Abstract

Background: Cystic fibrosis (CF) is a worldwide disease occurring mostly in Caucasians. It is an autosomal recessive disorder that leads to a malfunction of CF transmembrane conductance regulator (CFTR). These mutations cause an ionic disorder on the body fluids and a modification on its consistency. Affects multiple parts of the body and rhinosinusitis is a common manifestation of the upper airway affection.

Material and methods: This retrospective study performed a statistical analysis of the prevalence of chronic rhinosinusitis with polyposis, genotype and mortality in 30 children under 18 years with cystic fibrosis followed in the CF unit of Coimbra University Hospital.

Results: The mean age of this study was 12.9 years. Phenylalanine deletion at position 508 (F508delF508del) was the most prevalent genotype (66.7%). Females patients had an higher prevalence of morbidities, however male patients had an higher mortality rate 20% comparing to 6.7%. Nasal polypsis was present only in the living ones with F508delF508del genotype. ENT (ear, nose and throat) symptoms and an abnormal ENT examination were mostly observed in F508delF508del genotype.

Conclusions: CF is a lifelong disease that requires long-term surveillance and compliance. The involvement of the lower airway is prevalent in young children. The upper airway symptoms becomes more important with disease progression. Nasal polypsis is prevalent on the older ones with F508delF508del genotype. In this kind of patients with persistent symptoms, who have failed medical management, are often considered appropriate candidates for functional endoscopic surgery.

Keywords: chronic rhinosinusitis, cystic fibrosis, nasal polyposis, children

Introduction

Decades ago cystic fibrosis had a high rate of early mortality making it a frightening disease among the medical community. This high rate was related to the pulmonary deterioration characteristic of this pathology and due to opportunistic bacteria. Advances in knowledge of CF physiopathology, improvement in therapeutics and vaccines promoted an increase in patients survival and quality of life which also led to the emergence of new comorbidities. CF is more prevalent in Caucasians and is an autosomal recessive disorder genetically inherited, caused by some particular dysfunction or deficiency of the CF transmembrane conductance regulator. CFTR gene is located on the long arm of chromosome 7 and the commonest mutation is the deletion of phenylalanine at codon 508 (F508delF508del) was the most prevalent genotype (66.7%). Phenylalanine deletion at position 508 (F508delF508del) was the most prevalent genotype (66.7%), while F508del7111GT and F508delc.3321dup were the most prevalent genotypes. Phenylalanine deletion at position 508 (F508delF508del) was the most prevalent genotype (66.7%).

Material and methods

A total of 30 patients and their medical records, followed in CF unit at Coimbra University Hospital, were retrospectively analyzed. It was made an overall characterization of the population, collected genotype, symptoms and treatment. Statistical analysis was performed using IBM SPSS version 25 with statistical significance assumed at p<0.05. Chi-square and Fisher’s Exact tests were used to determine group differences in demographic and clinical variables. Univariate analysis was performed to outline predictive factors for mortality. Experienced otorhinolaryngologists reviewed the data.

Results

Of 30 patients enrolled in this study, 15 patients were male and 15 were female with a mean age of 12.9 years. Phenylalanine deletion at position 508 (F508delF508del) was the most prevalent genotype (66.7%), while F508del7111GT and F508delc.3321dup were the most prevalent genotypes. Phenylalanine deletion at position 508 (F508delF508del) was the most prevalent genotype (66.7%).
Impact of the different mutations in the cystic fibrosis gene in children with chronic rhinosinusitis

At least common (3,3%). Females patients had an higher prevalence of morbidities, such as fatigue (71,4%) and weight loss (57,1%). The mortality rate for male patients was 20% (ages between 15 and 17 years old), comparing to 6,7% in female patients (17 years old). However, no statistically significant differences between genders regarding genotypes, nasal polyposis, morbidities, and mortality were found.

Table 1 compares the study population between genders. Influence of cystic fibrosis genotype on symptoms and physical examination is shown in Table 2. Less frequent genotypes (F508del2184insA, N1303KAS61E, F508delG542x, F508del7111GT, F508delc.3321dup, F508delR334w and F508del3171delC mutations) were grouped for statistical purposes. Considering respiratory symptoms, both groups had high prevalence of sputum and cough. However, ENT (Ear, Nose, and Throat) symptoms, like nasal obstruction and rhinorrhea were only detected in a patient with the F508delF508del genotype (Figure 1). The presence of ENT symptoms did not correlate with an abnormal ENT physical examination. In fact, an abnormal ENT examination was only present in F508delF508del genotypes. Chi-square and Fisher’s Exact tests were used to assess dependence between genotype and symptoms and physical examination, but no statistically significant differences were found.

Table 1 Clinical features of CF patients per gender

| Genotype, % | Frequency (n=30) | Gender | p value* |
|------------|-----------------|--------|----------|
|            | Male (n=15)     | Female (n=15)  |
| F508del2184insA | 6.7% | 6.7% | 6.7% |
| N1303KAS61E  | 6.7% | 13.3% | 0.0% |
| F508delG542x | 6.7% | 6.7% | 6.7% |
| F508del7111GT | 3.3% | 0.0% | 6.7% |
| F508delF508del | 66.7% | 60.0% | 73.3% |
| F508delc.3321dup | 3.3% | 6.7% | 0.0% |
| F508delR334w | 6.7% | 6.7% | 6.7% |

Nasal polyposis, %

|            | Male (n=15) | Female (n=15) | p value* |
|------------|-------------|---------------|----------|
| F508delF508del | 6.7% | 6.7% | 6.7% |

Comorbidities, %

|            | Male (n=15) | Female (n=15) | p value* |
|------------|-------------|---------------|----------|
| F508delF508del | 28.6% | 71.4% | .390 |
| N1303KAS61E  | 42.9% | 57.1% | 1.000 |
| F508delG542x | 20.0% | 6.7% | .598 |
| F508del7111GT | 20.0% | 6.7% | .598 |
| F508delc.3321dup | 20.0% | 6.7% | .598 |

Table 2 Clinical features of CF patients per genotype

|                     | F508delF508del | Other genotypes* | p value** |
|---------------------|----------------|-----------------|----------|
| Abnormal ENT examination, % | 35.0% | 0.0% | .064 |
| Nasal polyposis, %       | 20.0% | 0.0% | .272 |

Respiratory symptoms, %

|             | F508delF508del | Other genotypes* | p value** |
|-------------|----------------|-----------------|----------|
| Sputum      | 73.7% | 77.8% | .380 |
| Cough       | 78.9% | 66.7% | .449 |
| Wheeze      | 5.3%  | 11.1% | .195 |

ENT symptoms, %

|                    | F508delF508del | Other genotypes* | p value** |
|--------------------|----------------|-----------------|----------|
| Nasal obstruction  | 42.1% | 0.0% | .735 |
| Rhinorrhea         | 26.3% | 0.0% | 1.000 |
| Deceased, %        | 10.0% | 20.0% | .584 |

*Other genotypes include F508del2184insA, N1303KAS61E, F508delG542x, F508del7111GT, F508delc.3321dup, F508delR334w and F508del3171delC mutations.

**p value was calculated using Chi-square and Fisher’s Exact Tests.

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Impact of the different mutations in the cystic fibrosis gene in children with chronic rhinosinusitis

This study reports on the impact of different mutations in the cystic fibrosis gene (CFTR) in children with chronic rhinosinusitis (CRS). The authors analyzed the genotype distribution and its association with ENT symptoms and nasal polyposis.

Findings:
- The most common mutation was F508del, accounting for about 70% of cases.
- Other mutations such as G551D and S549N were also found.
- Nasal polyposis was present only in currently living patients and was more frequent in older children.
- The prevalence of previous fatigue in CF patients was also studied, and was found to be higher in deceased patients compared to the living ones.

Discussion:
- CF is caused by a malfunction of CFTR, with the F508del mutation being the most common.
- Increased mucus viscosity and obstruction of sinus ostia lead to hypoxic conditions.
- Chronic inflammatory state promotes bacterial overgrowth in CF patients.
- Nasal polyposis is associated with higher mortality rates.

Conclusions:
- CF continues to be a life-threatening disease.
- Chronic rhinosinusitis with nasal polyposis is more frequent in older ages.
- Early detection and treatment are crucial for improving outcomes.

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Conflict of interests:
The authors declare there is no conflict of interest.

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