.08	0.36	17.3	0.37	17.8	102.89	2.78
FET100%(s)	---	4.47	---	4.55	---	---	1.79
ELA (Years)	38	122					

INTERPRETATION

Pre : ESA Obstruction (PEF<70%PredPEF or FEF<70%PredFEF)

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Post-treatment spirometry FEV1/FVC 64.78

LIMITATIONS OF THIS STUDY

- This case study was greatly limited by availability of the clinical cases.
- It is limited to perform invasive diagnostic test like saccharine test, exhaled NO, ciliary beat frequency, gene testing and electron microscopy.
- It is a single study would have benefitted if more cases were added to the study the spectrum or presentation of KS and effectiveness of homoeopathic aid on KS.

DISCUSSION

KS, a rare autosomal genetic disorder could be treated by homoeopathic aid effectively. This case study shows efficacy of homoeopathic medicine, viz., Tuberculinum in 50 millisemal scale which contain Nano particle of the tubercular organism initiate a good response to ameliorate the symptoms in comparison to antibiotics of different generation and inhalation of steroid which in turn culminate an iatrogenic disease and drug resistance to the patient. In this context WHO in this year raised their voice against microbial resistance they make themes of World Health Day 2011 as "Antimicrobial – resistance no action today, no cure tomorrow".

Existing studies are done by different researchers of modern medicine, in Lancet Journal few cases (about 9 cases) are published, last case published in 2009 (VinayKapur, SandeepChowhan, Sanjay D. Cruz, Prof. AtulSachdevet al.).

In BMJ (British Medical Journal) there are some few case studies are seen and in the Journal 'Nature' no such studies are found.

Thorough scrutiny of different homoeopathic periodical journal and webnet site, no case study relating with KS is found till date.

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