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Recovery of non-invasive *Aspergillus* sinusitis by endoscopic sinus surgery*

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SUMMARY

No previous data regarding non-invasive Aspergillus sinusitis (NIAS) treated by endoscopic sinus surgery (ESS) has stated any relevance to pre-operative evaluations, disease entities, and the reversibility of symptoms and the sinus mucosa. This prospective study of 31 patients with NIAS and treated by ESS (Stammberger's method) was designed to tackle the above problems. All patients were followed post-operatively by endoscopy once a week. The most refractory symptom was post-nasal dripping. The other symptoms such as foul odour showed progressive improvement by the second post-operative week. Prolonged saccharin time and disease history longer than two years showed the warning signs of a poor recovery. Most patients belonged to the chronic indolent sinusitis group with 55.5% having a complete recovery within the 9th to 12th post-operative weeks. Most patients of allergic Aspergillus sinusitis manifested a recurrent course within months following a post-ESS silent period. All patients of aspergilloma completely recovered prior to the 8th post-operative week.

Keywords: fungal sinusitis, aspergillosis, endoscopy

INTRODUCTION

Aspergillus infection of the nose and sinuses has been recognized since 1885 (cf., Stammberger et al., 1984). Aspergillosis, especially nosocomial *Aspergillus* infection, is becoming an important cause of morbidity and mortality. There has been an increase in aspergillosis of the sinonasal tract in recent years (Hartwick and Batskis, 1991). *Aspergillus fumigatus* is the species most often implicated in paranasal sinus disease (Stammberger et al., 1984; Jahrsdoerfer et al., 1979). Aspergillosis of the paranasal sinuses may be classified as invasive or non-invasive (Hora, 1965). Treatment of the non-invasive form of infectious aspergillosis is surgical debridement and drainage (Waxman et al., 1987). Surgical debridement of the primary affected sinus, most often through a Caldwell-Luc operation, is the treatment of choice (Parnes et al., 1989). However, Stammberger feels that in the proper hands adequate excision and drainage is possible by utilizing endoscopic surgery alone (Stammberger, 1985).

The emphasis of previous reports focused upon the infectious forms of aspergillosis of the paranasal sinuses and their treatment (McGuirt and Harrill, 1979; Stevens, 1981). None of the earlier reports describing non-invasive *Aspergillus* sinusitis (NIAS) treated by endoscopic sinus surgery (ESS) have discussed the prognostic factors, reversibility and the time course for complete recovery of the symptoms and the sinus mucosa. The aim of this prospective study has been to evaluate the pre-operative profiles, reversibility of the symptoms and the sinus mucosa, the time course for recovery, and a discussion of their relevance in the recovery and treatment of NIAS.

MATERIAL AND METHODS

Starting in 1989, a prospective study of 31 patients with NIAS in National Cheng Kung University Hospital at Taiwan was undertaken. There were 8 male and 23 female patients with their age ranging from 8 to 62 years. Pre-operative evaluations including duration of history, symptoms, saccharin time test, skin test using 10 common Taiwan allergens (Fang et al., 1988), CT scans and a history of systemic diseases were done. All the operative procedures were done by the author himself following the Messerklinger-Stammberger method (Stammberger, 1985). If complete clearance of the fungal masses could not be achieved through endoscopy, the antrum was opened via the anterior canine fossa to clean any residual fungal masses and preserve the mucosa as best as possible (Stammberger, 1985). Using the Gomori methenamine silver stain, all cases were microscopically proven to be positive or negative by identifying the specific fungal hyphae, even if the culture presented a false-negative (Jahrsdoerfer, 1979; Stevens, 1981; Hartwick and Batskis, 1991). These cases were classified into one of the following three

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Table 1. Three non-invasive forms of *Aspergillus* involvement of the paranasal sinuses.

type of sinus involvement	predisposition or vulnerability	extent of involvement and pathologic changes
indolent, chronic sinusitis	usually healthy host; no associated lung disease	maxillary and/or ethmoids; active granulomatous chronic inflammation and/or bone erosion
aspergilloma	usually healthy host or one with chronic sinus disease; post-traumatic; foreign body; no associated lung disease	single sinus, usually maxillary; non-specific chronic inflammation with cavitary "fungus ball"
allergic *Aspergillus* sinusitis	asthma with nasal polyps; atopic or healthy host; usually no associated lung disease	"allergic" inspissated mucin ball or plug no fungus ball, no bone erosion.

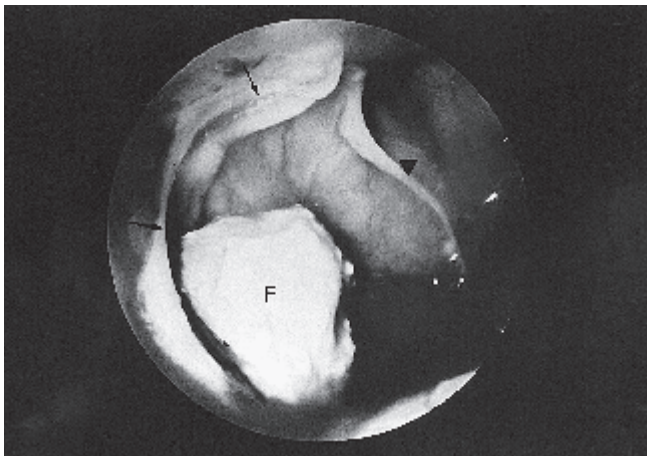

Figure 1. A case of aspergilloma. A fungal ball (F) was present in the maxillary sinus. Scanty mucopus (arrowhead) in the antrum was also noted through the dilated antral-meatal opening (arrows; 4-mm 30° Storz endoscope).

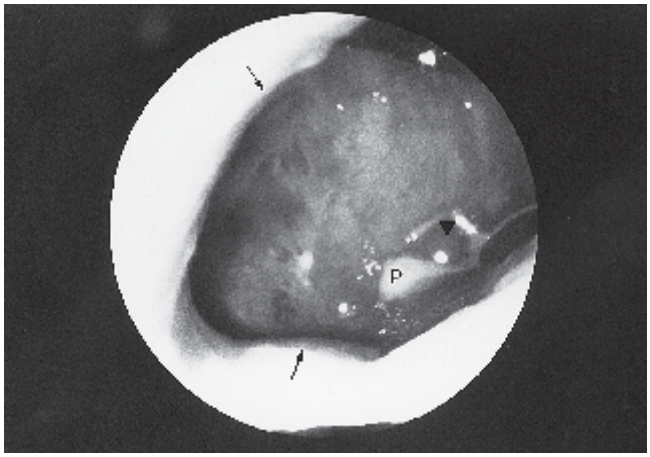

Figure 2. The persistent disease was found in a case of chronic indolent sinusitis at the 16th week of post-ESS course. A residual polypoid mucosa (arrowhead) with thick mucopus (p) was still noted through the antral opening (arrows; 4-mm 30° Storz endoscope).

clinical entities: (1) chronic indolent sinusitis (CIS): 18 cases; (2) aspergilloma: 7 cases (Figure 1); and (3) allergic *Aspergillus* sinusitis (AAS): 6 cases. This classification was based upon clinical characteristics, operative findings and pathological changes (Table 1), as proposed by Hartwick and Batskis (1991).

All patients were followed once a week during their post-ESS course and the recovery of their clinical symptoms was recorded. Irrigation of the sinuses through the dilated antral opening using normal saline and evaluation of sinus mucosa were done by endoscopy during the follow-up. All AAS subjects received topical betamethasone nasal sprays; however, no additional systemic steroids or antibiotics were used. A complete recovery was characterized by the absence of subjective symptoms and a sinus mucosa that was grossly normal and lacking residual mucopus. A persistent disease was noted when the sinus mucosa presented an abnormal appearance and/or had mucopus discharge after the 16th week of post-ESS (Figure 2). In order to better irrigate the sinuses, a revised ESS was used to dilate the sinus openings on 4 cases due to a meatal stenosis found in their post-operative course.

RESULTS

According to the history of NIAS, patients were classified into 3 groups: (A) more than 2 years: 8 cases; (B) less than 1 year: 10 cases; and (C) between A and B: 13 cases. All the cases in group B had completely recovered by the 12th week of their post-ESS course. Five cases from group A and 3 cases from group C converted into a persistent disease.

The saccharin times for the 31 patients ranged from 12 to 57 min (mean±s.d.: 21.3±4.2 min). Twenty-five patients whose saccharin times were less than 30 min, recovered almost completely before the 12th week of the post-ESS course, although 4 of these cases developed the persistent disease. However, 4 out of the 6 patients whose saccharin times were greater than 30 min developed the persistent disease.

A total of 14 cases had positive skin tests to *Aspergillus fumigatus* only, 4 cases had negative skin tests to *Aspergillus* but positive skin tests to other allergens, and 13 cases were skin test negative to all 10 allergens. In this study, the reversibility of NIAS had no relationship to the allergic skin test results.

Sinus CT-scans of NIAS in this series showed 4 cases with bone erosion, 8 cases with metal concretions and 23 cases with opacifications. Reversibility of these cases had no correlation to the radiological findings. In this study, 24 patients had no systemic diseases, 3 patients had diabetes, and 4 patients had hyper-

tension. The sinusitis of the 3 diabetic patients whose diabetes was under control, was CIS. Two of them had complete recoveries, however, one had persistent disease.

The most common symptoms of NIAS in this series were post-nasal dripping and nasal obstruction (29/31) followed in descending order by foul-odour smelling (20/31), bloody rhinorrhoea (15/31), and headache (14/31). The time for the recovery of each symptom after ESS is shown in Table 2. Relief of these symptoms (i.e., foul odour, bloody rhinorrhoea and headache) generally occurred before the second week of the post-ESS course, although relief of nasal obstruction usually occurred prior to the 4th week. Post-nasal dripping was the most refractory symptom with recovery, usually being noted during the 12th week of the post-ESS course.

Table 2. The time for the relief of nasal symptoms in NIAS after ESS (PND: post-nasal dripping; NO: nasal obstruction; FO: foul odour; BR: bloody rhinorrhoea; Head: headache).

post-ESS time	nasal symptoms (No. of cases)				
	PND	NO	FO	RR	Head
2nd week	0	9 (31%)	15 (75%)	13 (87%)	12 (86%)
4th week	2 (9%)	11 (38%)	3 (15%)	1 (7%)	2 (14%)
6th week	2 (9%)	3 (10%)	2 (10%)	1 (7%)	0
8th week	4 (14%)	4 (14%)	0	0	0
12th week	12 (41%)	0	0	0	0
16th week	1 (3%)	0	0	0	0
persistent	8 (28%)	2 (9%)	0	0	0
total (n)	29	29	20	15	14

In this study, there were 16 cases of CIS with maxillary sinus and/or ethmoid sinus involvement, and in 2 cases only the sphenoid sinus was involved involvement. All 9 subjects who required the combined anterior canine fossa approach belonged to the CIS group. There were 7 cases of aspergilloma involving the maxillary sinus only. All 6 cases of AAS had pan-sinusitis. Recovery of NIAS is shown in Figure 3, classified by the disease entity. All cases of aspergilloma demonstrated complete recovery and usually recovered before the 8th week of the post-ESS course. The cases of CIS generally showed recovery during the 9th to 12th week of the post-ESS course. However, 5 out of 6 AAS cases developed the persistent disease.

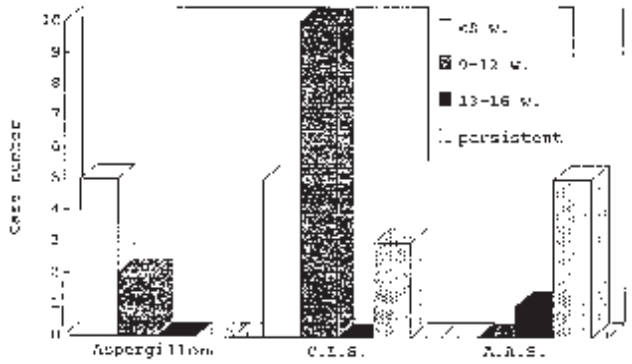

Figure 3. The time for complete recovery of NIAS after ESS according to the disease entities.

DISCUSSION

Five of the eight cases whose histories were longer than 2 years (group A) developed the persistent disease. Coincidentally, all these 5 patients belonged to the AAS group in this series. This prolonged history may be due to the fact that the patients had overlooked their symptoms (which are similar to those of chronic sinusitis) or that the physician might have neglected the allergic characteristics of the patient's disease. However, those patients with alarming symptoms such as foul odour, bloody rhinorrhoea or headache should have visited the otolaryngologist earlier. Their history would have been shorter and have lead to a better recovery. For example, all the patients with histories shorter than 1 year recovered completely prior to the 12th week of the post-ESS course. Additionally, the distinction between invasive and non-invasive forms is not well defined. Given enough time, non-invasive aspergillosis will probably become invasive (Jahrsdoerfer et al., 1979). The duration of infection appears to be the greatest factor (Jahrsdoerfer et al., 1979). Hence, it is important to decrease the likelihood of overlooking the clinical signs of the non-invasive forms of *Aspergillus* sinusitis, resulting in an earlier treatment of this disease.

Most patients had a short history of disease which correlates with a short saccharin time. Only 6 patients demonstrated a prolonged saccharin time (more than 30 min) and their history of disease was also longer (Katzenstein et al., 1983a). However, 4 of these 6 patients developed the persistent disease.

In chronic bronchitis, the ciliary transport rate decreases with increasing severity and duration of disease (Puchelle et al., 1981). In chronic sinusitis, increased severity of disease correlates with a slower nasal particle transport (Sakakura et al., 1978; Stanley et al., 1984). Impairment of mucociliary function is a significant factor in the delayed recovery of chronic sinusitis subjects (Fang, 1994). Thus, a pre-operatively prolonged saccharin time may predict poor recovery in NIAS subjects.

There were 14 patients (45%) with a positive skin test to *Aspergillus fumigatus*. Hence, skin tests may not be a reliable diagnostic tool in diagnosing NIAS and it may have no significant relationship with patient recovery.

Metal concretions in the CT scans were found in only 8 cases (26%), in contrast to the 46% reported in Stammberger's study (Stammberger et al., 1984). Four cases with bone erosion, mostly found in the medial wall of the antrum, were noted. Bone erosion rarely occurs in the non-invasive form (Parnes et al., 1989). When the patients with bone erosion are compared to those with radiopaque sinuses, then ther is no significant realtionship between recovery of sinusitis and the radiological findings.

In this study, 80% of the cases had no diabetes, hypertension or any other major systemic disease. These patients did not belong to the group predisposed to mycoses by severe diabetes and immunological disease (Stammberger, 1985). Most of the *Aspergillus* mycoses of the paranasal sinus were secondary to recurrent chronic sinusitis (Stammberger, 1985). NIAS subjects frequently have bacterial infections. Also, the residual antral mucopus in the NIAS subjects with persistent disease is frequently associated with bacterial infection, often being caused by *Staphylococcus aureus*, *Bacteroides fragilis*, and *Prevotella* species.

Diagnosis of *Aspergillus* infection in this series was made through microscopical findings (Katzenstein et al., 1983b). Fungal cultures may show false-negative results in a considerable number of microscopically proven cases. Hence, fungal cultures are not definitive enough to rule out mycotic sinusitis (Jahrsdoerfer et al., 1979; Parnes et al., 1989; Jonathan et al., 1989). Often, the diagnosis of Aspergillus is made post-operatively, based upon the morphological appearance of the tissue removed at the time of surgery (Jahrsdoerfer et al., 1979). AAS subjects had all of the following criteria: nasal polyps, asthma history, inspissated allergic mucin (Figures 4a-b), positive Aspergillus skin test, and no evidence of mycetoma or bone invasion (Meikle et al., 1985; Waxman et al., 1987; Jonathan et al., 1989; Hartwick and Batskis, 1991; Fang, 1994).

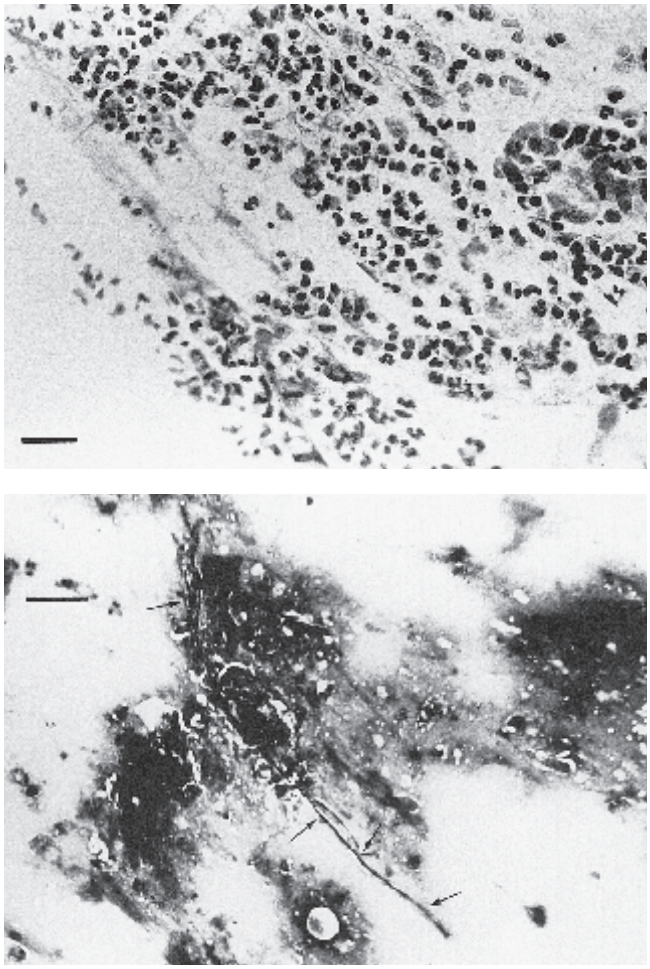

Figure 4. Smear of allergic mucin from the patient with AAS. (A): allergic mucin with clusters of eosinophils and chronic inflammatory cells (haematoxylin and eosin stain); (B): scattered *Aspergillus* hyphae (arrows) with septae and acute-angle branching (Gomori methenamine silver stain; bar represents 50 μm).

The treatment regimen should strive for clearance of the fungal mass as well as proper drainage and ventilation of the affected sinuses (Parnes et al., 1989). However, AAS subjects should be given additional steroid treatment, either locally or systemically. Irrigation with normal saline through endoscopy should be performed once a week during the post-operative follow-up session. Its purpose is to remove any residual fungal mass and to keep the sinuses open, yielding good drainage and ventilation since the fungus favours hypoxic or anaerobic conditions (Stevens, 1978; Jahrsdoerfer et al., 1979; Parnes et al., 1989).

The most common symptoms of NIAS were post-nasal dripping and nasal obstruction. The most refractory symptom was post-nasal dripping during the post-ESS course. This finding shares similarities to a previous study discussing patients diagnosed with chronic paranasal sinusitis combined with nasal polyps (Fang, 1994). The symptoms, i.e. foul odour, bloody rhinorrhoea and headache, cleared post-operatively within 2 weeks due to the good drainage and ventilation achieved quickly using ESS. In general, most of the symptoms of NIAS were reversed by ESS before the 12th week of the post-ESS course.

The most common cases of NIAS belonged to CIS subjects. The affected area mainly involved the maxillary and ethmoid sinuses. Through the ESS, 83.3% of them had a complete recovery before the 12th week, and 55.5% recovered during the 9th to 12th week of the post-ESS course. Curiously, all of the CIS subjects with persistent disease had ESS combined with the anterior canine fossa approach. If complete clearance of the fungal masses is not achieved by ESS alone, then utilizing the anterior cannine fossa approach may be insufficient and lead to this persistent disease. Hence, during endoscopy, if clearance of all fungal masses cannot be achieved, then the Caldwell-Luc operation should be reconsidered. In this study, the aspergilloma subjects mainly had maxillary sinus involvement (Jahrsdoerfer et al., 1979; McGill et al., 1980; Bassiouny et al., 1982). Most of them (71.4%) recovered completely before the 8th week of the post-ESS course.

AAS is a relatively new form of chronic sinusitis. The 6 AAS cases were post-operatively given local steroids; however, no systemic steroids or antifungal agents were administered (Waxman et al., 1987; Goldstein et al., 1988). This treatment method was utilized to diminished any conflicting effects. This study demanded a comparison among the three groups focusing on the effects of local drainage and irrigation by endoscopy in NIAS. Thus, no systemic steroid was used in order to cause minimal changes. With the exception of post-nasal dripping, the symptoms of the AAS subjects showed excellent improvement. However, they were unstable because some of these patients became markedly symptomatic within 6 to 10 weeks following a post-ESS-silent period. A portion of the patients with allergic *Aspergillus* sinusitis will be "cured" using this surgical procedure alone. However, some may manifest recurrent disease within months, while another group may have recurrence after a longer period (Waxman et al., 1987). Emphasis must be placed on early diagnosis. A careful evaluation of the patient's history and allergies will lead to an early diagnosis and, thus, an earlier treatment. It is important that otolaryngologists improve their therapeutic strategies to resolve these recurrent symptoms in allergic *Aspergillus* sinusitis.

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