Journal of Cystic Fibrosis 12 (2013) 266–270

Journal of Cystic Fibrosis

www.elsevier.com/locate/jcf

Original Article

Nasal polyposis in lung transplant recipients with cystic fibrosis

Domenic Vital [a], David Holzmann [a], Annette Boehler [b], Markus Hofer [b,*]

[a] Division of Otorhinolaryngology Head and Neck Surgery, University Hospital, Zurich, Switzerland
[b] Division of Pulmonary Medicine, University Hospital, 8091 Zurich, Switzerland

Received 22 April 2012; revised 14 July 2012; accepted 17 August 2012
Available online 18 September 2012

Abstract

Background: Chronic rhinosinusitis with nasal polyposis is common in patients with cystic fibrosis (CF). There are still many open questions regarding factors related to this condition. Furthermore, the prevalence of nasal polyposis and its implications for the outcomes in lung transplant recipients with cystic fibrosis are unknown.
Methods: All CF patients who underwent lung transplantation at our centre between November 1992 and December 2009 were included. Nasal polyp status was determined endoscopically at time sinus surgery and its relationships to gender, age at lung transplantation, Liou raw score, body mass index, FEV_1%predicted, diabetes mellitus, pre-transplant pseudomonas colonisation of the sinuses and the lungs, pre-transplant corticosteroid use and type of mutation of the CFTR gene were analysed. The post-transplant survival times and the incidence of bronchiolitis obliterans syndrome in patients with or without nasal polyposis were compared.
Results: Nasal polyps were found in 19% (17 patients) of the 89 lung transplant recipients, whose data was available for statistical analysis. None of the factors analysed was related to the nasal polyp status. The post-transplant survival times and the incidence of bronchiolitis obliterans syndrome did not significantly differ between patients with or without nasal polyposis.
Conclusions: CF-related nasal polyposis occurs in a relevant fraction of lung transplant recipients. A specific effect of nasal polyposis on post-transplant outcome could not be confirmed. Nevertheless, there was a trend to NP recurrence in patients with post-transplant sinonasal pseudomonas colonisation and is a tendency of less chronic rejection in CF patients with nasal polyps.

Keywords: Cystic fibrosis; Lung transplantation; Chronic rhinosinusitis; Nasal polyposis; Survival; Bronchiolitis obliterans syndrome

1. Introduction

Chronic rhinosinusitis with nasal polyposis (NP) is common in patients with cystic fibrosis (CF), with an estimated prevalence of 6–48% [1–7]. Despite its frequency, there are still many open questions regarding the origin of polyp growth. Some argue that the CF genotype may play a major role [1,8–10], and chronic colonisation with *Pseudomonas aeruginosa* might be a co-factor for NP [11].

Some studies have suggested that CF patients with NP show milder lung disease and have better survival rates than patients without NP [1,5,6,9], whereas others found no relationship between NP status and the severity of CF [12]. Moreover, the influence of a potentially specific CF phenotype with NP on bronchiolitis obliterans syndrome (BOS) and survival after lung transplantation (LTx) is not known, but might have both practical and prognostic implications in this group of patients with terminal CF lung disease.

The aim of this study was to determine the prevalence of NP in CF patients undergoing lung transplantation, to identify potential predictors for NP and to examine the survival and cumulative incidence of BOS of lung transplant recipients with and without NP.

* Corresponding author at: Division of Pulmonary Medicine, University Hospital Zurich, Raemistrasse 100, 8091 Zürich, Switzerland. Tel.: +41 44 255 39 26; fax: +41 44 255 89 97.
E-mail address: mhofer@hispeed.ch (M. Hofer).

1569-1993/$ -see front matter
http://dx.doi.org/10.1016/j.jcf.2012.08.013

2. Methods

All CF patients undergoing LTx at our centre between November 1992 and December 2009 were included in this study, and the data was collected retrospectively. The lung transplant recipients were followed until the end of December 2011, representing a minimum follow-up of two years per patient. The candidates for LTx were carefully selected following the international guidelines of the ISHLT Pulmonary Scientific Council [13]. The transplantation type was a sequential bilateral lung transplantation as described previously [14].

The standard protocol of immunosuppression (cyclosporine, azathioprine or mycophenolate mofetil and prednisolone) and induction therapy (anti-thymocyte globulin or basiliximab) was followed as described by Speich et al. [15]. On the basis of the sputum cultures, all patients were treated with a combination of at least two antibiotics for *Pseudomonas aeruginosa* (PA) for at least the first two weeks after LTx [14]. Further prophylactic therapy included cotrimoxazole, acyclovir/valacyclovir, oral itraconazole and nebulised amphotericin B. In addition, all transplant recipients with CF received a nebulised therapy with Colistin as prophylaxis against infection [14]. Inhalations with Colistin started immediately after LTx and were continued lifelong if patients had airway cultures positive for PA.

After the patient recovered from the transplantation, routine sinus surgery was performed as described previously [16]. Nasal polyp (NP) status was determined using the rigid endoscope at time of sinus surgery. The surgery consisted of an endoscopic fronto-spheno-ethmoidectomy as descried elsewhere [17,18]. In this procedure, all sinuses are widely opened and explored no matter how well they are pneumatised [16]. Daily nasal douching with isotonic saline solution was initiated on the second day after surgery. A potential relapse of NP was determined at the post-transplant follow-up visits by nasal endoscopy.

Microbiological sampling was performed with bronchoscopy and bronchoalveolar lavage (BAL) along with nasal endoscopy and aspiration of sinus secretions. Bacterial colonisation with PA was considered significant if bacterial counts were 10^4 colony-forming units/ml or more.

The diagnostic criteria for bronchiolitis obliterans syndrome (BOS) were applied as described elsewhere [19]: BOS 0 was defined as FEV_1 (forced expiratory volume in 1 s) >90% of baseline and FEF25-75 (mid-expiratory flow rate) >75% of baseline; BOS 0-p as FEV_1: 81 to 90% of baseline and/or FEF_{25-75}: ≤75% of baseline; BOS 1 as FEV_1: 66 to 80%; BOS 2 as FEV_1: 51 to 65%; and BOS 3, FEV_1: ≤50% of baseline. Estimated pre-LTx survival was calculated according to Liou et al. [20].

3. Statistical analysis

Descriptive statistics were used, and the mean and 95% confidence intervals (95% CI) are reported. Two groups were defined: Patients with nasal polyps (with NP) and without nasal polyps (without NP) at time of sinus surgery. Mann–Whitney tests and Fisher's Exact Tests (2×2 tables) were used to compare these groups, and a p-level <0.05 was considered as significant (two-tailed).

Survival and BOS following LTx were evaluated using Kaplan–Meier estimates. The groups with or without NP were compared with log rank tests. A multivariate analysis for the development of NP was performed. The following parameters were evaluated: gender, pre-transplant FEV_1, BMI, estimated survival without LTx, pre-transplant sinonasal and pulmonary PA colonisation (prePA-nose and prePA-lung), systemic pre-transplant corticosteroid treatment (preCS-use), pre-transplant diabetes (CFDM) and dF508 homozygosity. NP relapse rates and its relation to post-transplant sinonasal and pulmonary PA colonisation (postPA-nose and postPA-lung) were analysed using Fisher's Exact Tests (2×2 tables). IBM® SPSS® Statistics version 19 was used for the statistical analysis.

The institutional review board of the University Hospital Zurich (Kantonale Ethikkommission Zurich) approved this retrospective study.

4. Results

Five of the 94 CF patients did not undergo sinus surgery due to allograft deficiency, multiorgan failure or severe infection/sepsis and were excluded due to missing information on NP. The 89 evaluated patients (44 females, 49%) had a mean age of 26.9 years (95%CI 25.2–28.6 years) at LTx, a pre-LTx FEV_1 of 1.0 l (0.65–1.40 l) (26% of predicted FEV_1 (24–27%)) and an estimated 5-year survival without LTx of 33% (30–36%) (Table 1). Seventeen patients (19%) had nasal polyps by rigid endoscopy.

No difference was found regarding gender, pre-transplant FEV_1 or BMI, estimated survival without LTx, pre-transplant sinonasal or pulmonary PA colonisation, systemic pre-transplant corticosteroid treatment, pre-transplant diabetes or the presence or absence of dF508 homozygosity of the CFTR gene (Table 1). In the uni- and multivariate analysis none of the investigated parameters (gender, pre-transplant FEV_1, BMI, estimated survival without LTx, prePA-nose, prePA-lung, preCS-use, CFDM and type of mutation of the CFTR gene) favoured the development of NP.

Table 1
Characteristics of CF patients with and without nasal polyps (NP).

	With NP	Without NP
N, %	17 (19)	72 (81)
Female/male (*n*, %)	9/8 (53/47)	35/37 (49/51)
Age at LTx (year (95%CI))	26 (22–30)	27 (25–29)
Body mass index (kg/m^2, 95%CI)	16.6 (15.8–17.5)	17.7 (17.0–18.3)
FEV_1 (litres, 95%CI)	0.74 (0.65–0.83)	1.09 (0.62–1.55)
FEV_1%predicted (%,95%CI) (%,95%CI)	23 (19–26)	26 (25–28)
Survival without LTx at 5 years (%,95%CI)	31 (24–38)	33 (30–37)
PrePA-nose (*n*, %)	15 (88)	59 (82)
PrePA-lung (*n*, %)	15 (88)	55 (76)
PreCS-use (*n*, %)	4 (24)	23 (33)
dF508 homozygotes (*n*, %)	9 (53)	40 (56)
CFDM (*n*, %)	8 (47)	48 (67)