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ETIOLOGICAL PROFILE OF CHRONIC DIFFUSE INFILTRATING PNEUMOPATHIES

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ABSTRACT

Introduction: Chronic diffuse infiltrating pneumonias (DIP) form a heterogeneous group of pathologies, the classification of which is regularly modified; the latest from 2015 highlights 5 major families of chronic DIP. The etiological diagnosis of chronic diffuse infiltrating pneumonia is based on a range of elements discussed, necessarily, during a multidisciplinary discussion meeting (MDD) for etiological diagnostic decision. The aim of this work is to describe the etiological profile of the various chronic DIP followed at the Hassan II hospital in Fez. **Methods:** This is a retrospective analytical descriptive study conducted at the various follow-up consultations of patients with chronic DIP in the pneumology department of the Hassan II University Hospital Center in Fez. It was spread over a period of 03 years**. Results:** Of the 315 patients solicited, the age is between 21 and 89 years old, with an average age of 58.49 years. The female gender has a significant predominance with a percentage of 71.11%. Of the 315 chronic DIP files received at consultations, 76.5% were discussed in a multidisciplinary meeting with an average delay of 4.6 months. Of all the files discussed in DMD (N = 241), 71% concluded with an etiological diagnosis, 22.8% the diagnosis was not confirmed, the rest is being explored. We analyzed the 315 records of chronic DIP patients. The etiologies were retained on the results of the thoracic scans, the results of the BAL, the bronchial biopsies and the results of the immunological assessments. The results according to the ATS/ERS 2015 classification showed that the sarcoidosis-type granulomatosis etiology is the leading etiology, neck and neck with DIP of known cause with respective percentages of 32% and 36%, followed by the idiopathic DIP with 25%, then the particular DIP with 7% and finally the IPAF entity with a single case. The leader of the DIP of known causes, are the connectivities with more than 50%. The leader of idiopathic diffuse infiltrating pneumopathies is idiopathic pulmonary fibrosis with 49.3%. The eosinophilia lung (50%) represents half of particular DIP. **Conclusion:** DIP constitute a very heterogeneous group, whose etiological diagnosis remains complex and necessary for a good therapeutic attitude. Faced with the diversity and heterogeneity of etiologies evoked in chronic DIP, the diagnostic and therapeutic strategy requires a judicious elaboration between clinicians, radiologists and pathologists after which a multidisciplinary decision is taken (MDD).

KEYWORDS:

INTRODUCTION

Chronic diffuse infiltrating pneumonias (DIP) form a heterogeneous group of pathologies where the contribution of imaging is decisive. They are due to diffuse infiltration, mainly of the pulmonary interstitium; but also of the distal alveolar and bronchiolar air spaces and of the small vessels, by cellular or non-cellular lesions.[1]

From the current pathophysiological point of view, it is suggested that DIP develop from a genetically "vulnerable" alveolar epithelium, subjected to environmental "attacks" and repeated comorbidities.[2] Impaired re-epithelialization of the alveolar surface and its repair leads to remodeling of the parenchymal structure and development of areas of pulmonary fibrosis.[3]

From the radiological point of view, it is the attack of the different components of the connective tissue, which is the interstitium of the lung, which gives the different radiological lesions specific to each etiology of chronic DIP[4], thus explaining the diversity of etiologies chronic DIP.

The main international pulmonology bodies update the classifications of chronic diffuse infiltrating pneumopathies on an ongoing basis. The classification of the American Thoracic Society and the European Respiratory Society (ATS/ERS) 2013, which was slightly modified in 2015 by adding a new entity which

is the IPAF; highlights 4 major families of chronic DIP[5]:

• Sarcoidosis or Besnier-Boeck-Schaumann (BBS) lymphogranulomatosis disease.
• DIP of known causes: Hypersensitivity pneumonitis (HSP), Connectivitis, Vasculitis, Toxic, Pneumoconiosis,
• Idiopathic DIP: Idiopathic Pulmonary Fibrosis (IPF), Nonspecific Interstitial Pneumonitis (NSIP), Cryptogenic Organizing Pneumonitis (POC), etc.
• IPAF, a diffuse interstitial lung disease with autoimmune signs without however fulfilling the criteria for connectivity.
• Particular DIP with specific histopathological lesions: Langerhans cell histiocytosis, lymphangioleiomyomatosis, chronic eosinophilic pneumonitis.

The etiological diagnosis of chronic diffuse infiltrating pneumonia is based on the interrogation, the clinic, the biology, bronchoalveolar lavage (BAL), biopsy specimens by bronchial or extrathoracic endoscopy, and radiographic imaging, in particular the chest scanner. All discussed, necessarily, during a multidisciplinary discussion meeting (MDD) for etiological diagnostic decision.

The interest of recognizing the different etiologies of chronic DIP present in a population is projected on the actions to be taken in front of any DIP received by the practitioner.

The aim of this work is to describe the etiological profile of the various chronic DIP followed at the Hassan II hospital in Fez.

METHODS

Type of study

This is a retrospective analytical descriptive study conducted at the various follow-up consultations of patients with chronic diffuse infiltrating pneumonia in the pneumology department of the Hassan II University Hospital Center in Fez.

The study was spread over a period of 03 years; running from March 1, 2019 to February 28, 2022.

Target population

1. Inclusion criteria

All patients, female and male, aged 18 and over, followed at various follow-up consultations for chronic diffuse infiltrating pneumonia confirmed by high-resolution chest CT.

2. Exclusion criteria

Were excluded from the study, patients who were received only once in consultation then lost to follow-up, and those received for management of an acute or subacute diffuse infiltrating pneumonia.

Collection tools

The collection of data concerning the epidemiological elements was carried out on the detailed observations of the patients on the digital systematized register of the university hospital center Hassan II of Fez. The data concerning the etiology, the delay between the consultation and the diagnosis, the contribution of the multidisciplinary meeting (the DMD), were collected thanks to the DMD sheets which include the data and the decisions taken in the meeting. The classification used is that of the ATS/ERS 2015.

The collection was made thanks to a well-conducted exploitation sheet, including the demographic and etiological variants, as well as the variants concerning DMD.

The statistical study was carried out by Microsoft Excel software, SPSS software and EPI info version 2010.

Ethics

Ethical rules have been respected, and no conflict of interest has been reported.

RESULTS

Over the 03-year period, we solicited 315 patients, who were followed for diffuse infiltrative pneumonia in our training on the various consultations.

The average age of 58.49 years with extremes ranging from 21 years to 89 years. More than half is represented by the age group between 50 and 69, with a percentage of 64.8%; As for the age group under 30, it only represents less than 2% (Figure 1).

The analysis of our series (N = 315) showed that the female sex has a significant predominance with a percentage of 71.11%. The sex ratio is 0.4 (Figure 2). The female predominance is respected for all age groups except for those under 30 where there is only one woman against three men.

Of the 315 chronic DIP files received at consultations, 76.5% were discussed at a DMD meeting.

The average time between the first consultation and the diagnosis of DMD is 4.6 months, with a maximum of 25 months and a minimum of 01 month.

Of all the files discussed in DMD (N = 241), an etiological diagnosis was concluded in 71%, no diagnosis could be retained in 22.8% of cases, the rest is being explored.

We analyzed the 315 records of chronic DIP patients. The etiologies were retained in a DMD meeting on the results of chest CT scans, the results of BAL, bronchial biopsies and the results of immunological assessments.

The results were distributed according to the ATS/ERS 2013 classification, which was slightly modified in 2015 by Fisher by adding a new entity, which is IPAF or PISA (interstitial lung disease with autoimmune manifestations).

We eliminated 55 files whose etiology of DIP is not labeled. The etiologies retained on the other files (N=260) showed that the etiology granulomatosis type sarcoidosis is the leader of the etiologies, elbow to elbow with DIP of known cause with respective percentages of 32% and 36%, followed by idiopathic DIP with 25%, then particular DIP with 7% and finally the IPAF entity with a single case. (Table 1).

DIP of known causes are due to connectivitis in more than 50% of cases (represented by Rheumatoid arthritis (RA) in 34% of cases, scleroderma in 24% of, Gougeröt in 23% of cases, Systemic lupus erythematosus in 6% of cases, dermatomyositis in 4% of cases). Hypersensitivity pneumopathy is noted in 32.3% of patients, vasculitis is only represented in 4.3% of cases, followed by toxic DIP (in particular drug-induced DIP and post-radiation) and pneumoconioses equivocally in 3.2% of cases. (Table 2)

The leader of idiopathic diffuse infiltrating pneumonia is idiopathic pulmonary fibrosis with 49.3%, followed by NSIP-Idiopathic with 38.4% and cryptogenic organizing pneumonia with 12.3% (Table 3).

Individual DIP overall represent only 7% of all chronic DIP. The eosinophilic lung (50%) represents half of the etiologies; the other half is shared between lymphangioleiomyomatosis with four cases, histiocytosis with three cases, and finally lymphoid interstitial pneumonitis with two cases (Table 4)

DISCUSSION

Our study showed that sarcoidosis represents 31.9%, i.e. the largest share of DIP etiologies all combined, as do the majority of studies which retain that sarcoidosis is the most frequent cause of DIP before the age of 40.[6-12] Its incidence of 10 to 20 per 100,000. A localization.[6,7,15-21] (Table 5).

Connectivity represents 20.4% of all chronic DIP etiologies in our series. As for the different responsible connectivities, scleroderma and RA are the most common etiologies in terms of DIP secondary to connectivities. The same for other series, where RA with scleroderma present 58% of etiologies by connectivitis.[7-10, 15-21] (Table 6).

Hypersensitivity pneumonitis (HSP) or allergic alveolitis represent 11.5% in our series, the percentages differing from the studies (Table 5) depending on the population studied, because HSP is strongly linked to exposure to antigens.[11, 15-20]

Pneumoconiosis belong to the very heterogeneous group of “diffuse interstitial pneumonias” (DIP). For our series, whose sample represents the general population, pneumoconiosis are present with a percentage of 1.2%. If they are rare in the general population (2-4%), they are on the contrary frequent in particular groups. (eg, silicosis in underground miners or dental technicians).[12]

IPF is the most common idiopathic DIP (60-70%). Worldwide, the prevalence of idiopathic pulmonary fibrosis is estimated at between 14 and 43 cases per 100,000, according to an analysis of health system data.[13] 12.3% of our patients' chronic DIP were labeled IPF, a much lower percentage than the majority of populations in other studies[7,18] (Table 7), this could be due to the environment changing the lung's predisposition to develop pathology labeled idiopathic.

IPAF, an entity that remains rare or underdiagnosed, represents only 0.4% in our series. It is a recent and new entity, an interstitial lung disease which presents autoimmune manifestations but insufficient to retain the diagnosis of connective tissue disease.

Multidisciplinary discussion (MDD) is crucial for the management of chronic diffuse interstitial lung disease (DIP). One of its roles is to identify the etiology responsible for interstitial lung disease and therefore to decide on management. Diagnostic agreement is good for IPF and DIP associated with connective tissue.[14]

The DMD meeting discussed the files of 76.5% of patients, thus concluding with a definitive etiological diagnosis in 71% of cases, which confirms its essential contribution for the etiological diagnosis of DIP.

CONCLUSION

DIP constitute a very heterogeneous group, whose etiological diagnosis remains complex and necessary for a good therapeutic attitude. Various entities are now well individualized within chronic DIP and accurately diagnosing each of them is of significant practical interest, since each presents well-identified characteristics.

Faced with the diversity and heterogeneity of etiologies evoked in chronic DIP, the diagnostic and therapeutic strategy requires a judicious elaboration between clinicians, radiologists and pathologists after which a multidisciplinary decision is taken (DMD).

In the end, a precise and early etiological diagnosis, as well as an adapted treatment makes it possible to delay the installation of fibrosis and the occurrence of complications, thus improving the prognosis, quality of life and survival.

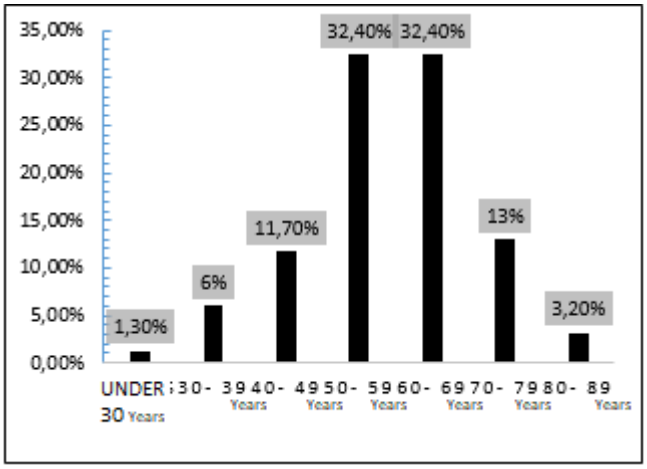

Figure 1: Distribution of ages in the series of chronic DIP in the pulmonology department, Hassan II hospital center, Fez.

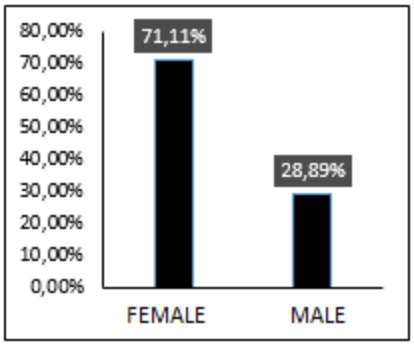

Figure 2: Gender distribution in the series of chronic DIP from the pulmonology department, Hassan II hospital center, Fez.

Table 1: Distribution of the different etiologies found in patients followed up with chronic DIP in the pulmonology department, Hassan II hospital center, Fez.

Etiologies		***N***	***%***
Sarcoidosis		83	31,9%
Known cause DIP N=93	HSP	30	11 ,5%
	connectivity	53	20,4%
	vasculitis	4	1,5%
	toxic	3	1,2%
	pneumoconiosis	3	1,2%
Idiopathic DIP N=65	PFI	32	12,3%
	NSIP	25	9,6%
	COP	8	3%
IPAF		1	0,4%
Particular DIP N=18	histocytosis	3	1,2%
	MLA	4	1,5%
	LIP	1	0,4%
	PAL	1	0,4%
	EOSINOPHILIC LUNG	9	3,5%
Total		241	100%

Table 2: Distribution of the different etiologies of chronic DIP with causes known to the pulmonology department, Hassan II hospital center, Fez.

Etiologies		***N***	***%***
Known cause DIP N=93	HSP	30	32,3%
	connectivity	53	57%
	vasculitis	4	4,3%
	toxic	3	3,2%
	pneumoconiosis	3	3,2%

Table 3: Distribution of the different etiologies of chronic DIP from idiopathic causes in the pneumology department, Hassan II hospital center, Fez.

Etiologies		***N***	***%***
Idiopathic DIP N=65	PFI	32	49,3%
	NSIP	25	38,4%
	COP	8	12,3%

Table 4: Distribution of the different etiologies of chronic DIP from specific causes in the pulmonology department, Hassan II hospital centre, Fez.

Etiologies		***N***	***%***
Particular DIP N=18	histocytosis	3	16,7%
	MLA	4	22,3%
	LIP	1	5,5%
	PAL	1	5,5%
	EOSINOPHILIC LUNG	9	50%

Table 5: Distribution of chronic DIP on different studies.

Studies	***Sarcoidosis %***	***Connectivity %***	***HSP%***	***Toxic%***
M.Lahroussi[15]	34	20		
S.Jridi[16]	23,4	23,3		
Niang[17]	20,63	14,28		
Berri[18]	20,54	8,21	21,4	
Abderahim[19]	37	7,4	14,8	
S. Debbiche[20]	27,1	16,5		2 ,3

Table 6: The frequency of the different types of connectivitis responsible for chronic DIP.

Studies	***RA%***	***SCLERODERMA%***	***LUPUS%***
Niang[7]	3,24	6,34	3,24
Bensalem[21]		53,75	2,5

Table 7: The frequency of idiopathic pulmonary fibrosis in different series of chronic DIP.

Studies	***PFI %***
Niang[7]	23,80
Berri[18]	39,73

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