

SUPPLEMENTARY MATERIAL

Chart S1 - STANDARDIZED FORM- INTERSTITIAL LUNG DISEASE

Center _____ Initial evaluation date ___/___/___ No. _____
Gender Male ; Female Age: ___ yo. Smoker: No , Current , Past
Compromised Host: No Yes Disease (s) _____

Time history: ___ months

Cough: Absent Present

Dyspnea: Absent ; Great efforts , Moderate efforts , Small efforts , Rest , Impaired evaluation or mMRC _____

Family history of ILD: No , Yes

Connective tissue diseases: No Systemic sclerosis , Rheumatoid arthritis , Systemic lupus erythematosus , Mixed connective tissue disease , Sjogren's Syndrome , Dermatopolymyositis , Interstitial Pneumonia with Autoimmune Findings , Antisynthetase Syndrome

Symptoms of GERD: No , Past , Current

GERD exams: No , Esophagitis , distal hypotonia , PHmetry-normal ; distal proximal

Drugs: No , Amiodarone , Bleomycin , Methotrexate ; Nitrofurantoin , Carbamazepine , Radiation Others _____

Hypersensitivity Pneumonitis exposures – Birds (Pigeons, parakeets, parrots, canaries, cockatiels): No , Yes ; Mold , Paints , Feather pillow

Occupational exposure - No , Silicosis , Asbestosis , Dust mixed , Berylliosis , Metals , Gases/vapors Chemicals agents

Physical exam: Normal , Digital clubbing , Skin lesions _____ Raynaud , Mechanic's hands , Arthritis , Ocular , Lymph nodes , Heart disease , Velcro crackles , Squeaks , Hepatomegaly , Splenomegaly , Others _____

Lung function test: FVC% _____ FEV1% _____ FEV1/FVC _____ DLCO % _____

SaO2 rest _____ SpO2 exercise _____

Autoantibodies: Antinuclear Factor _____ Rheumatoid Factor _____ Other _____

Transbronchial biopsy or **CRYOBIOPSY** : Diagnosis ; Compatible histological findings ; Nonspecific abnormalities ; Normal/negative findings

Bronchoalveolar lavage: Macrophages% _____ Neutrophils% _____ Lymphocytes% _____ Eosinophils% _____

Surgical Lung Biopsy Date / /

Biopsy from another site _____

Diagnosis- Date / / Unclassifiable Interstitial Lung Disease ;
 Idiopathic Pulmonary Fibrosis 1; ; Sarcoidosis ; Hypersensitivity Pneumonitis ;
 Cryptogenic organization pneumonia ; Non-Specific Interstitial Pneumonia (NSIP) ;
 Respiratory bronchiolitis - ILD/ Desquamative Interstitial Pneumonia ;
 Acute Interstitial Pneumonia ; Pneumoconiosis ;
 Lymphangioleiomyomatosis ; Pulmonary Langerhans Cell Histiocytosis ;
 Alveolar proteinosis ; Eosinophilic Pneumonia ; Bronchiolitis ; Vasculitis ;
 CTD (Systemic sclerosis, Rheumatoid arthritis, Systemic Lupus Erythematosus ,
 Mixed Connective Tissue Disease , Sjogren's Syndrome , Dermatopoliomyositis ,
 Interstitial Pneumonia with Autoimmunity Findings , Antisynthetase Syndrome);
 Airway centered fibrosis ; Carcinomatosis ; Drugs ; Others ; _____, Terminal lung ;
 Microaspiration ; Family ILD

Multidisciplinary discussion:

Diagnosis _____

Chest tomography date / /

Findings	YES
Craniocaudal Distribution	
Predominantly upper lobes	
Predominant lower lobes	
Diffuse	
Axial Distribution	
Central / peribronchovascular	
Peripheral/ subpleural	
Central and peripheral	
Unilateral predominance	
Decreased volume of upper lobes	
Lower lobe volume reduction	
Reticular opacities	
Reticular non-septal (irregular)	
Reticular septal	
Subpleural lines	
Parenchymal bands	
Nodules-Size	
small (below1 cm)	
Large (above1 cm)	
Large- conglomerates/masses	
Excavated	
Nodules -Distribution:	
Miliary	
Centrilobular	
Peribronchovascular	
Subpleural	
Tree in bud	

Increased opacity	
Possible dependent	
Ground glass	
No fibrosis	
With findings of fibrosis	
Consolidation	
At random	
Peribronchial	
Peripheral	
Hypertransparencies	
Honeycombing	
Cysts	
Emphysema	
Bronchiolectasis / bronchiectasis	
Non-traction bronchiectasis	
Mosaic perfusion	
Expiratory air trapping	
Pleura	
Thickening/Plaques/Calcifications	
Pleural effusion	
Pneumothorax	
Pulmonary Artery > Aorta	
Adenopathy	
Hilar	
Mediastinal	
Calcifications	

Chart S2 - ENVIRONMENTAL EXPOSURE QUESTIONNAIRE

	YES	NO	OBSERVATION
Do you live on a farm and have silos?			
Do you have birds at home? a) Pigeon b) Parakeet c) Parrot d) Canary e) Cockatiel f) Rabbit			
Air conditioning units at home or at work?			
Humidifier or vaporizer at home or work?			
Accumulation of fungus or mold at home or work on walls, floors or furniture or on the mattress?			
Musty smell at home or at work?			
Do you have water leaks at home?			
Do you go to hot water saunas?			
Do you have a pool at home?			
Do you have an internal water source at home?			
Pillows, or quilted or feather cushion?			
Feather decoration?			
Do you work/have you worked with paints or varnishes?			
Do you work or have you worked in furniture factories?			
Do you work or have you worked with wood/sawmills?			
Do you work or have you worked exposed to metallic fluids?			
Do you work or have you worked with foam sprays?			
Do you work or have you worked with bird or fish food?			
Do you work or have you worked with wheat flour?			
Do you have plants and handle soil or fertilizers?			
Exposure to insecticides? Exposure to copper sulfate?			
Do you have a fungus plantation (shiitake)?			
Do you play wind instruments?			

Table S1 - General characteristics of the most frequent ILD among 1406 patients in 6 centers in Brazil

	CTD-ILD	HP	IPF	Unclassifiable ILD	Sarcoidosis
N patients n (%)	376 (26,8)	327(23,2)	199 (14,1)	143 (10,2)	89 (6,3)
Age \bar{x} (± SD)	55,6 (± 12,7)	63,6 (± 12,6)	71,7 (± 6,9)	67,8 (± 11,1)	50,2 (± 11,4)
Sex, F, n (%)	287 (76,3)	188 (57,5)	52 (26,1)	67 (46,9)	51 (57,3)
Smoking n (%)	137 (36,7)	134 (41,2)	132 (66,7)	81 (57,4)	29 (33)
Family History n (%)	10 (3,3)	36 (13,3)	36 (23,8)	23 (20,2)	-
Relevant exposure n (%)	139 (39,4)	317 (96,9)	88 (44,6)	93 (68,4)	18 (25)
Symptoms of GER n (%)	216 (60,5)	142 (46,5)	85 (46,4)	66 (50,4)	23 (31,5)
Autoantibodies n (%)	315 (86,8)	36 (12,6)	8 (5,1)	17 (13,8)	2 (2,2)
Crackle n (%)	192 (52,3)	168 (52,3)	172 (89,1)	99 (72,8)	7 (8,1)
Honeycombing n (%)	54 (14,4)	53 (16,2)	142 (71,4)	29 (20,3)	1 (1,1)
Fibrotic ILD n (%)	289 (76,9)	269 (82,3)	199 (14,1%)	130 (90,9)	16 (18,0)
FVC % \bar{x} (± SD)	65,0 (± 18,0)	64,4 (± 19,2)	69,9 (± 18,6)	64,3 (± 18,0)	79,6 (± 16,5)

Note: GER: gastroesophageal reflux, FVC: forced vital capacity; IPF: idiopathic pulmonary fibrosis; HP: hypersensitivity pneumonitis; CTD-ILD: interstitial lung disease related to connective tissue disease

Table S2 – Distribution of the sample of 1406 patients with ILD according to the center of origin

Center of origin	Frequency (n)	Percentage (%)
Hospital of the Federal University of São Paulo	437	31,1
Hospital of the Federal University of Minas Gerais	285	20,3
CACP Pulmonology Clinic in São Paulo	259	18,4
Julia Kubistchek Hospital in Belo Horizonte	191	13,6
Sao Rafael Hospital in Salvador	128	9,1
Hospital of the Federal University of Goiás	106	7,5
Total	1406	100

Note: UNIFESP: Federal University of São Paulo; UFMG: Federal University of Minas Gerais; UFG: Federal University of Goiás

Table S3 - Total and variation in the main ILD diagnoses among the 6 centers in Brazil

Center of origin	Diagnostics %				
	CTD-ILD	HP	Unclassifiable ILD	IPF	Sarcoidosis
Hospital of the UNIFESP (n=437)	28,1	20,4	11,4	6,4	9,4
Hospital of the UFMG (n=285)	27,7	36,5	7,4	16,5	3,2
Private Clinic in São Paulo (n=259)	15,0	21,2	9,3	22,3	8,8
Julia Kubistchek Hospital in Belo Horizonte)(n=191)	38,2	14,1	12,6	19,9	4,2
São Rafael Salvador (n=128)	24,2	29,7	3,1	14,8	6,2
Hospital of the UFG (n=106)	29,2	13,2	18,9	8,5	0,0

Note: $\chi^2= 312,37$; $p < 0,001$. IPF: idiopathic pulmonary fibrosis; HP: hypersensitivity pneumonitis; CTD-ILD: interstitial lung disease related to connective tissue disease, UNIFESP: Federal University of São Paulo; UFMG: Federal University of Minas Gerais; UFG: Federal University of Goiás

Table S4 - Presence of autoantibodies in 1219 cases of ILD in 6 centers in Brazil from 2013 to 2019

Variables	n (%)
Positive	398 (32,6%)
ANA \geq 1:320 (isolated or associated)	260 (21,3%)
Rheumatoid Factor	80 (6,6%)
Anti-Ro	66 (5,4%)
Antisynthetase antibody	36 (2,9%)
Anti-Scl 70	41 (3,4%)
Isolated	283 (23,2%)
Combined	117 (9,6%)

Note: ANA: Antinuclear antibodies

Table S5 - Distribution of types of lung biopsies among the 6 centers in Brazil from 2013 to 2020

N (%)	TBB	SLB	Another biopsy site	TBB + SLB	Combinations	Total per center
Hospital of the UNIFESP	164 (57,1)	30 (14,6)	16 (34,8)	16 (51,6)	4 (80)	230 (39,8)
CACP Pulmonology Clinic in São Paulo	32 (11,1)	64 (31,1)	14 (30,4)	8 (25,8)	3 (86,7)	121 (20,9)
Hospital of the UFMG Julia Kubistchek	31 (10,8)	44 (21,4)	3 (6,5)	7 (22,6)	0	85 (14,7)
Hospital in Belo Horizonte São Rafael	29 (10,1)	27 (13,1)	11 (23,9)	0	0	67 (11,6)
Hospital in Salvador	22 (7,7)	27 (13,1)	2 (4,3)	0	1 (33,3)	52 (9,0)
Hospital of the UFG	9 (3,1)	14 (6,8)	0	0	0	23 (4,0)
Total by biopsy type (N)	287	206	46	31	8	578

Nota: TBB: transbronchial biopsy, SLB: surgical lung biopsy

Table S6 - Diagnostic yield of transbronchial biopsy in ILD in a cohort from 6 centers in Brazil

Transbronchial biopsy	N (%)
Total	323 (22,9)
Diagnostic/Compatible	116 (36%)
Sarcoidosis (n=36)	23 (63,9%)
HP (n=105)	33 (31,4%)
CTD-ILD (n=52)	13 (25%)
Silicosis (n=14)	11 (78,6%)
Drugs (n=13)	10 (76,9%)
IFP (n=18)	4 (22,2)
Others (n=22)	22 (29,3%)

Note: IPF: idiopathic pulmonary fibrosis; HP: hypersensitivity pneumonitis; CTD-ILD: interstitial lung disease related to connective tissue disease

Table S7 - Histological patterns obtained by surgical lung biopsy and final clinical diagnoses

SURGICAL LUNG BIOPSY	N (%)
Total	241 (17,1%)
Inconclusive	10 (4,1%) *
Bronchiolocentric fibrosis	58 (24,1%)
UIP	34 (14,1%)
HP	41 (17,0%)
Diffuse alveolar damage	1 (0,41%)
Organizational pneumonia	16 (6,6%)
Various bronchiolitis	10 (4,1%)
NSIP	18 (7,5%)
Granuloma	17 (7,0%)
Others	27 (11,2%)
OP and NSIP	6 (2,5%)
UIP and Bronchiolocentric fibrosis	2 (0,8%)
Bronchiolocentric fibrosis and NSIP	1 (0,4%)

Note: UIP: Usual interstitial pneumonia; HP: hypersensitivity pneumonitis, NSIP: Non-specific interstitial pneumonia; OP: Organizational pneumonia