Case report

How are the ancient cystic fibrosis patients? Cystic fibrosis diagnosed over 60 years-old

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A R T I C L E I N F O

A B S T R A C T

Background and aims: To specify the prevalence of patients diagnosed with CF at age of ≥60 year-old and to analyze their characteristics.
Patients and methods: Observational study of CF patients which were diagnosed at age ≥60 year-old. The analyzed variables were: age, sex, nationality, lung function parameters, conditions present at diagnosis, microbiological characteristics and genetic findings.
Results: eight patients were included. 7 patients were female (87.5%) with a mean age of 70.6 years (median 71.5 years, range 60—78 years). The most important findings were: sweat test >60 mEq/l; heterozygotes F508del; bronchiectasis in CT; methicillin-sensitive Staphylococcus aureus (50%) in sputum. The most patients presented a normal or mild obstructive lung function.
Conclusions: CF must also be considered a disease diagnosed in adulthood, incorporating the sweat test within the usual techniques of differential diagnosis in patients with different diseases associated with CF, because genetic counselling is esencial.

1. Background

Until recently, cystic fibrosis (CF) had been considered a childhood disease. Therapeutic advances and specialist units have contributed towards this disease ceasing to be lethal in childhood [1—3]. However, although current survival time can exceed 40 years, mostly in the case of patients from pediatric units, a diagnosis at over 40 years of age is still unusual, but the possibility of diagnosis at over 60 years of age still exists [4,5]. Awareness of the clinical characteristics of patients diagnosed at advanced ages could be important in order to consider CF in adults of 60 years, since few studies have been carried out so far. Diagnosis of CF is important because it implies a prognosis and provision of appropriate treatment, not to mention genetic counselling in families [1,4].

As a result we propose, as the main objective of our study, to look into the percentage of CF patients diagnosed at over 60 years of age. We would also analyze the reasons for which these patients were referred to CF Units, their most common clinical manifestations, and the genetic mutations found. This will serve, in the future, to understand that the age of the patient need not be a limiting factor for the diagnosis of CF.

2. Patients and method

An observational, cross-sectional and descriptive study of patients older than 60 years and diagnosed with CF at the multidisciplinary Units of Madrid Community (university hospitals La Paz, Ramón y Cajal, Doce de Octubre, La Princesa and Niño Jesús) and university hospital La Fe of Valencia was carried out between 1st of March and 31st of May 2012 [4].

The genetic, microbiological, demographic and clinical characteristics of each individual were analyzed. The CF diagnosis was established in accordance with international guidelines [6,7].

All patients underwent a genetic study involving 47 mutations in each simple using the test Inmunogenetics®, Innolipa CF-17, CF-19 and Deletions CFTR +6 and it was expanded if the mutation was unknown. At the time of writing, the genetic study was pending completion.

The lung function parameters studied were: forced vital capacity (FVC) in milliliters and percentage of predicted (ppFVC), forced expiratory volume in one second (FEV1) in milliliters and percentage of predicted (ppFEV1) and FEV1/FVC relation. The

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Table 1
Demographic characteristics.

Clinical and demographic characteristics	N = 8	%	Median	Range
Gender (females/males)	7/1	87.5%/12.5%		
Age at diagnosis (years)			70.6	60—78
Nationality:				
Spain	8	87.5%		
Ecuador	1	12.5%		
Clinical characteristics:				
Bronchiectasis	**8**	**100%**		
Pancreatic insufficiency	**2**	**25%**		
Rheumatoid arthritis	**1**	**12.5%**		
Familiar history of CF	**0**	**0%**		
2 or more pathologies at diagnosis	**3**	**37.5%**		

chronic or intermittent bronchial infection in these patients was analyzed, taking the microbiological data of bacteria, mycobacteria and fungi. These variables were studied at the time of data collection (or the closest possible).

Statistical analysis was performed using SPSS version 22.0 statistics. Quantitative variables were expressed as median and interquartile range. The qualitative variables were expressed as number of patients and their percentage.

Data was taken from the medical records of each patient. The study followed the ethical standards of research of the Centers.

3. Results

Eight patients ≥60 years-old were included within 89 diagnosed at ≥18 years-old (8.9%) in our monographic CF Units, and 1.3% of the total patients treated in these Units. Seven patients were women (87.5%) and one male (12.5%) with a mean age of 70.6 (median 71.5 (60—78)) years-old. 7 patients (87.5%) were Spanish and the remaining one was a citizen of Ecuador (Table 1).

The sweat test permitted the diagnosis of all patients studied and the most frequently detected mutation was delF508/delF508 (p.Phe508X). In three cases, we can find mutations whose frequency are less than 1.5%.

The clinical finding at the diagnosis time in all patients was the presence of bronchiectasis, principal reason which motivated the study of CF in this subgroup of patients older than 60 years-old. In addition, pancreatic insufficiency was observed in 2 patients (25%) at the time of diagnosis (Table 1).

The most frequent colonizing microorganism was meticilline sensitive Staphylococcus aureus (MSSA) in 4 out of 8 patients (50%) (Table 2).

Regarding the respiratory function parameters studied, the results showed that most patients had normal lung function or mild obstructive ventilatory impairment (Table 3).

4. Discussion

In The United States, before neonatal screening, the average of

Table 2
Microbiology.

Microorganisms	No cases (n = 8)	%
No colonization	2	25%
Pseudomonas aeruginosa	1	12.5%
MRSA[a]	0	0%
MSSA[b]	4	50%
Haemophilus Influenzae	0	0%
2 or more (Stenotrophomona + Mycobacterium avium intracelulare)	1	12.5%

[a] MRSA: methicillin-resistant Staphilococcus aureus.
[b] MSSA: methicillin-sensitive Staphilococcus aureus.

Table 3
Pulmonary function.

	Mean (n = 8)	Median	Standard deviation	Range
FEV1 (litres)[a]	1.790	1.880	0.430	(1.15—2.30)
FEV1 (%)	89.33%	94%%	29.11	(42—128)
FVC (litres)[b]	1.577	1.510	0.650	(0.8—2.60)
FVC (%)	83.3%	89%	38.8	(30—138)
FEV1/FVC	70.05%	74.5%	17.73	(43—87)

[a] FVC: forced vital capacity.
[b] FEV1: forced expiratory volume in one second.

the diagnosis was 6 months-old, although 90% of the patients were diagnosed at eight years of age [3,8]. The peculiarity of our study is that patients were diagnosed at ages when many units no longer consider this disease as likely, so it is rare that even a sweat test is applied.

In other European series, which cases with suspected diffuse bronchiectasis were studied, the incidence of CF was 7.6%, with an average age of 31 (18—56) years-old. No patient exceeded 60 years-old, as in our series [6]. In our Units, the most part of the patients presented pancreatic sufficiency and only two of them had pancreatic insufficiency at the time of diagnosis, similar to other studies [2,3,5,9].

Among our patients, MSSA bronchial infection was the most frequent, being the P. aeruginosa bronchial infection, the second one in frequency (12.5%). The chronic bronchial infections and bronchiectasis were the most typical pulmonary complications.

Our patients have a mean ppFEV1 of 89%, in contrast to other series, in which the estimated ppFEV1 was lower [6,9,10]. Perhaps this is due to the patients being firstly diagnosed with other diseases, like asthma or COPD, so they were "misdiagnosed and wrongly treated" for many years [5,6].

Another possible explanation could be that the patients who are diagnosed at above 40 years of age, would be carriers of mutations considered mild or of low risk, with predominantly negative or borderline sweat tests, which would be associated with better prognosis [11]. In these cases, other diagnostic techniques should be considered, such as the study of differential nasal potential, especially in those with undetermined chloride ion concentration values (40—60 mEq/L) or questionable genetic tests [11—14].

Other causes leading to diagnosis found in our study were male sterility, allergic bronchopulmonary aspergillosis (ABPA) and recurrent respiratory infections. None of our patients have recurrent pancreatitis, despite that being one of the most common clinical manifestations and diagnostic suspicions in other series, both children and adults with CF [7,15,16].

Thus, CF should also be considered a disease to be diagnosed in adulthood, including the sweat test within the usual tests of differential diagnosis in patients with diseases, such as bronchiectasis or chronic bronchial infection of unknown etiology. It is important

that diagnosis be made because this disease involves an indispensable genetic counselling procedure in their families.

Conflict of interest

Neither of the patients have conflict of interests and agree with the manuscript.

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