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Review Article

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Atelectasis with Torpid Evolution in Patients with Cystic Fibrosis

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Background

Cystic fibrosis (CF) is a chronic and progressive disease. Respiratory complications, usually, afect the quality of life, morbidity and prognosis of the disease [1-4]. Within respiratory complications, atelectasis is which the least medical literature has generated, without consensus on its etiology, prognosis and treatment [5]. In a previous study of our group, the incidence was 2.66%, 2.33% were lobar and 1.33% segmental [6]. Among the causes would be the existence of mucus plugs or alterations of the pulmonary architecture in which, the progressive and irreversible damage of the airway could cause distortion, obstruction and bronchial dilatation [5,7-11].

Currently, there are very few studies with a small number of cases that analyze the impact of atelectasis in the prognosis of CF. Atelectasis could be a variable of bad prognosis as a complication in CF. In this paper, we describe eleven cases, whose evolution was affected after being diagnosed with a pulmonary atelectasis, either by dying, entering the waiting list of lung transplant or, finally arriving at a lung transplant. We would like to show that patients suffering from these complications can have a worse prognosis and a lower survival.

Presentation of the Cases

This study is part of a more complex work in which patients with cystic fibrosis who have suffered at least one episode of atelectasis are being analyzed. We analyzed 46 patients who had suffered an episode of atelectasis in multidisciplinary CF units at a national and international level, collected from their beginning until July 2017. The follow-up of the cases has been carried out from the appearance of the complication until, at least, two years later. From this broader work, we have studied the cases of torpid evolution (Table 1, Table 2a and Table 2b).

Results

In our study, 11 out of of 46 patients (23.9%) who had suffered atelectasis during their follow-up, had a torpid evolution. Of these, six patients were women (54.5%). The mean age of the patients at the moment of lung transplantation and their death was 32-years-old.

Five patients died (45.5%), of which one was during the transplant surgery, another on the lung transplant list and three others without being able to access the waiting list for lung transplantation due to the rapidity of the respiratory worsening. Phe508del was the most frequent. Most of them had pancreatic insufficiency (72.7%). With respect to other pulmonary complications, the most striking finding was that three patients had hemoptysis (27.3%), of which two required embolization (18.2%) (Table 1).

According to microbiology at the time of atelectasis, most of them had chronic bronchial infection (81.8%): *Pseudomonas aeruginosa* stood out in eight of 11 patients (72.7%), followed by *methicillin-sensitive Staphylococcus aureus* in six of them (54.5%) (Table 1).

Regarding the location of atelectasis, five patients

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Table 2a: Evolution of pulmonary function and exacerbations.

	Spirometry closest to atelectasis (FEV1%-1)	Spirometer 6 months after atelectasis (FEV1%-2)	Spirometer 12 months after atelectasis (FEV1%-3)	Spirometer 24 months after atelectasis (FEV1%-4)	Last available spirometer (FEV1%-5)
Case n° 1					
FEV1	2340 ml/52%		1750 ml/38%	2110 ml/46%	770 ml/17%
FVC	3550 ml/66%		3020 ml/56%	3410 ml/63%	1270 ml/23%
FEV1/FVC	65.97%		58%	62%	61%
Exacerbations	Previous year to atelectasis: 2 O, 0 IV		Year after atelectasis: 6 O, 8 IV		Last year of follow up: 1 O, 2 IV
Case n° 2					
FEV1	1760 ml/52%		1760 ml/52%	1620 ml/48%	830 ml/26%
FVC	2610 ml/67%		2630 ml/68%	2570 ml/67%	1580 ml/42%
FEV1/FVC	61%		61%	62%	57%
Exacerbations	Previous year to atelectasis: 3 O, 1 IV		Year after atelectasis: 9 O, 2 IV		Last year of follow up: 4 O, 3 IV
Case n° 3					
FEV1	760 ml/27%	1190 ml/37.50%	1270 ml/40.30%	1360 ml/43.10%	1360 ml/43.10%
FVC	2280 ml/64%	1950 ml/53%	2120 ml/58.6%	2330 ml/64.54%	2330 ml/64.54%
FEV1/FVC	33%	61%	60%	58.40%	58.40%
Exacerbations	Previous year to atelectasis: 3 O, 1 IV		Year after atelectasis: 3 O, 1 IV		Last year of follow up: 3 O, 1 IV
Case n° 4					
FEV1	1880 ml/62%	1810 ml/61%	2040 ml/67%		1130 ml/30%
FVC	4200 ml/97%	4400 ml/104%	5040 ml/116%		2300 ml/44%
FEV1/FVC	63%	60%	58%		58%
Exacerbations	Previous year to atelectasis: 2 O		Year after atelectasis: 2 O		Last year of follow up: 1 O, 2 IV
Case n° 5					
FEV1	2210 ml/65%				1110 ml/33% (Pre-transplant)
FVC	3320 ml/85%				2120 ml/51% (Pre-transplant)
FEV1/FVC	66.39%				52.54% (Pre-transplant)
Exacerbations					Last year of follow up: 4 O, 1 IV
Case n° 6					
FEV1	1570 ml/37%	1710 ml/41%	1760 ml/42%	1560 ml/37%	1290 ml/31% (Pre-transplant)
FVC	2880 ml/55%	3490 ml/68%	2970 ml/58%	2880 ml/56.50%	2740 ml/54% (Pre-transplant)
FEV1/FVC	55%	49%	59%	54%	47% (Pre-transplant)
Exacerbations	Previous year to atelectasis: 1 O, 3 IV		Year after atelectasis: 2 O		Last year of follow up: 4 O, 1 IV
Case n° 7					
FEV1	1160 ml/42%	600 ml/22%	750 ml/28%	410 ml/15%	410 ml/15%
FVC	2420 ml/76%	1840 ml/59%	2140 ml/68%	1220 ml/39%	1220 ml/39%
FEV1/FVC	47%	32.50%	35%	34%	34%
Exacerbations	Previous year to atelectasis: 1 O, 3 IV		Year after atelectasis: 2 O, 3IV		Last year of follow up: 6 O, 3 IV
Case **n° 8**					
FEV1	940 ml/26%	710 ml/20%	715 ml/20%	850 ml/24%	760 ml/23% (Post pneumonectomy)
FVC	1350 ml/30%	1270 ml/32%	1300 ml/32%	1330 ml/33%	1330 ml/34% (Post pneumonectomy)
FEV1/FVC	69%	55%	55%	64%	57% (Post pneumonectomy)
Exacerbations	Previous year to atelectasis: 3 O, 3 IV		Year after atelectasis: 2 O, 0 IV		Last year of follow up: 2 O, 1 IV

Case **n° 9**					
FEV1	630 ml/21.70%		670 ml/23.40%	640 ml/22.50%	2520 ml/77.20% (Post transplant)
FVC	1210 ml/36.40%		1610 ml/48.70%	1610 ml/49.20%	2690 ml/65.90% (Post transplant)
FEV1/FVC	51.89%		41.77%	39.70%	93% (Post transplant)
Exacerbations	Previous year to atelectasis: 2 O, 1 IV		Year after atelectasis: 1 VO		Last year of follow up: 1 VO
Case **n° 10**					
FEV1	1290 ml/31.9%		1110 ml/27%	3600 ml/87% (Post transplant)	3400 ml/83.1
FVC	2510 ml/52%		2180 ml/44%	3810 ml/78.3% (Post transplant)	4070 ml/83.9%
FEV1/FVC	51.40%		51%	94.61% (Post transplant)	84%
Exacerbations	Previous year to atelectasis: 5 O, 3 IV		Year after atelectasis: 7 O, 4 IV		Last year of follow up: 1 VO
Case **n° 11**					
FEV1	1100 ml/38%		850 ml/28%	2890 ml/95% (Post transplant)	2890 ml/95%
FVC	1870 ml/55%		1680 ml/45%	3420 ml/91% (Post transplant)	3420 ml/91%
FEV1/FVC	59%		51%	85% (Post transplant)	85%
Exacerbations	Previous year to atelectasis: 7 O		Year after atelectasis: 5 O, 3 IV		Last year of follow up: 3 O, 4 IV

FEV1: Forced expiratory volume in one second; FVC: Forced vital capacity; O: Oral; IV: intravenous; ml: milliliters.

Table 2b: Differences found in lung function during the evolution.

Patients	**Differences in FEV1 ml/ppd and FVC ml/ppd at the atelectasis diagnosis (0 months) vs. 6, 12 and 24 months and the last collected**			
	FEV1 (6-0) **FVC (0-6)**	**FEV1 (12-0)** **FVC (12-0)**	**FEV1 (24-0)** **FVC (24-0)**	**FEV1 (last-0)** **FVC (last-0)**
1		-590/-14 -530/-14	-230/-6 -140/-3	-1570/-35 -2280/-43
2		0/0 20/1	-140/-4 -40/0	-930/-26 -1030/-25
3	420/10.5 -330/-11	510/13.3 -130/-5.4	600/16.1 50/0.54	600/16.1 50/0.54
4	-70/-1 200/7	160/5 840/19		-750/-32 -1900/53
5				-1100/-32 -1200/-34
6	140/4 610/13	190/5 840/19	-10/0 0/1.5	-280/-7 -140/-1
7	-560/-20 -580/-17	-410/-14 -280/-8	-750/-25 -1200/-37	-750/-25 -1200/-37
8	-230/-6 -80/?	-225/-6 -50/?	-90/-2 -20/?	-180/-3 -20/?
9		40/1.7 400/12.3	10/0.8 400/12.3	1990/55.5 (post-Tx) 1480/29.5
10		-180/-4.9 -330/-8	2310/35.1 (post-Tx) 1300/26.3	2150/51.2 1560/31.9
11		-250/-10 -190/-10	1790/57 (post-Tx) 1550/36	1790/57 1150/36

FEV1: Forced expiratory volumen at first second; FVC: Forced vital capacity; ml: Mililitres; ppd: Predicted percentage; Tx: Transplant.

presented it in the right upper lobe, of which one of them evolved to complete pulmonary atelectasis. One patient presented segmental atelectasis and, finally, one patient suffered two episodes of atelectasis. None of them had

radiological resolution of the complication (Table 1).

Lung function after the onset of atelectasis had a tendency to fall during the follow-up period (Table 2a, Table 2b, Figure 1 and Figure 2). Although no statistical differences were observed, mean z-scores of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) decrease three, six and 12 months after the onset of atelectasis. Concerning CF respiratory exacerbations, we also founded a tendecy of increasing the number of exacerbations one year after the episode of atelectasis.

Discussion

Atelectasis are well-recognized pulmonary complications that affect the upper lobes due to mucoid occupation, infectious process or aspiration, being essential to favor the clearance of the airway as quickly as possible to avoid complete lung collapse [2,5,9-11], as we have observed in our work. Some authors considered that there might be a genetic predisposition towards a specific location, especially in children [5,12]. Although the incidence published was 4-11%, the one published by our group was 2.66% [6] .

In the current study, we found that 23.9% presented a poor evolution, which led us to believe that atelectasis could adversely affect the survival of patients with CF, by favoring respiratory infections and a worsening of lung function. The mean age of these patients was lower than those published (more than 40 years) [1]. It is well known that pulmonary exacerbations are associated with a aggravation of the disease [13,14]. In our cases, we have observed an increase in the number of exacerbations, which would explain their torpid evolution.

All the patients in our study, with the exception of one,

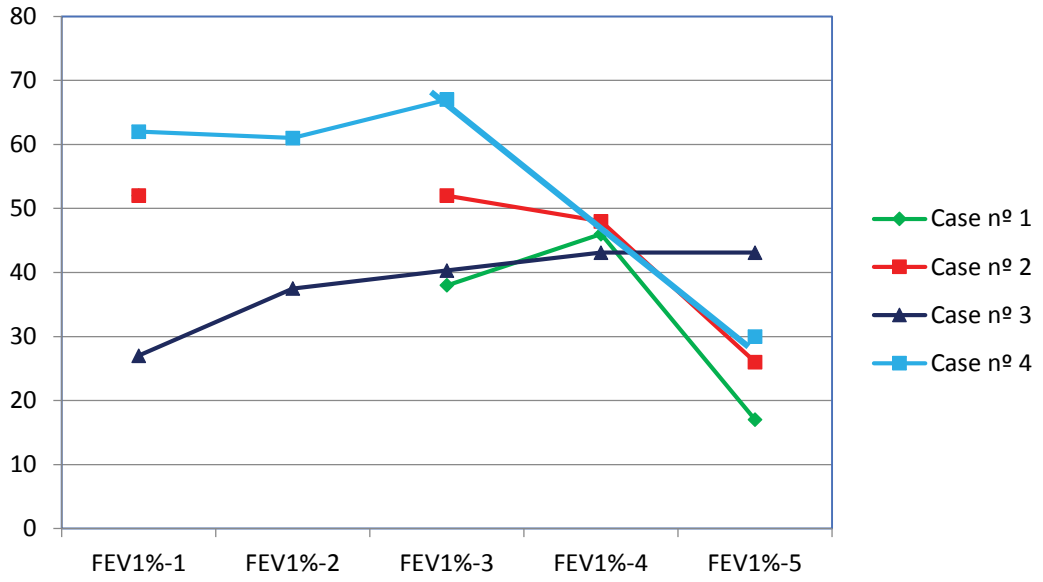

Figure 1: Evolution of FEV1 (predicted percentage) of died patients.

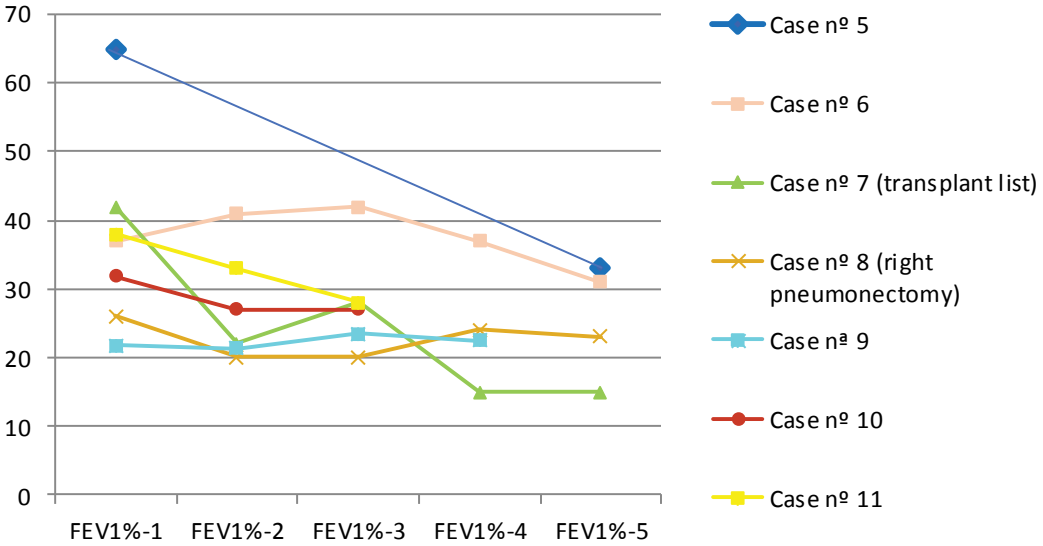

Figure 2: Evolution of FEV1 (predicted percentage) of the alive patients until the lung transplant.

were carriers of the Phe508del mutation. This mutation is associated with worse pulmonary function, more bronchial infections and other complications, and a worse prognosis [15].

Women presented a greater fall in lung function and showing the dysregulation in the production of mucus influenced by estrogen [13,16]. Despite the fact that, in general, women have a worse prognosis, we have not found a correlation between the atelectasis of torpid evolution and the female gender.

Different risk factors have been postulated in the development of atelectasis increasing the viscosity of the pulmonary mucus, such as chronic bronquial infection, hyperglycemia and hemoptysis [5]. The relationship of ABPA with the etiology of the atectasias is very controversial, since it could favor the development of mucosal impaction [3,6,13,17,18]. Three of our patients had episodes of hemoptysis. The atelectasis and its inflammation could trigger the onset of hemoptysis. But, likewise, the treatment of hemoptysis, when removing physiotherapy and inhaled therapy for its control, could cause them. In our work, all of our patients had a chronic bronchial infection.

The use of the flexible bronchoscope with instillation of substances with mucolytic effect has been described in patients with atelectasis who have not responded to the usual treatment or as a diagnostic method [18], but without There is no available bibliography on its effective value in the treatment of this complication [6,8,19]. Surgery as a treatment is of doubtful value and only justified by the persistence of atelectasis during a prolonged period with worsening of the disease [10]. In our study, a patient needed a right pneumonectomy, which led to clear clinical improvement and good subsequent evolution. Five patients required a fiberoptic bronchoscopy; saline serum was instilled in four of them, adding DNAse in only one case, without achieving radiological improvement.

According to our results of the present study, several risk factors could be established for the appearance of atelectasis with torpid evolution, such as the fact of being a carrier of the Phe508del mutation, taking into account that this mutation correlates with more severe clinical manifestations, location in the upper lobes, having comorbidities associated with CF, as well as presenting previous pulmonary complications, especially chronic bronchial infection and hemoptysis.

Conclusions

We can conclude that atelectasis seems to cause an increase in pulmonary exacerbations and rapid respiratory deterioration, so it is necessary to treat it early, mainly with different measurements to reduce the sputum viscosity. Among the limitations of the work we found: 1) The small number of patients which prevents concluding if the aggravation of these patients is due to the presence of atelectasis or the underlying disease; 2) This study is retrospective; but this would allow us to analyze the data and the characteristics of the patients more quickly. We believe that, after these results, it is necessary to continue analyzing this complication with multicentre studies.

Conflicts of Interest

"The authors declare no conflict of interest". "The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results".

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