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Original article

EXPLORING RARE INTERSTITIAL LUNG DISEASES: INSIGHTS FROM HIGH-RESOLUTION COMPUTED TOMOGRAPHY

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Abstract

Interstitial lung diseases (ILDs) pose significant diagnostic and therapeutic challenges due to their diverse and intricate nature. This study investigated rare ILDs, such as cryptogenic organizing pneumonia, eosinophilic pneumonia, lymphocytic interstitial pneumonia, hypersensitivity pneumonitis, and Langerhans cell histiocytosis, identified through high-resolution computed tomography (HRCT) in N. Macedonia.

A cohort of ten patients was recruited from the University Clinic for Pulmonology and Allergology in Skopje over a one-year period. HRCT scans were conducted using a 128-slice PHILIPS INCISIVE CT scanner, while clinical data were gathered from comprehensive medical records and questionnaires.

Analysis revealed a gender distribution of 6 females and 4 males, with ages ranging from 18 to 78 years (mean age: 50±17.2 years), predominantly residing in urban areas. Notably, six patients reported cough symptoms, while dyspnea was present in nine individuals. HRCT findings encompassed reticular shadows, high and low attenuation, and trapped air, exhibiting diverse distribution patterns.

This study contributes to elucidating the radiological patterns and distributions of rare ILDs, thereby enhancing diagnostic accuracy and facilitating effective management strategies.

Keywords: interstitial lung diseases, high-resolution computed tomography, rare cases

Introduction

The realm of rare interstitial lung diseases (ILDs) is diverse and intricate, presenting diagnostic and therapeutic challenges. With over 200 entities, ILDs exhibit varied clinical, radiological, and pathological features[1,2]. These diseases are categorized into various groups[3]. This review presents a selection of rare and ultra-rare ILDs in N. Macedonia, including cryptogenic organizing pneumonia, eosinophilic pneumonia, lymphocytic interstitial pneumonia, hypersensitivity pneumonitis, and Langerhans cell histiocytosis, identified via high-resolution computed tomography (HRCT).

Organizing pneumonia (OP) presents as interstitial pneumonia with acute or subacute onset, histologically resembling acute lung injury. Secondary OP follows recent peripheral bronchial infections, while cryptogenic organizing pneumonia (COP) lacks identifiable causes[4]. COP is distinguished clinically from secondary OP and may result from medical interventions, infections, or may be associated with vasculitis or malignancy[5,6].

Symptoms typically appear between 55-60 years, with no smoking association[7], as presented in Figure 1.

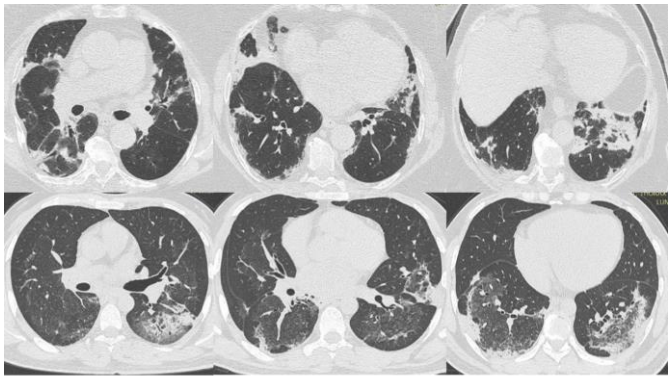

Fig. 1. HRCT Findings in Organizing Pneumonia
(from the author's personal archive)

HRCT reveals diverse COP changes, including sharply demarcated consolidations with a lobular pattern adjacent to broncho-vascular structures. Additional findings include bilateral subpleural-dominant consolidations and nodules[8-12]. Consolidations, often accompanied by air bronchograms, vary in distribution and localization, with a predilection for lower lung lobes, aiding differentiation from chronic eosinophilic pneumonia (Figure 1)[8].

Eosinophilic pneumonia comprises diseases marked by eosinophil infiltration in lung tissue, divided into idiopathic, secondary, eosinophilic vasculitis, and eosinophilic granulomatosis with polyangiitis[13]. Acute eosinophilic pneumonia (AEP) presents with a rapid onset of fever, severe dyspnea, and hypoxia, responding well to steroids with low relapse rates[14]. Imaging shows ARDS-like infiltrations, often with pleural effusions[15]. HRCT features include ground glass opacities, interlobular septal thickening, pleural effusion, bronchovascular bundle thickening, airspace consolidations, and centrilobular nodules, as presented in Figure 2[16].

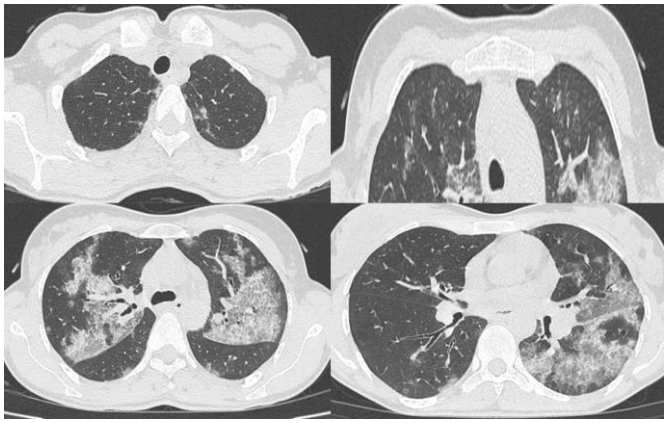

Fig. 2. HRCT Findings in Eosinophilic Pneumonia
(from the author's personal archive)

Lymphoid interstitial pneumonia (LIP) is a benign lymphoproliferative disorder marked by predominant lymphocytic lung infiltration, classified as a subtype of interstitial lung disease[17]. It affects adults predominantly aged 52-56, with a female predilection, potentially linked to autoimmune diseases like Sjögren's syndrome[18].

HRCT typically shows diffuse changes, with bronchovascular structure thickening, interstitial thickening along lymphatic channels, small pulmonary nodules, ground glass changes, scattered cystic lesions, and mediastinal lymphadenopathy[17,19,20]. LIP is an uncommon interstitial lung disease, with idiopathic forms being extremely rare. Treatment with corticosteroids may stabilize or improve symptoms, but survival remains uncertain, warranting further research (Figure 3)[21].

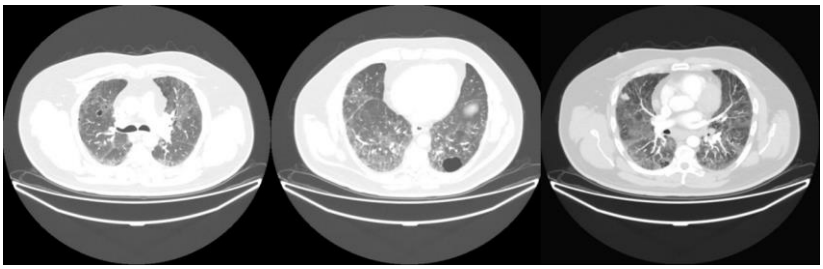

Fig. 3. HRCT Findings in Lymphoid Interstitial Pneumonia (LIP)
(from author's personal archive)

Hypersensitivity pneumonitis (HP) is a diffuse granulomatous interstitial lung disease resulting from exposure to various antigenic organic particles[22]. Diagnosis is challenging due to nonspecific clinical manifestations and radiological and histological patterns resembling other interstitial and small airway diseases[23].

Acute HP manifests suddenly within hours of severe antigen exposure in sensitized individuals. Subacute HP arises from intermittent or continuous low-dose antigen exposure, while chronic HP results from persistent or repeated low-level exposure, distinguished by fibrosis[22, 24].

In acute HP, HRCT may appear normal or show diffuse ground-glass opacities or centrilobular nodules. Subacute HP typically features ground-glass opacification, poorly defined centrilobular nodules, and areas of air trapping, often with mid-lung and upper-lung predominance (Figure 4) [25-30].

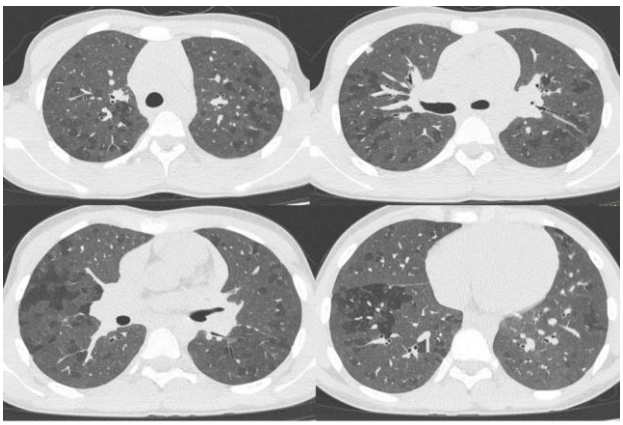

Fig. 4. HRCT Findings in Hypersensitivity Pneumonitis (HP)
(from author's personal archive)

Pulmonary Langerhans cell histiocytosis (PLCH) is a rare form of Langerhans cell histiocytosis characterized by granulomatous infiltration of distal bronchial walls with Langerhans cells, forming small nodules and affecting adjacent arterioles and the interstitium[31-33]. It primarily affects young adults but can occur across various age groups,

with no gender predilection[32]. PLCH is almost exclusively found in smokers (90–95%), classifying it as a smoking-related interstitial disease[34].

HRCT is more effective than plain chest radiography in identifying reticulonodular opacities and cysts. Distribution patterns, including a predilection for the middle and upper lung zones and sparing of certain regions, aid in distinguishing PLCH from other cystic lung diseases[35-37]. The prognosis is generally favorable, with spontaneous resolution or stabilization observed in over 50% of patients, particularly in those who quit smoking. However, in about 20% of cases, particularly among smokers, the disease may progress, leading to worsening respiratory function and eventual pulmonary fibrosis[38].

The study aimed to assess the distribution and radiological patterns of these rare ILDs identified via HRCT.

Materials and methods

Ten patients diagnosed with cryptogenic organizing pneumonia, eosinophilic pneumonia, Langerhans cell histiocytosis, lymphocytic pneumonia, and hypersensitivity pneumonitis were recruited from our University Clinic for Pulmonology and Allergology in Skopje over a one- year period. High-resolution computed tomography (HRCT) scans were performed using a 128-slice PHILIPS INCISIVE CT scanner, with 1 mm slices and high spatial resolution image reconstruction algorithms. Clinical data were obtained from the medical records system, "Moj Termin," and through medical questionnaires.

Statistical Analysis: Data analysis was conducted using SPSS 23.0. Categorical variables were presented as absolute and relative numbers, while numerical variables were expressed as means, standard deviations, minimum, and maximum values. Tabular and graphical representations were utilized to present the data of interest.

Results

This section presents an analysis of 10 patients diagnosed with interstitial pneumonia, comprising 3 cases of cryptogenic pneumonia, 3 of lymphoid pneumonia, 2 of eosinophilic pneumonia, 1 of Langerhans cell histiocytosis, and 1 of hypersensitivity pneumonitis. Among these patients, there were 6 females and 4 males, with ages ranging from 18 to 78 years and an average age of 50±17.2 years. The majority of patients (9 out of 10) came from urban areas. Among them, 2 were current smokers, while 4 reported being ex-smokers. Three patients had prior hospitalizations, and none had a family history of lung disease, as demonstrated in Table 1.

Six patients presented with cough, predominantly moderate in intensity (4) and productive (4). Dyspnea was reported by 9 out of 10 patients. Based on the MRC scale, six patients experienced dyspnea while walking quickly on level ground, two walked slower than their peers of the same age, and two experienced dyspnea after walking on level ground for several minutes. One patient reported a history of animal contact, two reported allergies, and seven had comorbidities.

HRCT findings revealed reticular shadows in the upper and middle zones of one patient, localized peripherally and sub-plurally. High attenuation was observed peripherally and sub-plurally in five patients, and peri-broncho-vascularly in five others. Additionally, low attenuation was noted peripherally and sub-plurally in three patients, and peri-broncho-vascularly in four. Trapped air was detected in three patients, with two showing it in the peripheral and subpleural regions, and one in the peri-broncho-vascular regions (Table 2).

Table 1. Summary of Patient Information Acquired from the Questionnaire

Variable	n (%)
Pneumonia	
Organizing cryptogenic	3(30)
Lymphoid Interstitial	3(30)
Eosinophilic	2(20)
Langerhans Histiocytosis	1(10)
Typical Hypersensitive	1(10)
Gender	
female	6(60)
male	4(40)
Age	
(mean ± SD)(min- max)	(50±17.2) (18-78)
Residence	
city	9(90)
village	1(10)
Smoker	
yes	2(20)
Ex- smoker	
yes	4(40)
no	6(60)
Prior hospitalizations	
yes	3(30)
no	7(70)
Family history of lung disease	
yes	0
no	10 (100)

Table 2. Distribution of HRCT Findings in Patients with Rare Interstitial Lung Diseases in Upper and Mid Zones

Upper and mid zones			n (%)
Reticular opacities	Peripheral and subpleural	**yes**	1(10)
		no	9(90)
	Peri-broncho-vascular	**yes**	
		no	10(100)
High attenuation	Peripheral and subpleural	**yes**	5(50)
		no	5(50)
	Peri-broncho-vascular	**yes**	5(50)
		no	5(50)
Low attenuation	Peripheral and subpleural	**yes**	3(30)
		no	7(70)
	Peri-broncho-vascular	**yes**	4(40)
		no	6(60)
Air trapping	Peripheral and subpleural	**yes**	2(20)
		no	8(80)
	Peri-broncho-vascular	**yes**	1(10)
		no	9(90)

HRCT revealed reticular shadows in the upper zones of the lungs in one patient, predominantly localized in the peripheral and subpleural regions. High attenuation was observed peripherally subpleural in five patients and peri-broncho-vascularly in five others. Additionally, low attenuation was noted peripherally subpleural in three patients and peri-broncho-vascularly in four. Trapped air was present in three patients, with two showing it

predominantly in the peripheral and subpleural regions and one in the peri-broncho-vascular regions. HRCT findings revealed predominantly basal subpleural and subpleural in one patient, with subpleural distribution found symmetrically in 3 patients and asymmetrically in 5. Both homogeneous and heterogeneous distributions were observed in all patients. Additionally, apicobasal localized findings were noted in 4 patients, while subpleural sparing was observed in 3 patients (Table 3).

Table 3: Distribution of HRCT Findings in Lower Lung Zones

Lower zones			**n (%)**
Reticular opacities	Peripheral and subpleural	**yes**	1(10)
		no	9(90)
	Peri-broncho-vascular	**yes**	
		no	10(100)
High attenuation	Peripheral and subpleural	**yes**	5(50)
		no	5(50)
	Peri-broncho-vascular	**yes**	5(50)
		no	5(50)
Low attenuation	Peripheral and subpleural	**yes**	2(20)
		no	8(80)
	Peri-broncho-vascular	**yes**	2(20)
		no	8(80)
Air trapping	Peripheral and subpleural	**yes**	1(10)
		no	9(90)
	Peri-broncho-vascular	**yes**	1(10)
		не	9(90)

Discussion

The assessment of rare interstitial lung diseases (ILDs) through high-resolution computed tomography (HRCT) offers crucial insights into their radiological manifestations, aiding in both diagnosis and management. This study investigated a spectrum of rare ILDs, including cryptogenic organizing pneumonia (COP), eosinophilic pneumonia, lymphocytic interstitial pneumonia (LIP), hypersensitivity pneumonitis (HP), and Langerhans cell histiocytosis (PLCH), within the context of N. Macedonia [1-22].

The findings of this study underscore the diagnostic challenges associated with rare ILDs, particularly in regions where they may be underrecognized or underreported. COP, characterized by diverse radiological patterns including consolidations, nodules, and subpleural-dominant lesions, often presents with nonspecific clinical features, necessitating a comprehensive diagnostic approach[4-8,10-12]. Similarly, eosinophilic pneumonia, marked by eosinophilic infiltration and diverse HRCT findings such as ground-glass opacities and interstitial thickening, poses diagnostic dilemmas owing to its variable clinical presentation[13-16].

The radiological evaluation of lymphocytic interstitial pneumonia (LIP) reveals diffuse changes, including bronchovascular structure thickening and scattered cystic lesions, underscoring the importance of HRCT in elucidating the disease extent and distribution[17-21]. Moreover, hypersensitivity pneumonitis (HP) and Langerhans cell histiocytosis (PLCH) exhibit distinct radiological features, ranging from ground-glass opacities and centrilobular nodules to reticulonodular opacities and cysts, emphasizing the need for accurate characterization to guide optimal management strategies[22-30].

In addition to highlighting the radiological diversity of rare ILDs, this study sheds light on their demographic and clinical profiles, including gender distribution, smoking history, and comorbidities. The prevalence of cough and dyspnea underscores the significant symptom burden associated with these conditions, necessitating timely diagnosis and intervention.

Conclusion

This study provides valuable insights into the distribution and radiological patterns of rare ILDs in N. Macedonia, elucidating their diagnostic challenges and clinical implications. The comprehensive evaluation of HRCT findings contributes to the enhanced understanding of these complex diseases, facilitating their early recognition and targeted management.

Moving forward, further research endeavors are warranted to expand our knowledge of rare ILDs, encompassing larger cohorts and longitudinal studies to delineate their natural history and treatment outcomes. Collaborative efforts involving multidisciplinary teams comprising pulmonologists, radiologists, and pathologists are essential to optimize the diagnosis and management of rare ILDs, ultimately improving patient outcomes and quality of life.

Conflict of interest statement. None declared.

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