Interstitial Lung Disease – An uncommon variant

Dr Sakshi Dubey
Department of Respiratory Medicine

36y/M, blacksmith by profession , no comorbidities

Onset of symptoms – March 2019

1. Breathlessness → MMRC grade 1, wheeze +

2. Cough → dry, on and off

No history of chest pain, palpitations, PND, orthopnea , hemoptysis, weight Loss, fever , loss of appetite

Clinical course

In August 2019, he was worked up at a private hospital for the above symptoms..

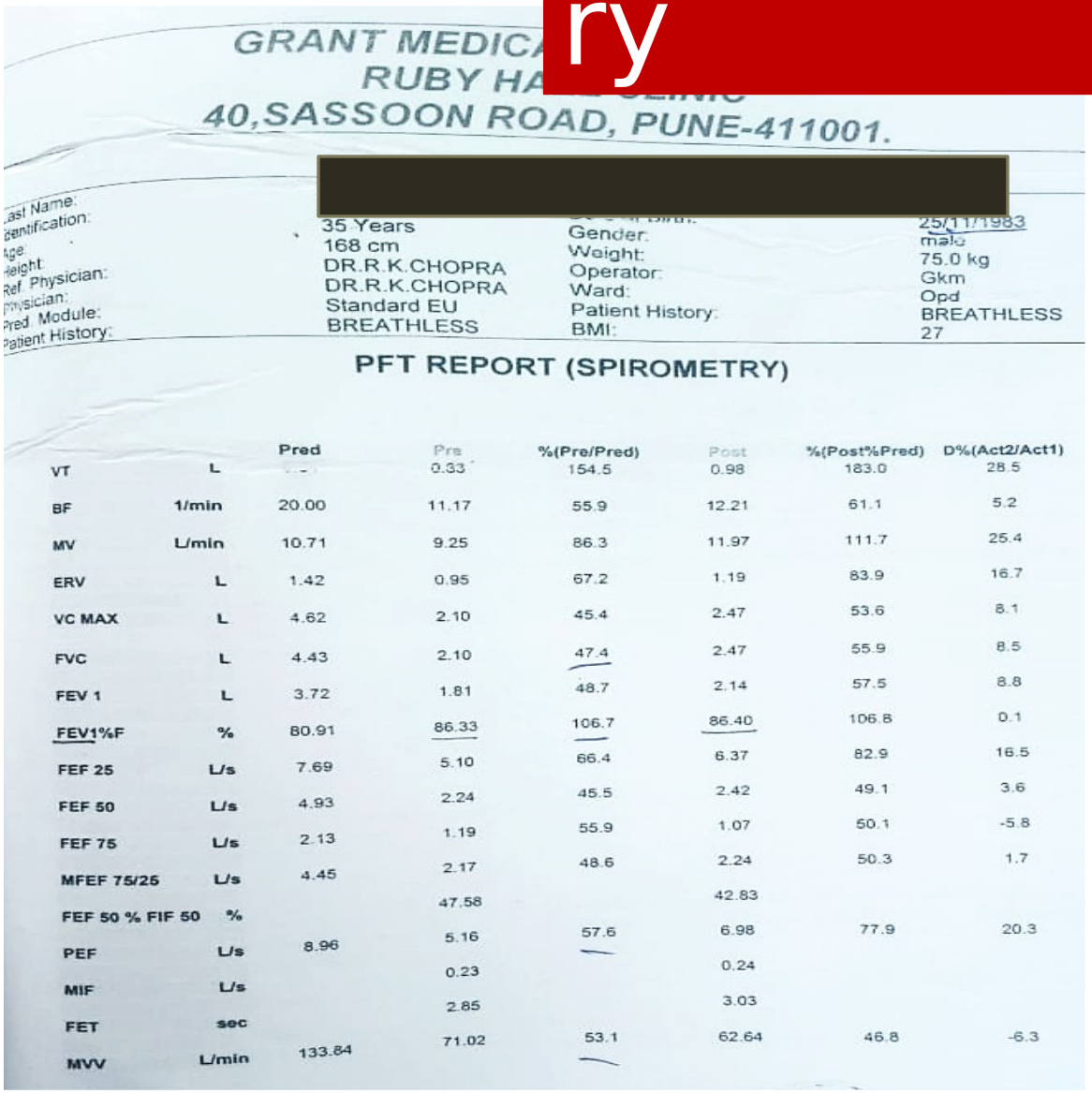
Hematology - within normal limits

Biochemistry - within normal limits

Chest Radiograph – **Diffuse bilateral reticulonodular pattern**

ECG - normal 2D ECHO - normal

Spirometry



GRANT MEDICA
RUBY HA
40,SASSOON ROAD, PUNE-411001.

[redacted]

Last Name:				
Identification:				
Age:	35 Years	Gender:		25/11/1983
Height:	168 cm	Weight:		male
Ref. Physician:	DR.R.K.CHOPRA	Operator:		75.0 kg
Physician:	DR.R.K.CHOPRA	Ward:		Gkm
Pred. Module:	Standard EU	Patient History:		Opd
Patient History:	BREATHLESS	BMI:		BREATHLESS
				27

PFT REPORT (SPIROMETRY)

		Pred	Pre	%(Pre/Pred)	Post	%(Post%Pred)	D%(Act2/Act1)
VT	L		0.33	154.5	0.98	183.0	28.5
BF	1/min	20.00	11.17	55.9	12.21	61.1	5.2
MV	L/min	10.71	9.25	86.3	11.97	111.7	25.4
ERV	L	1.42	0.95	67.2	1.19	83.9	16.7
VC MAX	L	4.62	2.10	45.4	2.47	53.6	8.1
FVC	L	4.43	2.10	47.4	2.47	55.9	8.5
FEV 1	L	3.72	1.81	48.7	2.14	57.5	8.8
FEV1%F	%	80.91	86.33	106.7	86.40	106.8	0.1
FEF 25	L/s	7.69	5.10	66.4	6.37	82.9	16.5
FEF 50	L/s	4.93	2.24	45.5	2.42	49.1	3.6
FEF 75	L/s	2.13	1.19	55.9	1.07	50.1	-5.8
MFEF 75/25	L/s	4.45	2.17	48.6	2.24	50.3	1.7
FEF 50 % FIF 50	%		47.58		42.83		
PEF	L/s	8.96	5.16	57.6	6.98	77.9	20.3
MIF	L/s		0.23		0.24		
FET	sec		2.85		3.03		
MVV	L/min	133.84	71.02	53.1	62.64	46.8	-6.3

- FEV_1- 1.81 (48.7%).
- FEV_1/FVC- 86.3 .
- FVC-2.10 L(47.4%).
- ⬇
- Moderate restriction.

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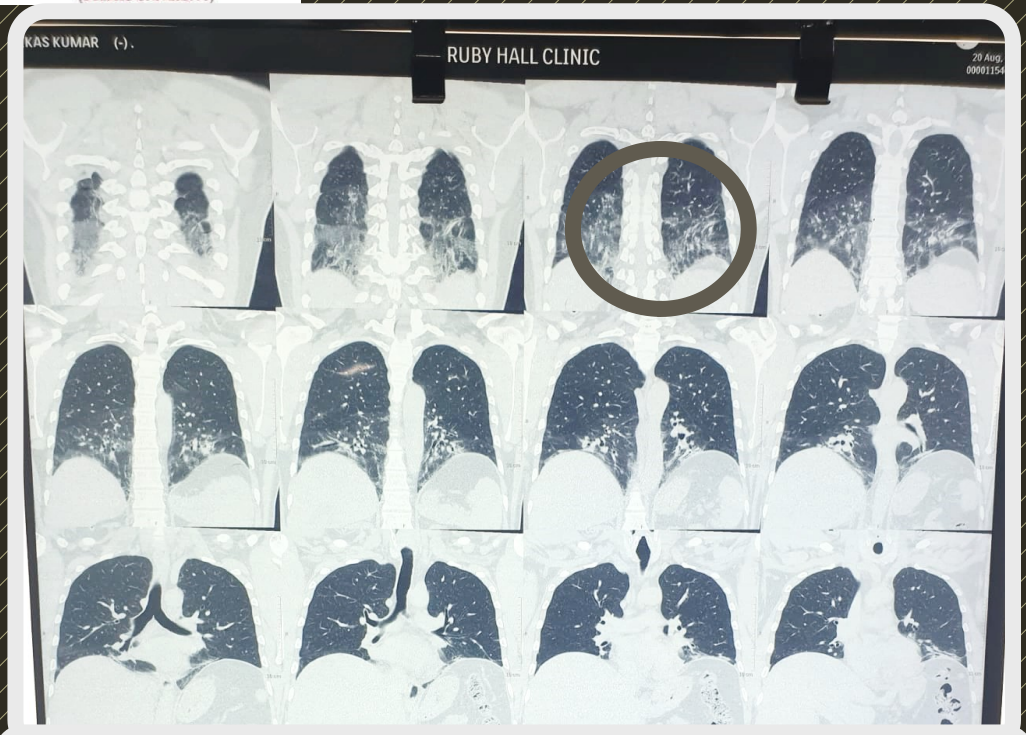

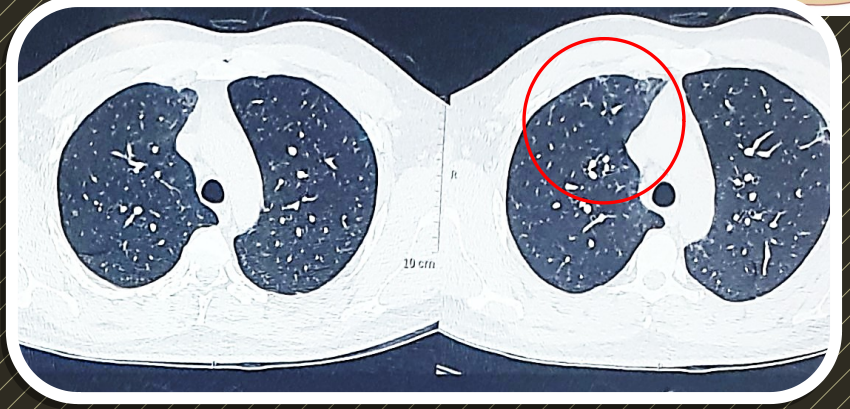

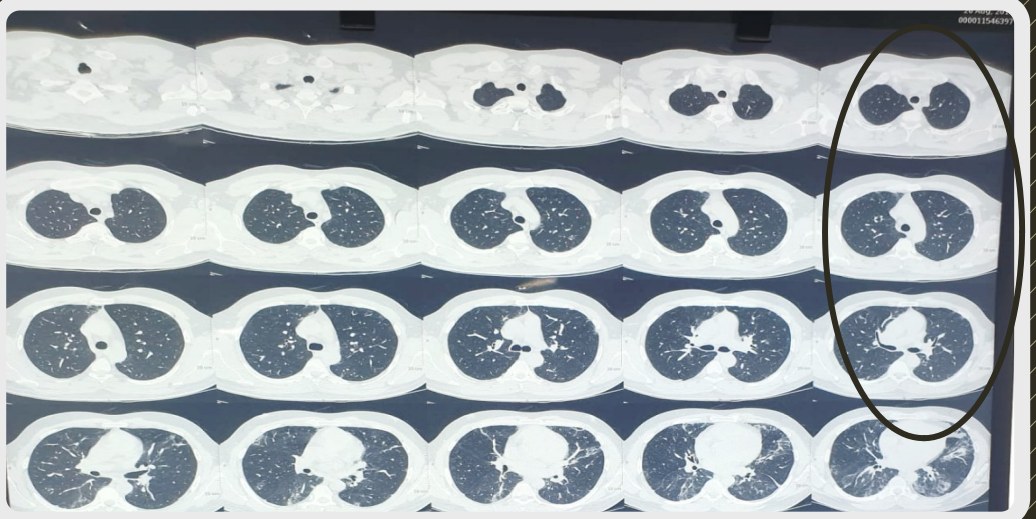

HRCT (thorax) suggestive of-

1.Subpleural areas of ground glass opacities in anterior segments of bilateral upper lobe, bilateral lower lobe, lingular lobe.

2.Fibrotic changes in lingular lobe

3.No evidence of honey combing, interlobular and intralobular interstitial thickening or traction bronchiectasis .

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Diagnosed as ILD ? NSIP (Non Specif ic Interstitial Pneumonia)

Started on Pirfenidone 200 mg TDS !!!!

Prednisolone 20 mg OD, nebulisation with budecort and asthalin

Continued treatment for 4 months but showed
no significant improvement

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Reported to our hospital in Nov 2019
with complaints of

Persistent Breathlessness and Cough

No history of chest pain, palpitation, PND, orthopnea , hemoptysis, weight Loss, fever , loss of appetite

Clinical Examination

General Examination - NAD

Vitals

- PR - 90bpm
- BP - 130/80 mmhg
- RR - 20/min
- SPO_2 - 98% on room air

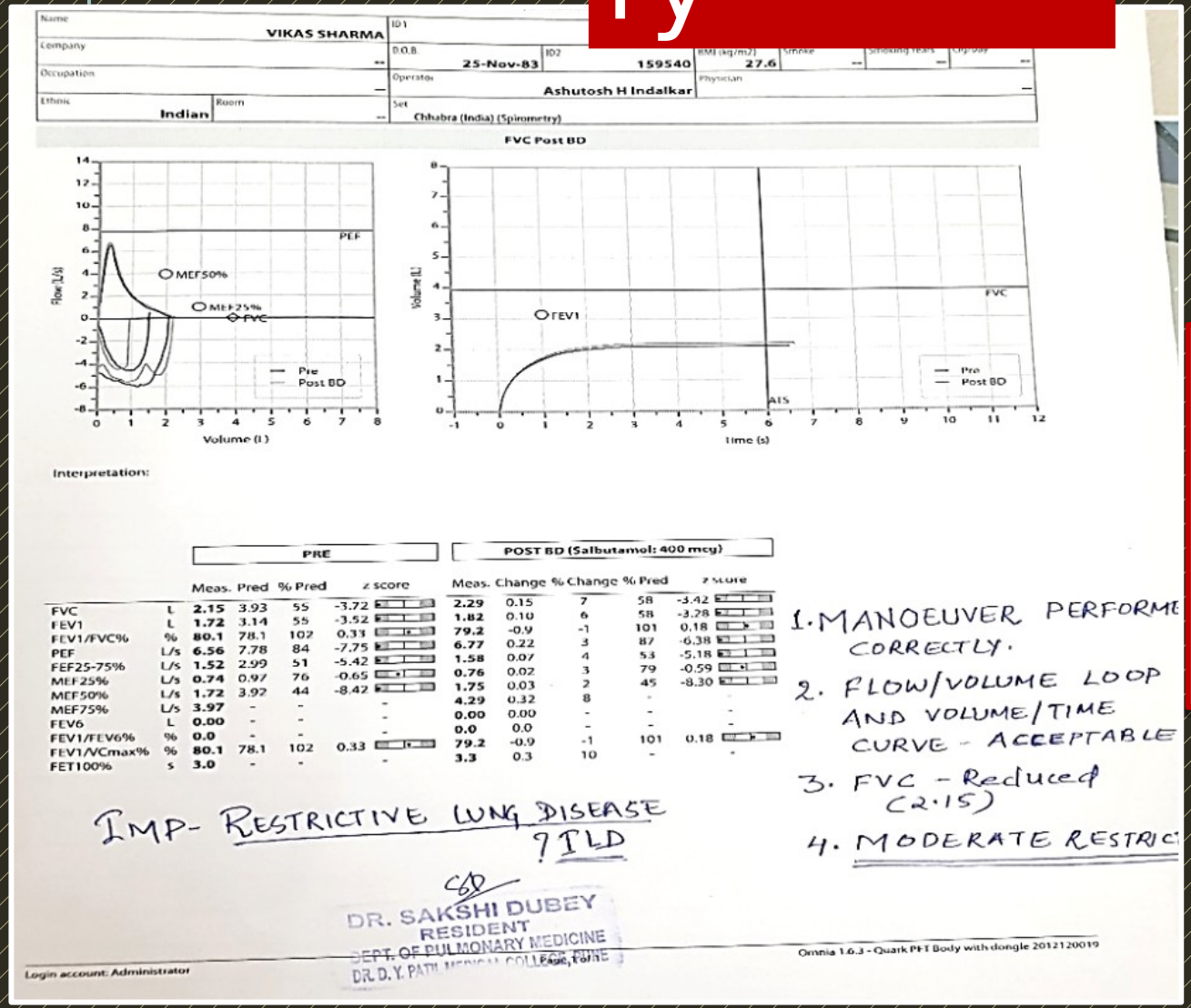
Respiratory System – Fine Late Inspiratory crackles in bilateral infrascapular area

Investigations

- ***Haematology*** Hb-15.70, TLC: 7,200,

  Platelets:2.33 lakhs
- ***Biochemistry*** (LFT's/RFT's) within normal limits
- ***RA*** factor Negative
- ***ANA*** Negative
- ***ECG*** Sinus rhythm
- [illegible] Showed 5% of Desaturation (98 to 93 percent)

Spirometry



Name: VIKAS SHARMA | ID1 | Company | D.O.B.: 25-Nov-83 | ID2: 159540 | BMI (kg/m2): 27.6 | Occupation | Operator: Ashutosh H Indalkar | Physician | Ethnic: Indian | Room | Set: Chhabra (India) (Spirometry)

FVC Post BD

Interpretation:

		PRE Meas.	Pred	% Pred	z score	POST BD (Salbutamol: 400 mcg) Meas.	Change	% Change	% Pred	z score
FVC	L	2.15	3.93	55	-3.72	2.29	0.15	7	58	-3.42
FEV1	L	1.72	3.14	55	-3.52	1.82	0.10	6	58	-3.28
FEV1/FVC%	%	80.1	78.1	102	0.33	79.2	-0.9	-1	101	0.18
PEF	L/s	6.56	7.78	84	-7.75	6.77	0.22	3	87	-6.38
FEF25-75%	L/s	1.52	2.99	51	-5.42	1.58	0.07	4	53	-5.18
MEF25%	L/s	0.74	0.97	76	-0.65	0.76	0.02	3	79	-0.59
MEF50%	L/s	1.72	3.92	44	-8.42	1.75	0.03	2	45	-8.30
MEF75%	L/s	3.97	-	-	-	4.29	0.32	8	-	-
FEV6	L	0.00	-	-	-	0.00	0.00	-	-	-
FEV1/FEV6%	%	0.0	-	-	-	0.0	0.0	-	-	-
FEV1/VCmax%	%	80.1	78.1	102	0.33	79.2	-0.9	-1	101	0.18
FET100%	s	3.0	-	-	-	3.3	0.3	10	-	-

IMP- RESTRICTIVE LUNG DISEASE
?ILD

1. MANOEUVER PERFORME CORRECTLY.
2. FLOW/VOLUME LOOP AND VOLUME/TIME CURVE - ACCEPTABLE
3. FVC - Reduced (2.15)
4. MODERATE RESTRIC

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- FEV_1-1.72(55%).
- FEV_1/FVC-78.1.
- FVC-2.15 (55%).
- Moderate restriction

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DLCO

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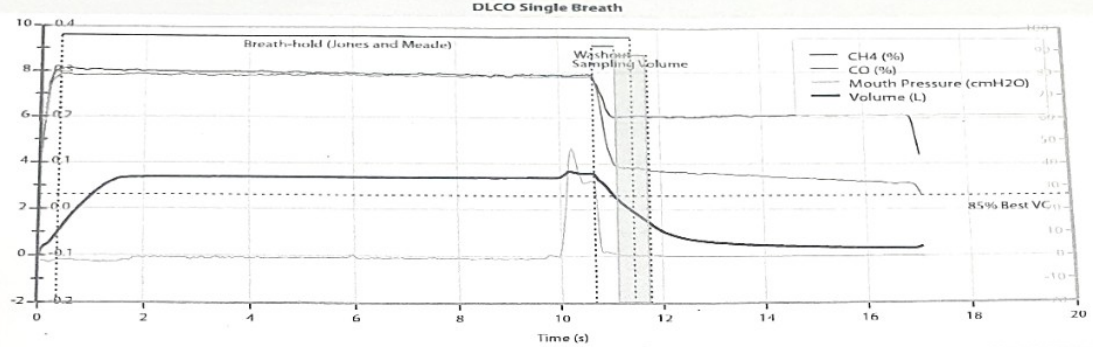
	VIKAS SHARMA	ID1 339973	Gender Male	Age 36	Weight (kg) 76.90	Height (cm) 167.0	
Company —		D.O.B. 01-May-83	ID2 —	BMI (kg/m2) 27.6	Smoke —	Smoking Years —	Cig/Day —
Occupation —		Operator Ashutosh H Indalkar		Physician —			
Ethnic Indian	Room —	Set ECCS extended (DLCO)					

DLCO Single Breath



DLCO Results

		Meas.	Normal Range	Pred	% Pred	z score
DLCO	mL/min/mmHg	**20.88**	23.36 - 37.24	30.30	69	-2.23
DLCO corr	mL/min/mmHg	**20.12**	23.36 - 37.24	30.30	66	-2.41
DLCO/VA	mL/min/mmHg/L	**4.52**	3.57 - 6.34	4.96	91	-0.52
VA	L	**4.46**	4.96 - 7.26	6.11	73	-2.37
TLC(DLCO)	L	**4.63**	5.11 - 7.41	6.26	74	-2.34
VC	L	**3.08**	3.55 - 5.06	4.31	72	-2.66
RV/TLC(DLCO)	%	**33.3**	19.0 - 37.0	28.0	119	0.97
RV(DLCO)	L	**1.54**	1.08 - 2.42	1.75	88	-0.51
Hb	g/dL	**16.0**	---	-	-	-

DLCO Trials Results

(*) Best Trial		Trial 1 11:19 AM (*)
DLCO	mL/min/mmHg	20.88
DLCO corr	mL/min/mmHg	20.12
DLCO/VA	mL/min/mmHg/L	4.52
VA	L	4.46
TLC(DLCO)	L	4.63
IV(DLCO)	L	3.35
DLCO 3eq	mL/min/mmHg	25.27
FiCO	%	0.296
FiCH4	%	0.306
FiO2	%	21.00
FaCO	%	0.091
FaCH4	%	0.204
Sample Vol	mL	1053
Washout Vol	mL	1067
Breath Hold Time	s	11.08
Hb	g/dL	16.0

1. MANOEUVER PERFORMED CORRECTLY
2. REDUCED DLCO
3. RESTRICTIVE LUNG DISEASE
   ILD

Imp -

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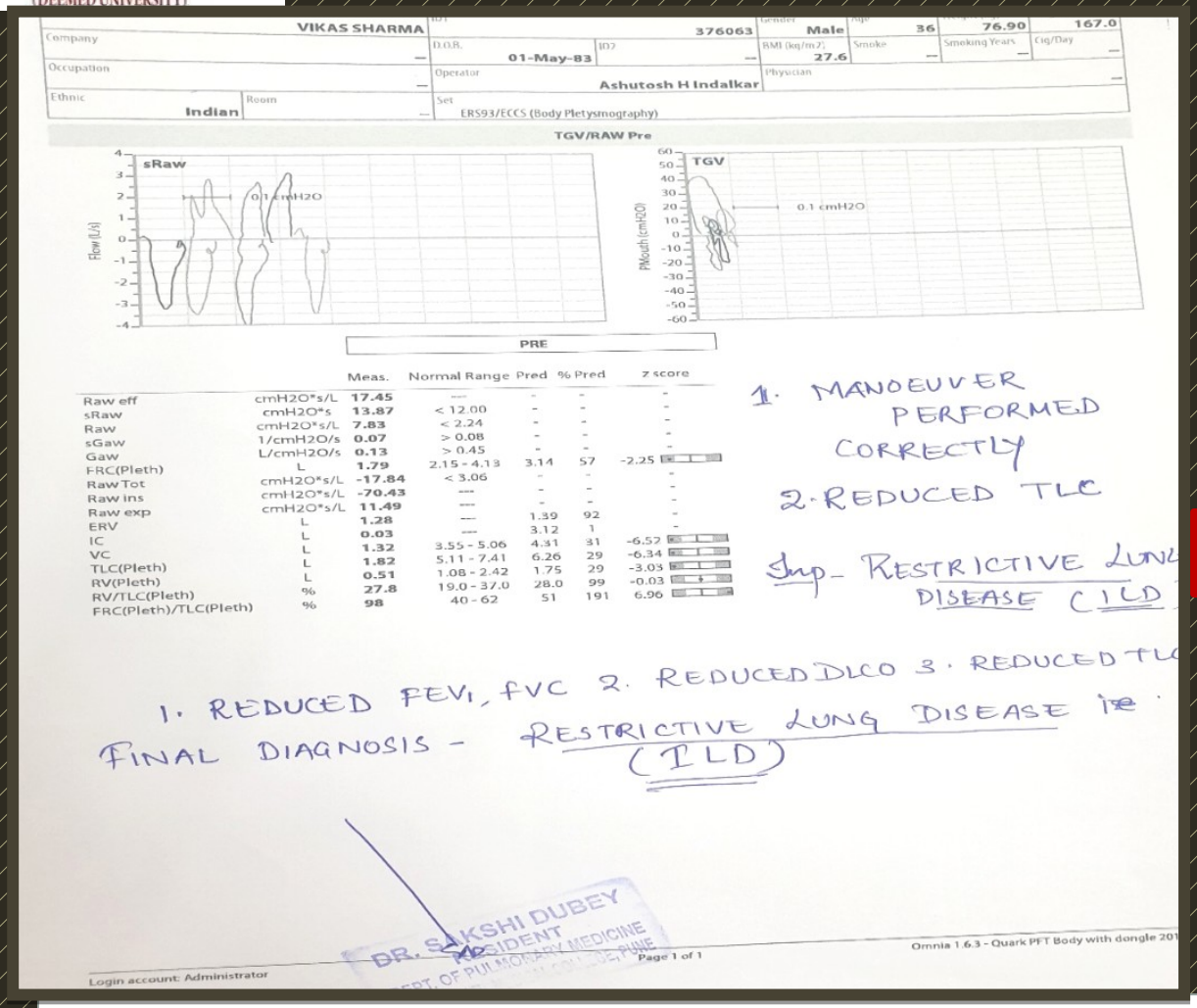
DLCO -20.12 (66 %)

Lung volume



VIKAS SHARMA | ID: 376063 | Gender: Male | Age: 36 | 76.90 | 167.0
Company: — | D.O.B.: 01-May-83 | ID2: — | BMI (kg/m2): 27.6 | Smoke: — | Smoking Years: — | Cig/Day: —
Occupation: — | Operator: Ashutosh H Indalkar | Physician: —
Ethnic: Indian | Room: — | Set: ERS93/ECCS (Body Pletysmography)

TGV/RAW Pre

PRE

		Meas.	Normal Range	Pred	% Pred	z score
Raw eff	cmH2O*s/L	17.45	---	-	-	-
sRaw	cmH2O*s	13.87	< 12.00	-	-	-
Raw	cmH2O*s/L	7.83	< 2.24	-	-	-
1/cmH2O/s		0.07	> 0.08	-	-	-
sGaw		0.13	> 0.45	-	-	-
Gaw	L/cmH2O/s	1.79	2.15 - 4.13	3.14	57	-2.25
FRC(Pleth)	L	-17.84	< 3.06	-	-	-
Raw Tot	cmH2O*s/L	-70.43	---	-	-	-
Raw ins	cmH2O*s/L	11.49	---	-	-	-
Raw exp	cmH2O*s/L	1.28	---	1.39	92	-
ERV	L	0.03	---	3.12	1	-
IC	L	1.32	3.55 - 5.06	4.31	31	-6.52
VC	L	1.82	5.11 - 7.41	6.26	29	-6.34
TLC(Pleth)	L	0.51	1.08 - 2.42	1.75	29	-3.03
RV(Pleth)	%	27.8	19.0 - 37.0	28.0	99	-0.03
RV/TLC(Pleth)	%	98	40 - 62	51	191	6.96
FRC(Pleth)/TLC(Pleth)						

1. MANOEUVER PERFORMED CORRECTLY
2. REDUCED TLC

Imp- RESTRICTIVE LUNG DISEASE (ILD)

1. REDUCED FEV1, FVC 2. REDUCED DLCO 3. REDUCED TLC

FINAL DIAGNOSIS - RESTRICTIVE LUNG DISEASE (ILD)

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TLC -1.82

1.Reduced FVC 2. Reduced DLCO 3. Reduced TLC.

FINAL DIAGNOSIS ON PFT- RESTRICTIVE LUNG DISEASE (ILD).

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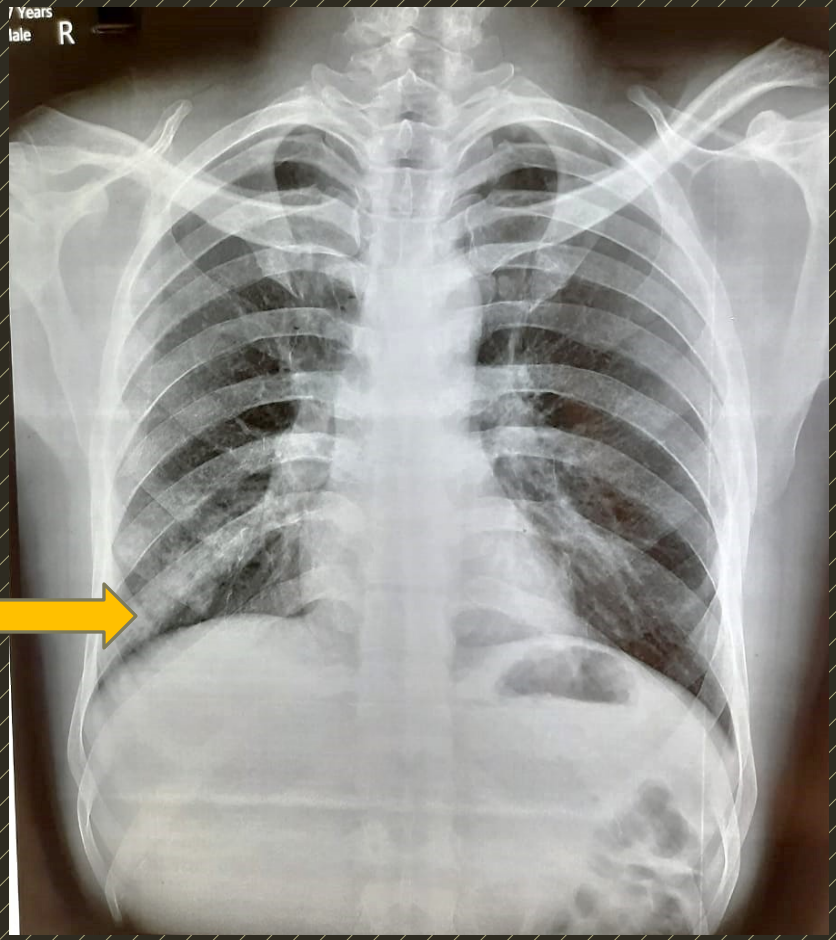
Chest radiograph- Bilateral ,lower zone reticulo-nodular opacities present.



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HRCT in Oct 2019

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Fiberoptic Bronchoscopy with Trans Bronchial Lung Biopsy done (TBLB).

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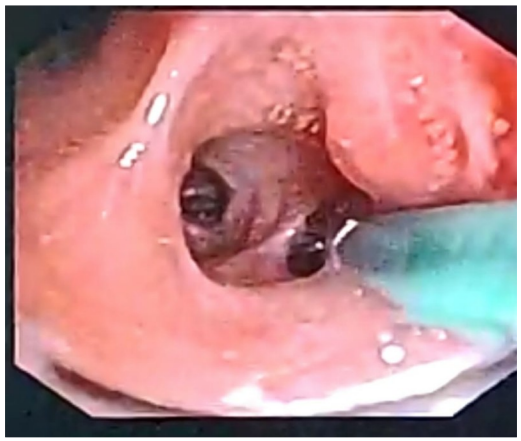
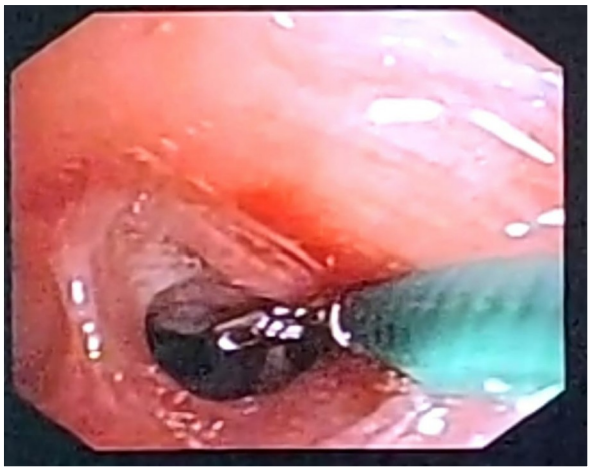
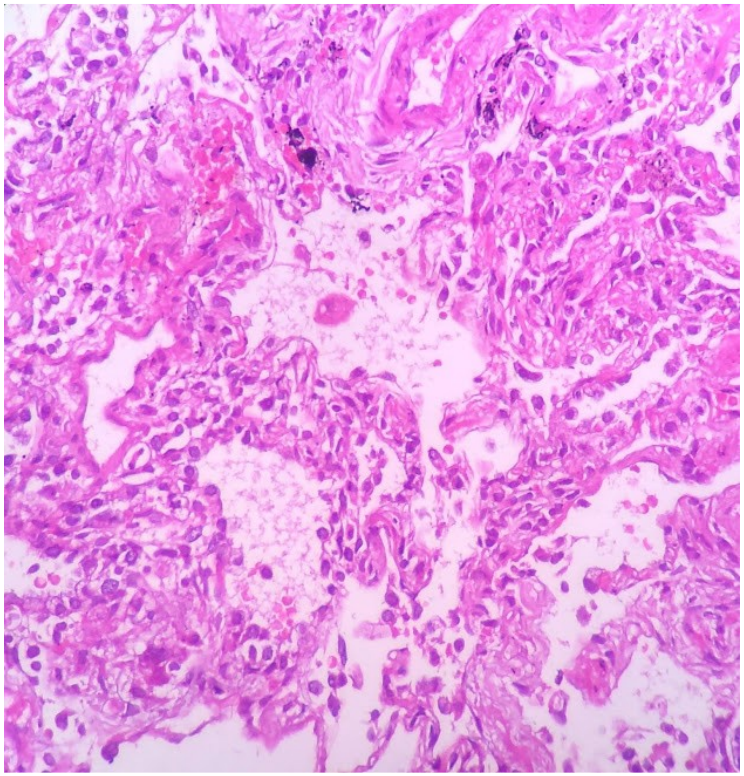
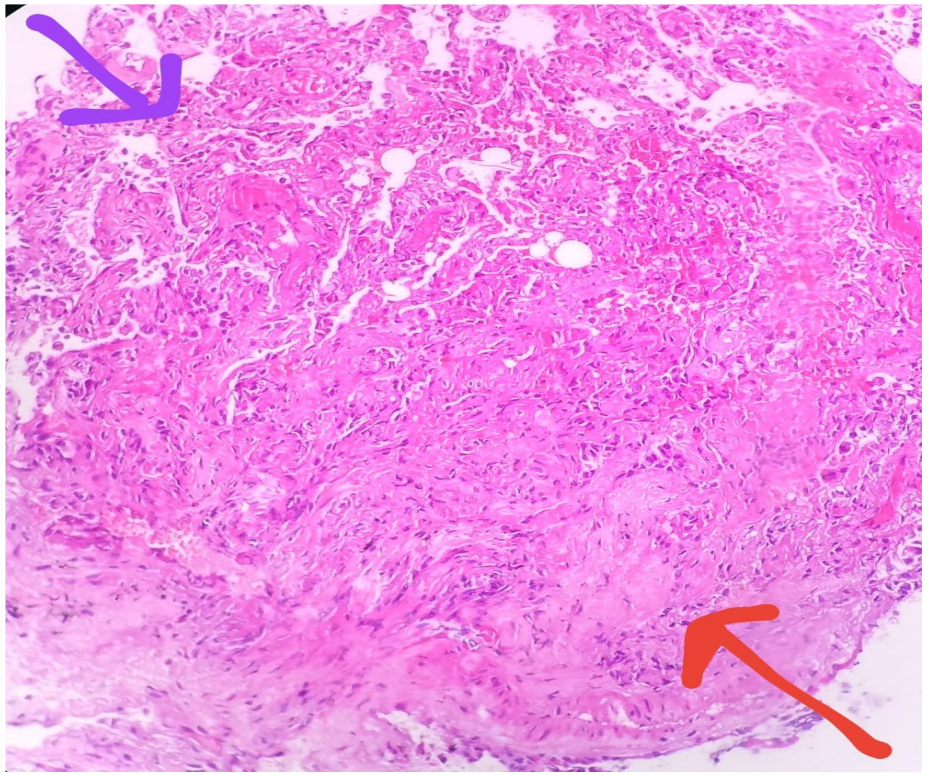




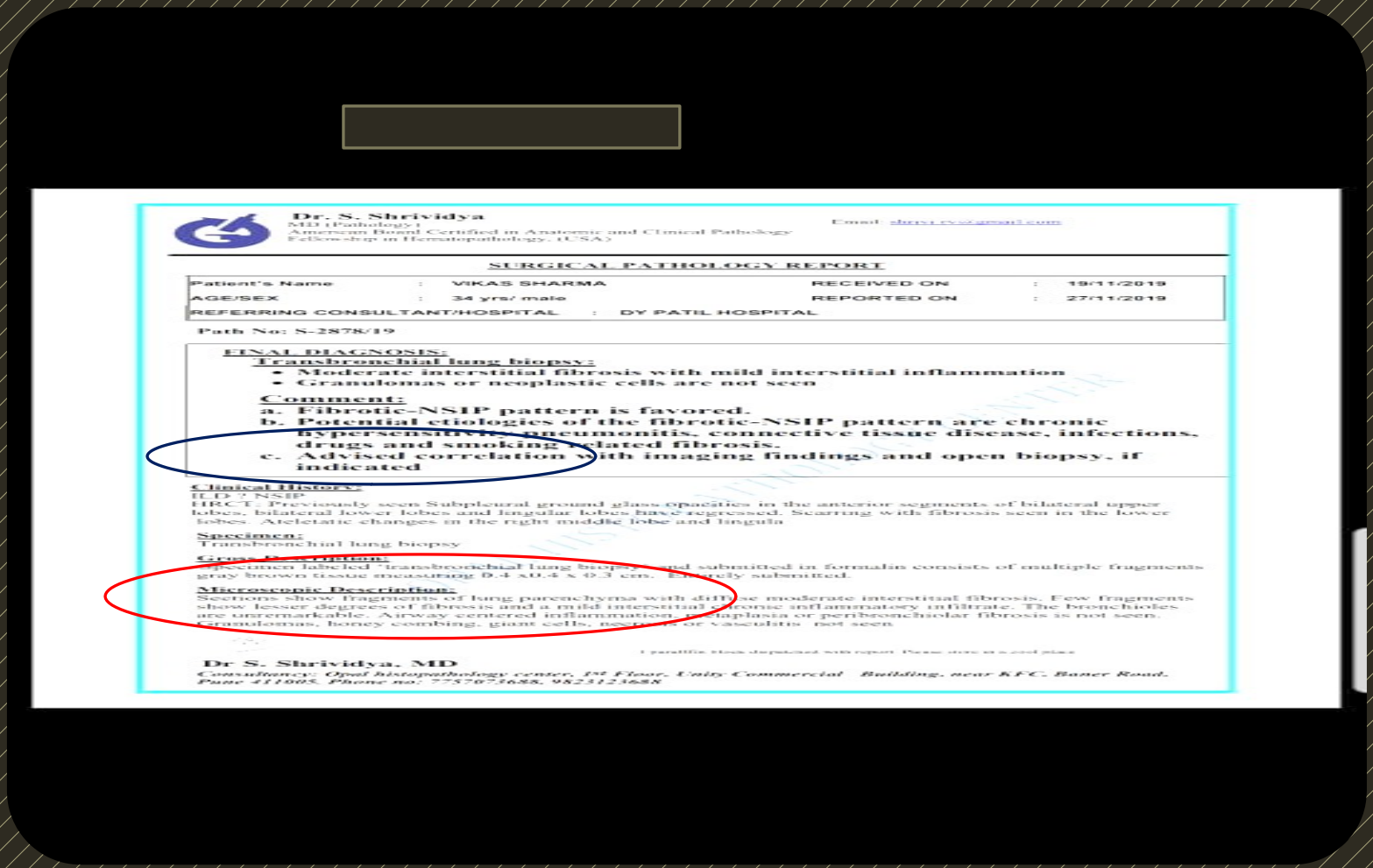
Histopathological Examination





1.Edematous, thickened alveolar septa prominently and uniformly infiltrated by chronic inflammatory cells and areas of interstitial fibrosis.
2. The alveolar space contain ocassional macrophage.
3. No granuloma or atypical cells are seen.

Trans Bronchial Lung Biopsy from Right lower lobe



Dr. S. Shrividya
MD (Pathology)
American Board Certified in Anatomic and Clinical Pathology
Fellowship in Hematopathology, (USA)

SURGICAL PATHOLOGY REPORT

Patient's Name	: VIKAS SHARMA	RECEIVED ON	: 19/11/2019
AGE/SEX	: 34 yrs/ male	REPORTED ON	: 27/11/2019
REFERRING CONSULTANT/HOSPITAL	: DY PATIL HOSPITAL		

Path No: S-2878/19

FINAL DIAGNOSIS:
Transbronchial lung biopsy:
- Moderate interstitial fibrosis with mild interstitial inflammation
- Granulomas or neoplastic cells are not seen

Comment:
a. Fibrotic–NSIP pattern is favored.
b. Potential etiologies of the fibrotic–NSIP pattern are chronic hypersensitivity pneumonitis, connective tissue disease, infections, drugs and smoking related fibrosis.
c. Advised correlation with imaging findings and open biopsy, if indicated

Clinical History:
ILD ? NSIP
HRCT: Previously seen Subpleural ground glass opacities in the anterior segments of bilateral upper lobes, bilateral lower lobes and lingular lobes have regressed. Scarring with fibrosis seen in the lower lobes. Atelectatic changes in the right middle lobe and lingula

Specimen:
Transbronchial lung biopsy

Gross Description:
Specimen labeled "transbronchial lung biopsy" and submitted in formalin consists of multiple fragments gray brown tissue measuring 0.4 x 0.4 x 0.3 cm. Entirely submitted.

Microscopic Description:
Sections show fragments of lung parenchyma with diffuse moderate interstitial fibrosis. Few fragments show lesser degrees of fibrosis and a mild interstitial chronic inflammatory infiltrate. The bronchioles are unremarkable. Airway centered inflammation, metaplasia or peribronchiolar fibrosis is not seen. Granulomas, honey combing, giant cells, necrosis or vasculitis not seen.

Dr S. Shrividya, MD
Consultancy: Opal histopathology center, 1st Floor, Unity Commercial Building, near KFC, Baner Road, Pune 411005. Phone no: 7757075688, 9823123688

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Diagnosis

NON SPECIFIC
INTERSTITIAL PNEUMONIA (FIBROTIC)

Management

- Pirfenidone was stopped !!!
- Started on Prednisolone 40 mg OD.
- Reviewed after 8 weeks.

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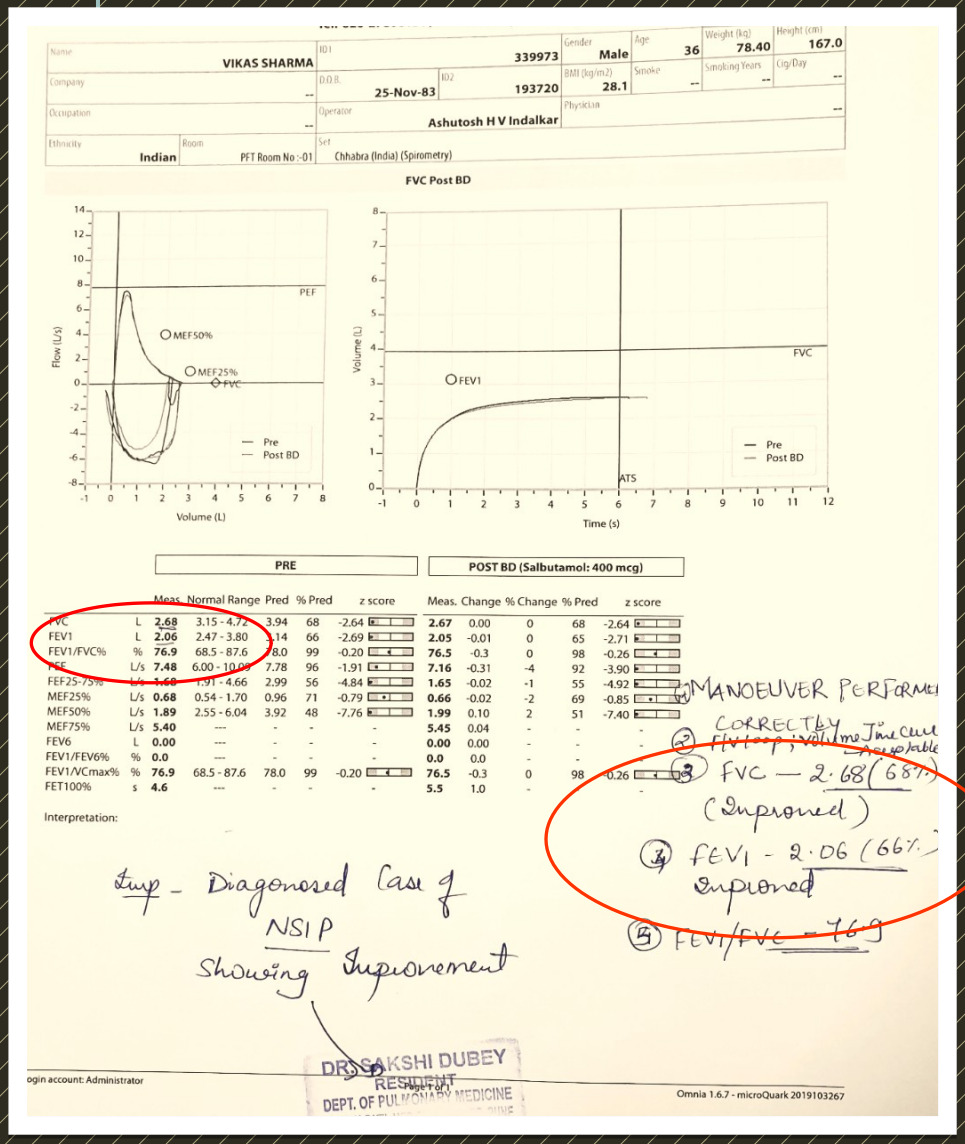
Follow up…2 months



Name	VIKAS SHARMA	ID1	339973	Gender	Male	Age	36
Company	--	D.O.B.	25-Nov-83	ID2	193720	BMI (kg/m2)	28.1
Occupation	--	Operator	Ashutosh H V Indalkar			Physician	--
Ethnicity	Indian	Room	PFT Room No :-01	Set	Chhabra (India) (Spirometry)		

Weight (kg): 78.40 | Height (cm): 167.0 | Smoke: -- | Smoking Years: -- | Cig/Day: --

FVC Post BD

PRE

		Meas.	Normal Range	Pred	% Pred	z score
FVC	L	2.68	3.15 - 4.72	3.94	68	-2.64
FEV1	L	2.06	2.47 - 3.80	3.14	66	-2.69
FEV1/FVC%	%	76.9	68.5 - 87.6	78.0	99	-0.20
PEF	L/s	7.48	6.00 - 10.09	7.78	96	-1.91
FEF25-75%	L/s	1.66	1.91 - 4.66	2.99	56	-4.84
MEF25%	L/s	0.68	0.54 - 1.70	0.96	71	-0.79
MEF50%	L/s	1.89	2.55 - 6.04	3.92	48	-7.76
MEF75%	L/s	5.40	---	-	-	-
FEV6	L	0.00	---	-	-	-
FEV1/FEV6%	%	0.0	---	-	-	-
FEV1/VCmax%	%	76.9	68.5 - 87.6	78.0	99	-0.20
FET100%	s	4.6	---	-	-	-

POST BD (Salbutamol: 400 mcg)

Meas.	Change	% Change	% Pred	z score
2.67	0.00	0	68	-2.64
2.05	-0.01	0	65	-2.71
76.5	-0.3	0	98	-0.26
7.16	-0.31	-4	92	-3.90
1.65	-0.02	-1	55	-4.92
0.66	-0.02	-2	69	-0.85
1.99	0.10	2	51	-7.40
5.45	0.04	-	-	-
0.00	0.00	-	-	-
0.0	0.0	-	-	-
76.5	-0.3	0	98	-0.26
5.5	1.0	-	-	-

Interpretation:

MANOEUVER PERFORMED CORRECTLY
FVC — 2.68 (68%) (Improved)
FEV1 - 2.06 (66%) Improved
FEV1/FVC - 76.9

Dup - Diagonosed Case of NSIP Showing Improvement

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- Symptomatic Improvement
- Marginal Improvement in FVC

- FEV_1-2.06(66%)
- FEV_1/FVC-76.9
- FVC-2.68 (68%)

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Discussion

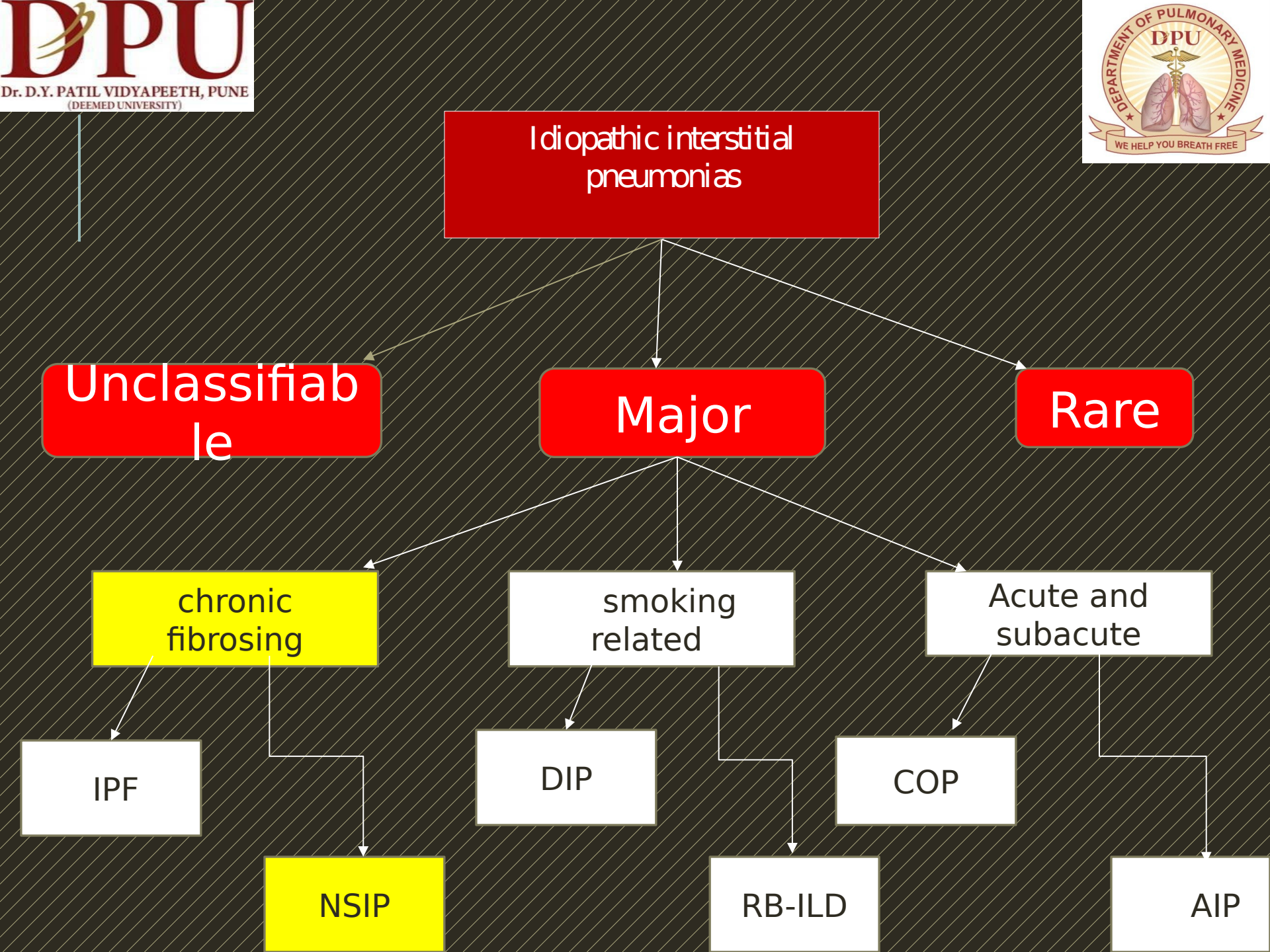
The term ILD refers to a heterogenous collection of more than one hundred disorders that tend to be grouped together because they share clinical, radiological, and pathological features.

These disorders are sometimes called DPLD, as interstitium is not the only the compartment involved.

Classification

Interstitial Lung Diseases

- Known cause or association (CTD, Occupation)
- Idiopathic Interstitial Pneumonias
- Granulomatous (Sarcoidosis, HP)
- other forms lymphangioleio -myomatosis, Histiocytosis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Idiopathic interstitial pneumonias
Unclassifiable
Major
Rare
chronic fibrosing
smoking related
Acute and subacute
IPF
NSIP
DIP
RB-ILD
COP
AIP

Clinical features

- Middle aged adults (20-40 years)
- Affects non smokers.
- Subacute onset of dyspnea and cough.
- Commonly associated with CTD except RA.
- Hypersensitivity Pneumonitis may also present with NSIP.

Investigations

PULMONARY FUNCTION TESTING

Restrictive ventilatory Defect characterised by

- ✓ Preserved FEV1/FVC
- ✓ Depressed

CHEST IMAGING

Peripheral, subpleural,basal symmetric ,ground glass opacities / reticular markings .

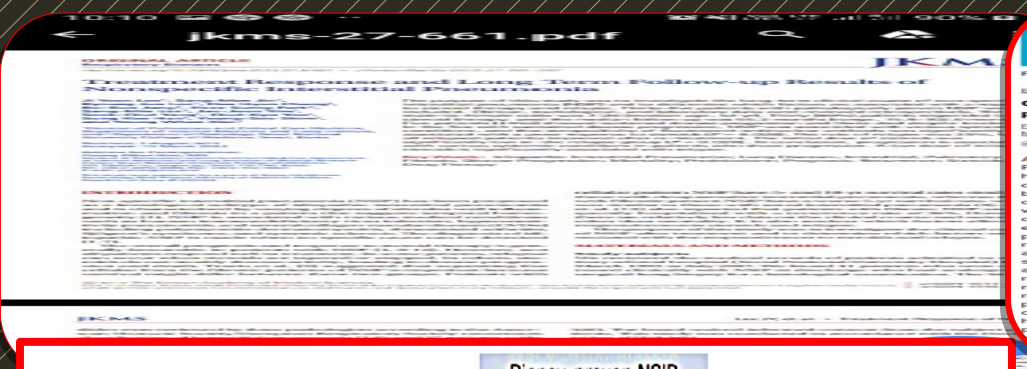
- Traction bronchiectasis.
- Very rare –microcystic honeycombing (fibrotic)

Pathological types

TYPES	PATHOLOGY
CELLULAR	DOMINATED BY ACTIVE INFLAMATION
FIBROTIC	DOMINATED BY ESTABLISHED FIBROSIS
MIXED	COMBINATION OF INFLAMMATION AND FIBROSIS BOTH.

Treatment

Corticosteroids



F-13
C-16

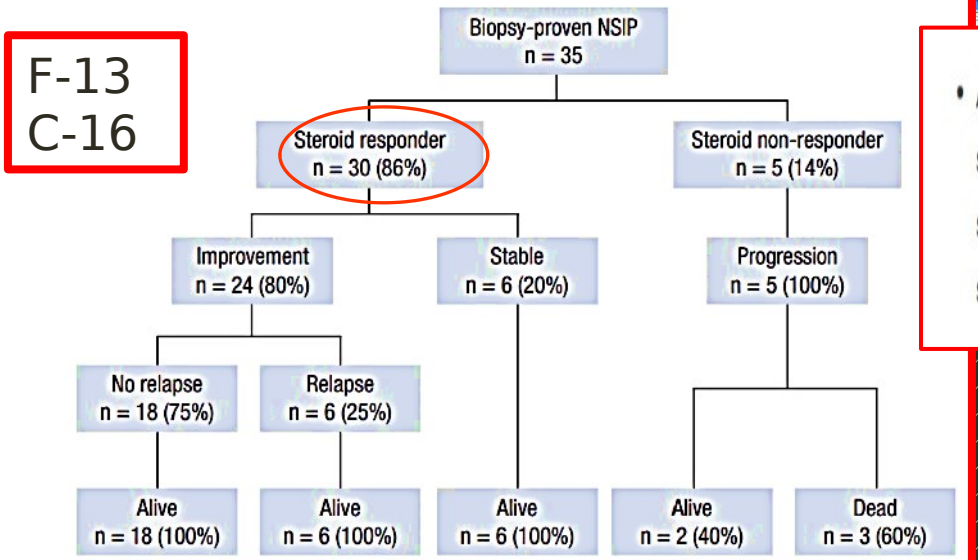


Table 2 Comparison between steroid responders and non-responders

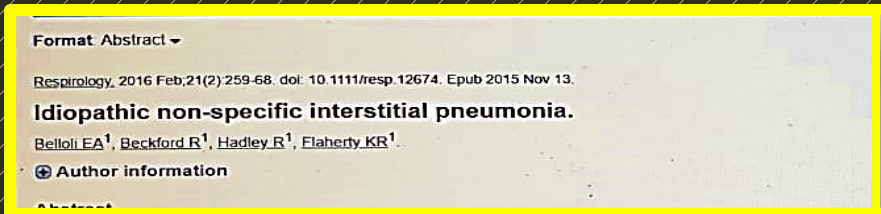
- Among a total of 47 patients from a number of smaller series (both idiopathic and secondary NSIP), treatment with glucocorticoids alone resulted in improvement in 35, stabilization in 6, and deterioration or death in 6 [5,8,10,11,14]. Despite an initial response, some patients subsequently experienced progressive worsening of lung function [11].

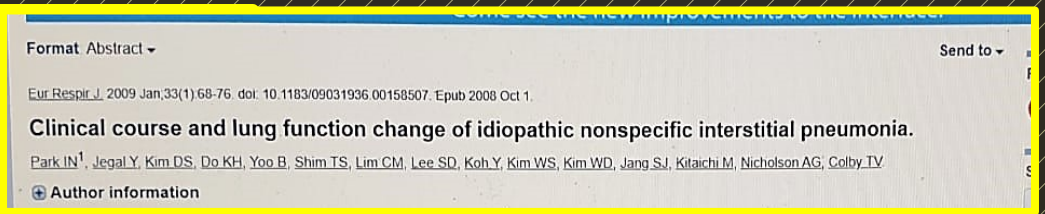
Recommended dose

To begin with, a dose of 0.5 to 1 mg/kg ideal body weight with maximum dose of 60mg/day for one month, followed by a tapering dose of 30 to 40 mg /day for 2 months.

If patient stabilizes with treatment , the dose is gradually tapered and discontinued after 6 to 9 months

Patient not responding to corticosteroid ,consider starting immunosuppressive agents .





Other Modalities

AZATHIOPRINE	**Fibrotic NSIP , not responding to steroids and NSIP associated with CTD shown better improvement with azathioprine when used along with steroids.** **Dose-25 to 50 mg/day.**
CYCLOPHOSPHAMIDE	**Best therapeutic evidence of cyclophosphamide was seen in ssc- ild .** **Dose- Montly intravenous dose**
MYCOPHENOLATE MOFETIL	**Used in ILD associated with scleroderma .** **Dose- 1.5 to 3 gm daily in 2 divided dose.**

Lung Transplant

Patient with severe NSIP that is progressive and disabling despite immunosuppressive therapy may be considered for lung transplant.

- ✓ Honey combing on HRCT.
- ✓ DLCO less than 35 % of predicted.
- ✓ 10 % or greater decrease in FVC or 15 % decrease in DLCO during 6 month follow up.

ROLE OF TBLB IN DIAGNOSIS OF ILD

TBLB is the procedure of choice when ILD is suspected, has a centrilobular distribution.

Sarcoidosis , Hypersensitivity pneumonitis , Lymphangitis Carcinomatosis , Eosinophilic

- The highest yield is in Sarcoidosis- around 71%

Studies suggest that in NSIP, TBLB is used when the radiological features are inconsistent with UIP/NSIP/Non responder.

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DEPARTMENT OF PATHOLOGY.
DEPARTMENT OF RADIOLOGY.

Thank