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RHINOLOGY

Posttransplant sinus surgery in lung transplant recipients with cystic fibrosis: a single institutional experience

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Abstract Chronic rhinosinusitis is hypothesised to play a major role in lung transplant recipients with cystic fibrosis. Paranasal sinuses are considered to accumulate a significant bacterial load, potentially leading to lung allograft infection with ensuing complications such as bronchiolitis obliterans syndrome, i.e. allograft rejection. We therefore would like to present our combined medical and surgical treatment plan, which consists of an endoscopic fronto-spheno-ethmoidectomy as well as a meticulous daily nasal care program. The microbiological results show that our combined concept is effective, whereas especially daily nasal care with isotonic saline solution is the cornerstone in preventing significant colonisation of the sinuses and spreading bacteria to the lower respiratory tract causing lung allograft infection. Regarding the surgical part of our treatment, it should be emphasised that all sinuses and ethmoidal air cells should be widely opened. Edges such as bony overhangs should be smoothened to avoid mucus retention and consecutive bacterial recolonisation requiring subsequent revision surgery.

Keywords Cystic fibrosis · Lung transplantation · Sinus surgery · Chronic rhinosinusitis · Microbiology

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Introduction

Chronic rhinosinusitis (CRS) is common in patients with cystic fibrosis (CF). CF patients may suffer from nasal obstruction due to nasal polyps and mucosal swelling or their sinuses are asymptomatically colonised with bacterial germs. CRS was hypothesised to play an important role in lung transplant recipients with CF as the sinuses can be considered as a bacterial reservoir, from where bacteria may be spread to the lower airways causing lung allograft infection [1–5]. Chronic bacterial infection with *Pseudomonas aeruginosa* and other bacteria leads to the accumulation of neutrophils as seen in bronchoalveolar lavage (BAL) fluid and to unopposed neutrophil elastase. The latter correlates with poor outcome due to bronchiolitis obliterans syndrome (BOS) and progressive irreversible graft dysfunction as described by Nunley et al. [6].

We support this hypothesis of a bacterial reservoir in the sinuses and consequently followed a combined medical and surgical treatment plan for CF-related CRS. This treatment approach was established at the beginning of our lung transplant program in 1992. The results of our 10-year experience were reported in 2004 [7]. There, we already could demonstrate a significant correlation of the sinus bacteriology obtained by sinus aspirates and BAL. Patients with a low colonisation rate in the paranasal sinuses had a significantly lower incidence of tracheobronchitis and pneumonia as well as a trend towards a lower incidence of BOS [7]. In contrast, some authors maintain that surgery is not effective in treating CRS in CF patients [8, 9]. However, they do not clearly define the extent of their surgery and the postoperative care regimen. The objective of this paper is to describe our surgical protocol such as the meticulous postoperative nasal care program and to study its efficacy by analysing microbiological data.

Method

Selection of candidates and timing of surgery

As all CF candidates for lung transplantation (LTx) are far too ill to undergo extensive sinus surgery, it became our standard to perform sinus surgery after LTx. After LTx, patients are treated with at least two antibiotics active against *P. aeruginosa* for a minimal duration of 2 weeks. Sinus surgery is performed after clinical recovery from lung transplantation. Exclusion criteria for sinus surgery are poor outcome after LTx including allograft deficiency, multi organ failure and severe infections/sepsis.

Surgical technique

The surgery begins with a fronto-spheno-ethmoidectomy as described elsewhere [10]. In this procedure, all sinuses are widely opened and explored no matter how well they are pneumatised. Taking into account that the nasal mucosa in CF patients will swell up due to subepithelial cysts, all ethmoidal cells and sinuses are exposed and opened widely to prevent fluid retention. By doing so, rinsing the sinuses will reach almost every corner of the nasal cavities and sinuses. To achieve such cavities, we use diamond drills to smoothen edges and bony overhangs as best as possible. If significant fluid retention with consecutive colonisation and/or polyp formation is encountered (see Fig. 1), revision surgery frequently comprises the removal of the middle turbinate on both sides. Figures 2, 3 shows such cavities.

Postoperative care

Nasal packs are removed the day after surgery. Patients start nasal irrigation with isotonic saline solution 6 h thereafter and continue this rinsing care twice daily. The postoperative follow-up visits are arranged in cooperation with the chest physicians. The objectives of these visits are to supervise and to instruct the nasal care as well as to detect potential infections by nasal inspection and endoscopy. Sinus aspirates are taken and sent for microbiological analysis. Bacterial colonisation was considered significant if CF-relevant pathogens (*P. aeruginosa*, *Staphylococcus aureus*, *Stenotrophomonas maltophilia*, *Achromobacter* (*Alcaligenes*) *xylodoxidans and Burkholderia cepacia complex*) were cultured and bacterial counts were 10^4 colony-forming units/ml or more. Patients with cultures positive

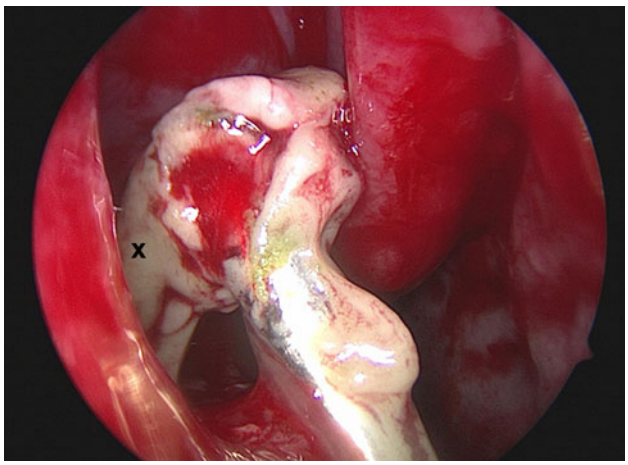

Fig. 1 Retention of purulent secretion and polyp formation in the right maxillary sinus (*cross*): typical intraoperative finding during endoscopic surgery

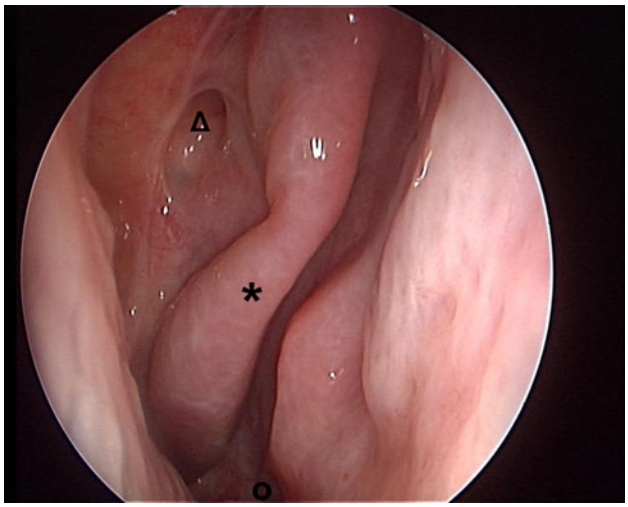

Fig. 2 Endoscopy of the right nasal cavity (2 years after fronto-spheno-ethmoidectomy with removal of the middle turbinate) showing the right sphenoethmoid recess with the sphenoid sinus (*open triangle*) and the superior turbinate (*asterisk*). *Open circle* indicating the direction of the choanae

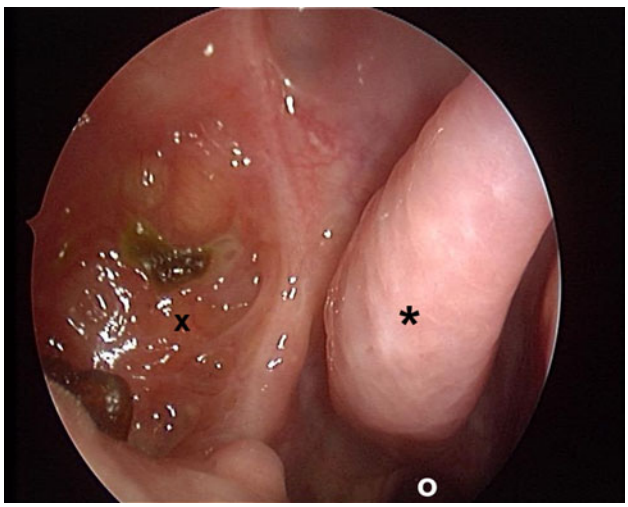

Fig. 3 Endoscopy of the right nasal cavity (2 years after fronto-spheno-ethmoidectomy with removal of the middle turbinate) showing the maxillary sinus with little crusting (*cross*), the superior turbinate (*asterisk*) and the choanae (*open circle*)

Table 1 Baseline characteristics of the CF patients, which underwent LTx between 1992 and 2009

Number of patients	94
Gender (F/M)	47/47 (50/50 %)
Mean age at LTx, years (95 % CI)	26.8 (25.1–28.5)
Sinus surgery	82 (87 %)
Complete data set	77 (82 %)

for these pathogens received specific antibiotic treatment according to the chest physician's recommendation and were instructed specifically to intensify nasal care. Postoperatively, the patient is seen on the occasion of every surveillance bronchoscopy, which is performed monthly during the first 6 months and depending on clinical findings thereafter. From the second year after LTx, sinonasal checks are performed depending on several parameters including inflammation of nasal mucosa, polyp formation, crusting and patient's compliance for nasal care. Emergency follow-ups are performed at the request of the chest physician to check the nasal and sinus cavities e.g. in case of lower airway infection or marked deterioration of FEV1.

Analysis of data

Microbiological culture results were assessed retrospectively and recorded for the period before (preSS), such as the period of the first 12 months after lung transplantation and sinus surgery (postSS). If three or more cultures postSS showed significant bacterial growth of CF-relevant bacteria, the sinuses were considered as "chronically colonised" despite sinus surgery and consecutive nasal care. The status of chronic colonisation postSS was correlated with the status of posttransplant allograft infection. Any growth of CF-relevant bacteria in bronchoalveolar lavage (BAL) fluid was defined as a posttransplant allograft infection. Statistical comparisons were performed using Fisher's exact test.

Results

Baseline characteristics of the patients were listed in Table 1. Since the beginning of our lung transplant program, only 12 (13 %) out of 94 CF lung transplant recipients had to be excluded from sinus surgery due to allograft deficiency, multiorgan failure or severe infections/sepsis. Further five patients (5 %) had to be excluded because of incomplete data sets.

Eradication of CF-relevant bacteria

Sixty-one of the 77 patients (79 %) were harbouring *P. aeruginosa* preSS of whom more than one-third could be eradicated with sinus surgery and consecutive daily nasal care. Of the six patients (8 %) with *S. aureus* in their sinuses preSS, 4 patients (5 %) had persistent sinonasal colonisation. The patients with *S. maltophilia* (3 patients, 4 %) and *A. xylodoxidans* (4 patients, 5 %) preSS were successfully eradicated. One (1 %) of the two patients (2 %) with *B. cepacia complex* had cultures positive for this pathogen postSS (Table 2).

Table 2 Sinus microbiology before (preSS) and after (postSS) sinus surgery

	PreSS	PostSS	Eradication rate (%)
S. aureus	6 (8 %)	4 (5 %)	33
P. aeruginosa	61 (79 %)	40 (52 %)	35
A. xyloxidans	4 (5 %)	0	100
S. maltophilia	3 (4 %)	0	100
B. cepacia complex	2 (3 %)	1 (1 %)	50

Absolute and relative numbers of patients which harboured CF-relevant bacteria preSS and postSS such as the relative number of patients eradicated for each pathogen are given

Table 3 Chronic sinonasal colonisation versus lung allograft infection

	Chronic sinonasal colonisation	
	Yes	No
Lung allograft infection		
Yes	19 (25 %)	3 (4 %)
No	17 (22 %)	38 (49 %)

Absolute and relative numbers of patients with or without chronic sinonasal colonisation and lung allograft infection are given in cross tabulation. Statistical correlations were performed using Fisher's exact test

Fisher's exact test $p < 0.0001$

Correlation of chronic sinonasal colonisation and allograft infection

Chronic sinonasal colonisation postSS could be prevented in 41 patients (53 %) of whom 38 patients (49 %) also had sterile BAL fluid. Nineteen patients (25 %) with chronic sinonasal colonisation showed allograft infection whereas 17 patients (22 %) had sterile BAL fluids although the sinuses were chronically colonised. Fisher's exact test showed a highly significant correlation of sinus colonisation and lung allograft infection ($p < 0.0001$, Table 3).

Evolution of the surgical concept

The first lung transplant recipients with CF underwent limited surgical procedures consisting of a bilateral

ethmoidectomy and wide exposure of the maxillary sinus. At that time, many patients required revision surgery due to recurrent bacterial colonisation of the sinuses and subsequent bronchopulmonal infections of allograft. We noticed in all revision cases mucus retention was due to insufficient exposure of the sinuses. Hence we are now exposing all sinuses aggressively to prevent mucous retention. Mucous and fluid retention correlate more with insufficient opening of the sinus than with its poor pneumatisation. Even small sinuses, e.g. the frontal or the sphenoid sinuses, may retain colonised fluid in CF-related rhinosinusitis. In all the patients requiring revision surgery, we found excavations with significant load of purulent mucus. Consequently, we learned that bony overhangs, especially the floor of the sphenoid sinus, should be removed extensively. We found this could be best achieved with the use of diamond drills. In this context, we also observed an advantage to remove the middle turbinate, which improves the sinus-rinsing process with isotonic saline solution. None of the patients, whose middle turbinate was resected, had any adverse effects.

Post-surgical care

Experiences from the posttransplant care showed that the main factor affecting outcome is patient's compliance in daily nasal care. Irrigation with isotonic saline solution is sufficient in most of the cases and topic antibiotics (e.g. tobramycin) are rarely used. Outcome was also dependent on early detection of infections and resistance-adjusted antimicrobial treatment. A close collaboration between chest physician and otorhinolaryngologist, therefore, is the condition sine qua non.

Discussion

There is an ongoing controversy regarding the effectiveness of sinus surgery in CRS of CF patients. Some authors conclude that sinus surgery might not be effective in preventing bacterial spread to the allograft [8, 9]: Leung et al. [8] recorded a persistent sinonasal colonisation with *P. aeruginosa* in 82 % of the cases and the patients of Osborn et al. [9] showed an identical flora before and after surgery in 49 %, whereas in only 15 % a preoperative pathogen was absent postoperatively. In contrast, sinus surgery with consecutive nasal care was able to eradicate *P. aeurignosa* in more than one-third of our patients and similar or higher rates in other pathogens. An absent pathologic sinonasal colonisation postSS furthermore had direct impact on the transplanted lung reducing allograft infections significantly.

We are convinced that only extensive surgery with wide opening of all sinuses *together* with a meticulous nasal care including regular follow-up visits lead to significant success with significant reduction of sinus colonisation with CF-relevant bacteria and prevention of allograft infection. Consequently, we conclude that the concepts of Leung et al. [8] and Osborn et al. [9] show two major deficits. First of all, their surgical techniques were not clearly defined and limited to the maxillary sinus and the ethmoid. Secondly, a postoperative nasal care program was not included in their concepts [8, 9].

It has been proved that the likelihood of penetration of the sinuses by irrigation is increased by enlarging the dimension of the sinus ostia [11] confirming our strategy of aggressive exposure of all sinuses. In this context, it is also beneficial to resect the middle turbinates, a decision taken in relation to the severity and impact of chronic rhinosinusitis. Bilateral middle turbinate resections are not indicated in most of the cases of non-CF associated rhinosinusitis. In the specific group of CF patients after lung transplantation, however, severity of the disease is mostly always high and its impact vital. According to our almost 20 year experience, we more and more recommend the resection of the middle turbinates so that nasal douching of the maxillary and ethmoid sinus becomes more effective. Up until now, none of our patients have had any side effects such as atrophic rhinitis, anosmia or other iatrogenic problems. The advantages of a better control of sinonasal colonisation by nasal care predominate. As we did, Soler et al. [12] observed a good outcome after bilateral middle turbinate resection with no apparent negative consequences in a non-CF population. Other options such as medialisation of the middle turbinate by sutures were not studied.

Good experiences regarding the effectiveness, handling and costs of a daily rinsing device were made by the use of the "Emser Nasendusche®" (SIEMENS & CO, Heilwasser und Quellenprodukte des Staatsbades Bad Ems GmbH & Co. KG). This device consists of a refillable plastic device (volume 250 ml) and a connection piece, which can be held to the nostrils while the twice daily rinsing is performed. The rinsing itself prevents sinonasal colonisation by increasing mucociliary flow, hydrating the mucosa and by flushing away toxic (microbial) agents [13, 14]. Regarding the osmolarity of saline solution, it is unclear whether iso- or hypertonic solution is more beneficial. Though hypertonic solution might increase mucociliary flow [13, 14], it may decrease patient's compliance due to the side effects of hyperosmolarity (e.g. nasal burning, pain or other irritations) so we prefer isotonic saline solution. Daily nasal care (and related patient's compliance) is the cornerstone in preventing significant colonisation of the nasal and sinus cavities leading to airway infection and consequently worse outcome.

Conclusion

Posttransplant sinus surgery in lung transplant recipients *combined* with postoperative daily nasal care is an effective way to treat CRS in patients with CF and its complications. A consequent postoperative daily nasal care is necessary and crucial for the effectiveness of the therapeutic approach.

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Conflict of interest The authors declare that they have no conflict of interest.

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