REVIEW ARTICLE

Surgical Management of Fungal Rhinosinusitis

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Abstract

Fungal rhinosinusitis is on the rise. Most current treatment protocols for fungal rhinosinusitis include surgery combined with medical therapy. Endoscopic sinus surgery has revolutionized the management of this disease limiting the use of the open surgical approaches to very extensive cases with orbital, soft tissue or intracranial involvement by invasive fungal rhinosinusitis. A regular and thorough follow-up is mandatory in all cases to check for recurrences. This article discusses the various forms of fungal rhinosinusitis and their surgical management.

Keywords: Fungal rhinosinusitis, fungus ball, invasive, endoscopic surgical procedures.

INTRODUCTION

Since the etiologic agent and the host immunity influence the choice of treatment, recent review of the treatment of fungal rhinosinusitis stresses the need for determining the type of disease: whether allergic, noninvasive or invasive.

In order to simplify the understanding of the rationale of surgical management in the various forms, we have given importance to each type separately.

ALLERGIC FUNGAL RHINOSINUSITIS(AFRS) AND EOSINOPHILIC MUCIN SINUSITIS

Surgery has played an important role in the management of AFRS since its earliest reports, and is required in almost all cases. In 1979, McGuirt et al stated, 'Without question, the treatment of paranasal sinus aspergillosis is surgical, the key to successful surgical treatment is the removal of the diseased mucosa and aeration and drainage of the involved sinus.[3] However, while surgery alone is not sufficient treatment for AFRS, it is a crucial step in the management.

In the early days, treatment options were based on the concern that the offensive fungal pathogen could probably have invasive potential. The clinical and radiological appearance of the disease often confused the underlying diagnosis, influencing surgeons to adopt a more radical approach. Radiologic evidence of invasion into adjacent anatomical areas such as the orbit or cranial cavity was frequently interpreted as invasive disease or malignancy and radical surgeries followed resulting in increased morbity and mortality in these cases. Treatment was generally aggressive, incorporating open surgical approaches as well as the use of systemic antifungal medications. Despite this aggressive approach, recidivism remained high.[1]

An improved understanding of the pathophysiology of AFRS led to a fundamental change in its management. Soon it was appreciated that AFRS is an immunologic rather than infectious disorder.[2] The acceptance of specific immunologic hypersensitivity as the cause of AFRS has led to dramatic changes in its management protocols, both medical as well as surgical. Whereas immunomodulators have largely replaced the systemic use of antifungal medications, radical surgery has given way to more conservative, tissue-sparing approaches. Mabry et al refer to this surgery as "conservative, but complete", relying almost completely on endoscopic techniques.

The very physical characteristics of AFRS (bone attenuation and extension into adjacent areas) that once merited a radical surgical approach form the basis of the conservative surgical approach. By nature, AFRS creates local inflammatory responses capable of producing allergic mucin and polyposis which can range from subtle to

extensive, resulting in distortion of local anatomy and hence, a loss of important surgical landmarks. Also, polyposis can result in severe bleeding during surgery which further increases the risk of iatrogenic injury especially in the presence of bone erosion. It is important for the surgeon to recognize these factors.

In AFRS, the disease pattern is more or less consistent: The involved paranasal sinus which is the reservoir for allergic mucin is the epicenter of the disease process, whereas the lining mucosa which is mildly inflamed acts as an intact barrier to the fungus.[5,6] More significant inflammation at the sinus ostium results in polyp formation which extend to the infundibulum, middle meatus, sphenoethmoid recess and nasal cavity. The surgeon has to follow the polyps to the disease. The expansile nature of polyposis also facilitates surgery by improving access to the sinuses. Enlargement of the nasal cavity, middle meatus and frontal recess provide the surgeon with access adequate to deal with the disease in even the most difficult areas, such as the frontal sinus.[4]

Based on this understanding of the pathophysiology, various treatment plans which account for its multiple contributing factors have emerged. Combination therapy using various combinations of antifungals, corticosteroids and immunotherapy in conjunction with surgery has helped in disease control to a varying degree.

The surgical treatment of AFRS and eosinophilic mucin sinusitis is aimed at removal of the fungal antigenic material by completely removing the allergic mucin and debris from the sinuses, while simultaneously treating the underlying inflammatory process with medical treatment (systemic and topical steroids).

It is beneficial to start systemic steroids 7-10 days prior to surgery since, it helps in dramatically reducing the inflammatory response of the mucosa to the fungal antigen and the nasal polyp bulk. We have seen a 40-50% improvement in the radiological picture (Figs 1 A and B) as well as in the symptoms (especially when orbital symptoms occur in patients with AFRS) with the judicious use of preoperative steroids. Additionally, preoperative antibiotics are started due to the frequency of concomitant post-obstructive bacterial sinusitis.[5]

The goals of surgical management in AFRS and eosinophilic mucin sinusitis include:

1. Achieving complete removal of all allergic mucin and fungal debris resulting in a greatly reduced antigenic inciting factor in the atopic individual. This is immensely helped by the expansile nature of this condition which provides access to relatively difficult areas such as the frontal recess.
2. Surgery should achieve permanent drainage and ventilation of the affected sinuses, while simultaneously

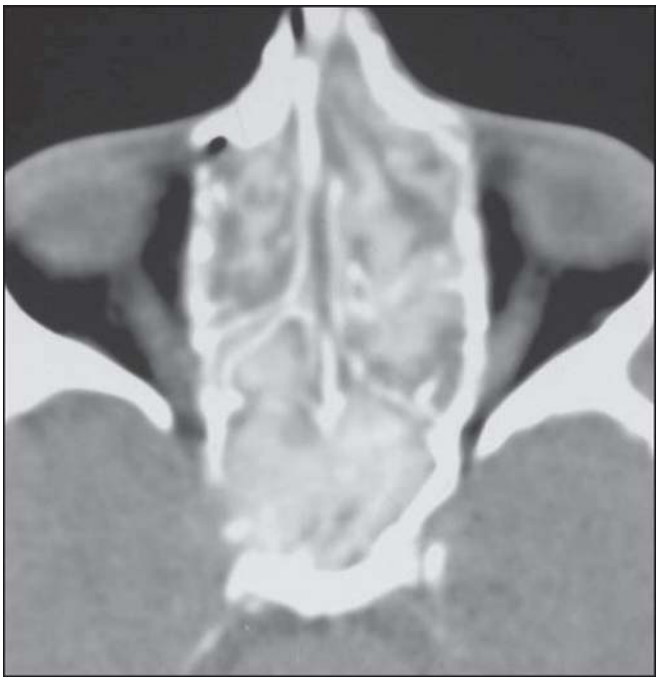

FIGURE 1A: Preoperative axial CT scan of a patient with allergic fungal rhinosinusitis, prior to steroid therapy. Note the erosion of the lamina papyracea in the region of the right orbital apex

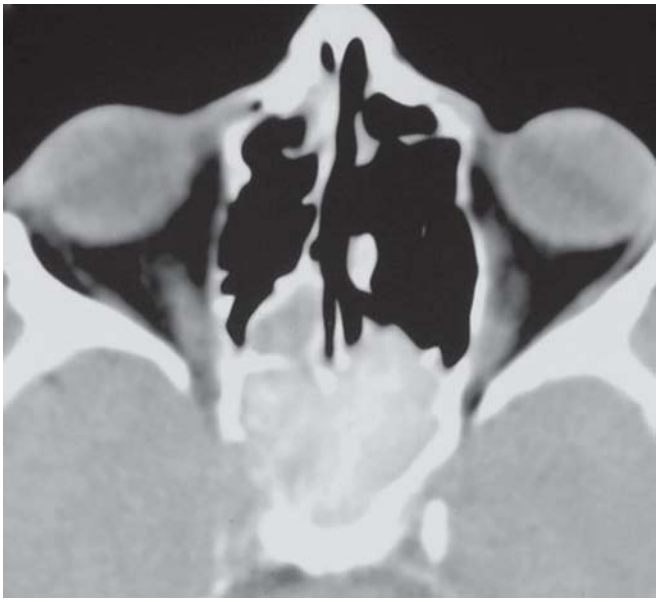

FIGURE 1B: Preoperative axial CT scan of the same patient (Fig. 1A) after ten days of systemic steroids, showing partial regression of the disease

preserving the integrity of the underlying mucosa. This has been improved greatly by the advent of tissue sparing instrumentation.[7] Even though sinonasal polyposis results in a distortion of anatomy, the careful use of powered instruments ensures preservation of the underlying mucosa which in turn, helps in preventing trauma to the underlying periosteum, dura or periorbita in the presence of bone erosion. Once adequate drainage and ventilation of the sinuses is achieved, the preserved underlying mucosa soon reverts back to normal (Fig. 2A).

3. The third and final goal of surgical treatment is to achieve postoperative access to previously diseased areas (Fig. 2B).

Today, widely employed endoscopic techniques yield excellent results.[8] Endoscopic powered instrumentation have made achieving the abovementioned goals relatively easy, as they help in preserving mucosa while carefully removing soft tissue and thin bone under vision. However, as with all instruments, expertise is required in the use of these powered instruments to prevent disastrous complications especially since bone erosion is known to occur in AFRS putting underlying structures such as the periorbita or dura at risk of damage. In the event of extensive bone remodeling or erosion, image-guided systems may be used.[8]

The pathologic behavior of AFRS increases the risk of complications during surgery. Polyposis, presence of huge amounts of allergic mucin and hemorrhage may cause spatial disorientation. Bony erosions may distort normal anatomy and confuse anatomic boundaries putting the orbit or intracranial structures at a risk of injury. An incomplete surgical procedure would result in almost certain and rapid recurrence of AFRS. The currently accepted pathophysiology of this condition emphasizes the absence of tissue invasion in the immunocompetent host. Also, what works to the surgeon's advantage is the fact that the disease is essentially extradural and extraperiorbital. The importance of mucosal preservation during surgical intervention cannot be stressed enough, since intracranial seeding of the fungal antigen has been reported by an inadvertent breach of dura during surgery. In addition to fungal or bacterial seeding, penetration of the dura or periorbita can result in grievous complications such as diplopia, blindness, hemorrhage, stroke, encephalocele formation or CSF leak.

Surgical treatment for recurrences is indicated only when intense medical management fails to clear an exacerbation. Allergic mucin is suctioned out as an office procedure from the sinus cavities and intensive medical therapy with low dose steroid orally usually helps in reverting the changes. However, massive recurrent polyposis with accumulation of huge quantities of mucin would merit revision surgery, the goals of revision surgery being the same as those for primary surgery.

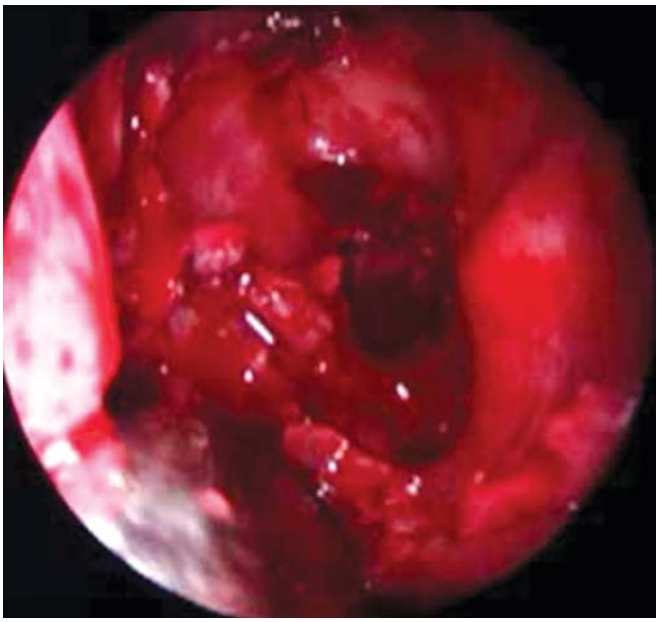

FIGURE 2A: Intraoperative endoscopic image of a patient with right sided allergic fungal rhinosinusitis, showing complete clearance of disease, with restoration of ventilation of all sinuses

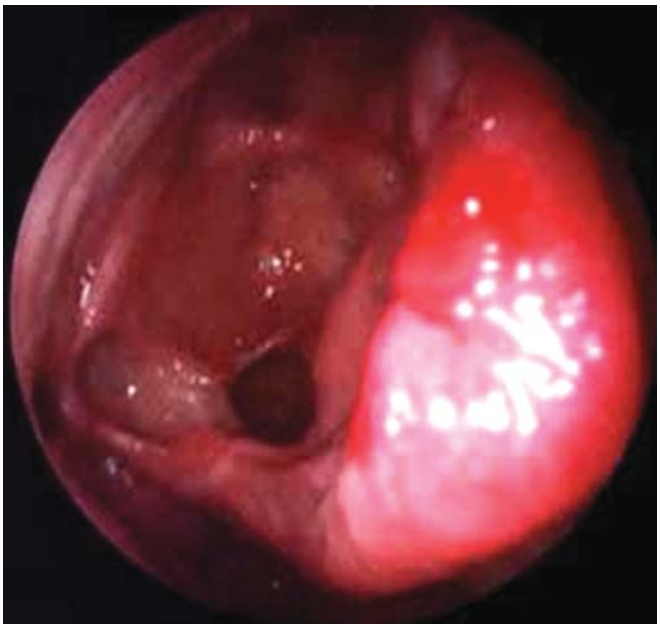

FIGURE 2B: Three-week postoperative endoscopic image of the same patient (Fig. 2A) showing a healed ethmoidectomy cavity, with normal appearing mucosa lining all the widely patent sinuses

FUNGAL BALLS

Fungus balls of the paranasal sinuses are commonly referred to as 'mycetomas' in literature. However, this is a misnomer as fungal balls are not true mycetomas. This form of fungal rhinosinusitis is commonly seen in immunocompetent individuals, and shows no evidence of invasion on histopathology. As it is noninvasive and nonlife-threatening a relatively conservative approach is advocated in its treatment. In cases where the immunity of the host gets compromised, these otherwise indolent forms of fungal rhinosinusitis may become invasive.

The goal of treatment for a fungal ball is surgical removal of the hyphal mass with re-establishing the drainage from the affected sinus. A symptomatic patient with opacification of the sinus and bone erosion merits surgical removal, however, the same line of management in a patient who is asymptomatic is controversial. Presence of coexisting asthma in a patient with a fungal ball merits surgery to prevent exacerbation of asthmatic attacks due to the fungal antigen.

Endoscopic sinus surgery to remove the fungal ball is the treatment of choice today and the erstwhile external approaches are obsolete. Irrigation of the sinus is performed to clear the sinus of all the fungal debris.

The maxillary sinus is cleared by widening the natural ostium (middle meatus antrostomy) and a canine puncture will help in visualizing the entire sinus cavity as well as serve the purpose of irrigation.

Sphenoid sinus fungal balls are also approached endoscopically by widening the natural ostium (Fig. 3). The sinus is irrigated to remove all debris thus preventing damage to important structures. Patients with sphenoid sinus fungal balls are at a risk of life-threatening complications if there is a bony dehiscence of the lateral sphenoid wall (as seen in 8% individuals) or if seeding occurs during aggressive endoscopic removal since, the sphenoid sinus is surrounded by important intracranial structures (cavernous sinus, carotid artery, etc). In patients who demonstrate bony lateral sphenoid dehiscence radiologically preoperatively, we start systemic antifungal agents such as oral iatraconazole 200 mg twice daily prior to surgery.

Frontal sinus fungal balls are rare. Endoscopic removal combined with irrigation through the anterior table was advocated by Klossek (1997).[9]

As described earlier in this section, the treatment of fungal balls is surgical removal endoscopically. Recurrence is rare but, has been reported to occur even as late as two years following surgery. In Klossek's (1997) series, the recurrence rate was 4%, whereas, Ferriero (1997) reported a slightly higher recurrence rate of 7%.[9,10] A regular follow-up is important as many of these recurrences can be addressed with simple irrigation or suctioning in the outpatient department or conservative endoscopic surgery.[9]

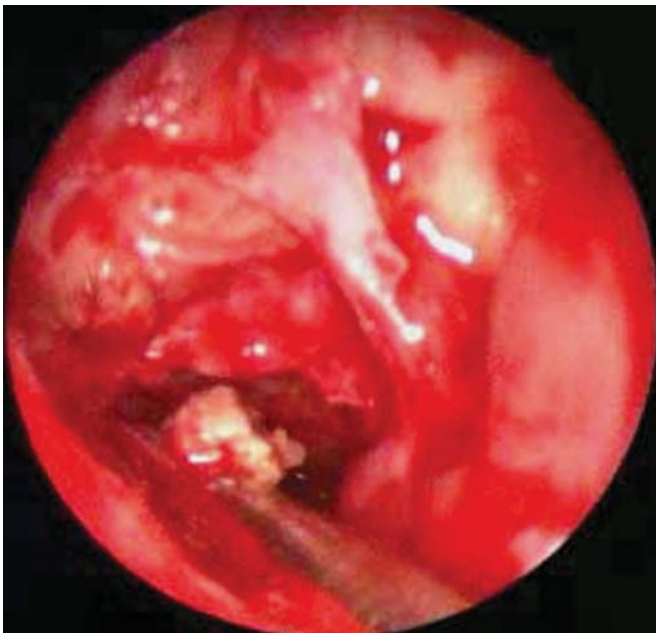

FIGURE 3: Endoscopic intraoperative image of a fungal ball being evacuated from the right sphenoid sinus

INVASIVE FUNGAL RHINOSINUSITIS

deShazo (1998) noted three types of invasive disease:[11] Acute fulminant invasive fungal sinusitis (AIFS), the Chronic invasive fungal sinusitis (CISF) and granulomatous invasive fungal sinusitis. For practical purposes, the term chronic invasive fungal sinusitis is used to describe both granulomatous and nongranulomatous nonfulminant but invasive disease.

Acute invasive fungal sinusitis (AIFS) is a life-threatening rapidly fulminant infection and a medical emergency, the challenge being to diagnose the disease early before it extends into the orbit or the cranial cavity.

Mucormycosis is frequently rapidly progressive, and antifungal therapy alone is often inadequate to control the infection. The numerous strains of mucormycosis have a broad range of susceptibility to antifungal agents; some strains may be highly resistant to amphotericin B. Furthermore, the hallmark angioinvasion, thrombosis, and tissue necrosis of this disease result in poor penetration of

anti-infective agents to the site of infection. Therefore, even if the causative organism is susceptible to the treating antifungal agent *in vitro*, the antifungal may be ineffective *in vivo*. Finally, surgery is necessary due to the massive amount of tissue necrosis seen in mucormycosis, which may not be prevented by killing the organism.[15] Surgical debridement of infected and necrotic tissue should be performed on an urgent basis.

Patients who develop AIFS are usually, but not always, immunocompromised.[12] The most effective treatment for AIFS is prevention of occurrence in an immunocompromised individual. The importance of surgical treatment for AIFS has long been assumed.[13] Surgery helps to acquire a specimen for diagnosis and culture thus, establishing the diagnosis and enabling appropriate medical treatment.[14] Surgery also reduces the local fungal burden in the tissues and augments the normal immune mechanisms for elimination of the fungal antigen.[14] Early aggressive surgery may slow disease progression and allow time for reversal of the underlying immunocompromise.[14] Surgical widening of the sinus ostia makes irrigation with antifungals and placement of packs soaked in Amphotericin B easier. However, one of the drawbacks of surgery is hemorrhage in neutropenic patients who are anemic and thrombocytopaenic. Surgery also creates mucosal defects which exposes the tissues to further fungal invasion. These issues must be considered when planning surgery for AIFS.[14] Available evidence suggests that patients treated with surgery have a better prognosis than those treated with medical therapy alone.[13] Surgery for AIFS should be performed on an urgent basis as soon as the diagnosis is confirmed. The goal of surgery is the debridement of all infected tissue within the nose and paranasal sinuses by the endoscopic approach. The external approach may be inevitable when there is extensive disease of the lateral nasal wall, or evidence of orbital, facial or intracranial extension. External procedures include any of the following: medial maxillectomy, total maxillectomy with or without orbital exenteration, or craniofacial resection. The extent of the surgery should be modified according to the overall prognosis.

In rhinocerebral mucormycosis, early surgical excision of the infected sinuses and appropriate debridement of the retrorbital space can often prevent the infection from extending into the eye, thereby obviating the need for enucleation and resulting in extremely high cure rates (85%).[16] Repeated surgical exploration of the sinuses and orbit may be necessary to ensure that all necrotic tissue has been debrided and the infection has not progressed. Published case series continue to support the need for surgical debridement to optimize outcomes. For example, in a case series totaling 49 patients with rhinocerebral mucormycosis, the mortality was 70% in cases treated with antifungal agents alone versus 14% in cases treated with antifungal agents plus surgery.[17,18] Nevertheless, the observational clinical data support the concept that surgical debridement is necessary to optimize cure rates. In most cases of invasive fungal rhinosinusitis with proptosis, it is a foregone conclusion to sacrifice the orbit. However, we have followed a surgical protocol, which is tailor-made to suit each patient; at the same time, continuing aggressive medical management using amphotericin B. Endoscopic debridement with regular and repeated follow-up forms the mainstay of our treatment. In our experience, posterior orbital disease (orbital apex involvement) merits an eventual orbital exenteration, while anterior orbital involvement (only lamina papyracea erosion or minimal anterior periorbital involvement) allows for eventual orbital conservation, with expectance for recovery of full ocular function. Any salvaged orbit should be closely followed up, and the decision to sacrifice the orbit, if at all, should be made within 10 to 12 days at the latest.

Repeated debridements at regular intervals are performed endoscopically until freely bleeding peripheral margins are obtained with simultaneous use of systemic amphotericin B and medications to reverse the immunocompromise. Once immunocompromise is reversed, the disease may resolve completely or take on the attributes of CIFS with a chronic indolent course.[23] Regular follow-up is required with endoscopic examination to rule out a recurrence. Any suspicious areas should be biopsied. The patient is asked to report any symptom such as rhinorrhea, facial pain or nasal congestion which may herald a recurrence.

Previously, cases of rhinocerebral mucormycosis were almost consistently fatal.[19] Although the mortality rate of rhinocerebral disease remains high, the infection can be cured when diagnosed early and treated with aggressive surgery and antifungal agents.[20] Recent series have described a mortality of approximately 40% in diabetics with rhinocerebral mucormycosis and a similar survival rate for rhinocerebral disease in patients with hematological malignancies.[16,18,21] The prognosis is much better if the disease has not penetrated beyond the sinus walls prior to surgical debridement; in local sinonasal disease, the mortality

has been reported to be approximately 10%.[16] The nature of the underlying disease and the reversibility of the immune dysfunction are also important determinants of survival. One study showed that 75% of patients with rhinocerebral disease who had no underlying immune compromise survived, while 60% of those with diabetes and only 20% of patients with other immunocompromised states were cured.[22] The overall survival rate of patients with mucormycosis is approximately 50%, although survival rates of upto 85% have been reported more recently. Much of the variability in outcome is due to the various forms of the disease. Rhinocerebral mucormycosis has a higher survival rate than does pulmonary or disseminated mucormycosis because the rhinocerebral disease can frequently be diagnosed earlier and the most common underlying cause, diabetic ketoacidosis, can be treated readily.

Chronic invasive fungal sinusitis (CIFS) is diagnosed by the clinical presentation and histopathologic report. A diagnosis of CISF is made in patients with a prolonged clinical course (symptoms persisting for more than 4 weeks), radiologic evidence of sinusitis and presence of hyphal forms in the tissue.[23,24] In CIFS, the fungal hyphae invade tissue but, unlike AIFS, vascular invasion is rarely seen. The non-granulomatous form is seen in immunocompromised individuals such as diabetics and has a poor prognosis whereas, the granulomatous form is seen in immunocompetent hosts.

Most cases of CISF have been treated with a combination of surgery and antifungal agents.[24] However, as this condition is relatively rare and the case series is small, there have been no systematic evaluations of therapy for CIFS. The consensus is that surgery is an important part of the treatment of CIFS (deShazo et al, 2000).[24,26,27] The preliminary goal of surgery for CISF is to secure an accurate diagnosis, since there are many differential diagnoses for this condition. However, histopathology is the single most reliable investigation to arrive at a confirmative diagnosis. There is no consensus regarding the extent of surgery required for this condition and whether the nongranulomatous form should be treated differently from the granulomatous form. It is rational to remove all diseased tissue without violating protective tissue planes such as periorbita and dura that may act as barriers to further spread of disease and without sacrificing important structures.[29] Radical surgery should be reserved for very aggressive cases. However, deShazo suggests aggressive surgical debridement for non-granulomatous chronic invasive fungal sinusitis similar to that used for the treatment of acute invasive fungal sinusitis.[25] Washburn et al (1988) recommend a prolonged course of amphoterecin B exceeding 2 gm for adults postoperatively in all cases of CIFS to prevent a recurrence. In contrast, deShazo et al (1997) state that granulomatous invasive fungal sinusitis responds well to surgical treatment alone and does not merit the use of systemic antifungals. In our experience, each patient needs to be assessed individually for appropriate surgical intervention and we combine surgery with the use of systemic antifungal agents in all cases.

Since the nature of this disease is chronic, it can be followed up easily by repeated endoscopy and even radiologically if required; and with the availability of specific antifungal therapy, an initial conservative surgical treatment protocol can be justifiably followed. The prognosis of this disease is uncertain and hence regular follow-up with endoscopic evaluation at 2-3 monthly intervals is mandatory. CT scanning is recommended one month after surgery for a baseline and then at regular intervals of 3 months to follow the progression/regression of the disease.[24,28,29]

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