Practice patterns regarding noninvasive rhinosinusitis in the immunosuppressed patient population

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ABSTRACT

The number of immunosuppressed patients is growing remarkably. Currently, there is no guideline on how treatment of noninvasive sinusitis in these patients may differ from that of the general population, and practice patterns vary widely across the country. The purpose of this survey was to examine practice patterns and management for this patient population. A survey and literature review were performed. The survey was sent to the membership list serve of the American Rhinologic Society. Twelve questions were asked. Four demographic questions were asked about the physicians and their practices. Four questions were asked about the type of immunocompromised patients they saw. Two questions were asked about management in the setting of significant acute and chronic sinusitis. The responses were collected and analyzed using Pearson independent chi-square testing. Of 871 members on the list serve only 89 physicians responded. The majority of responders were sinus and skull base surgeons practicing in an academic setting. There was a large range of geographic location, years in practice, and patient population. Two significant findings related years in practice to management of chronic sinus immunocompromised patients ($p = 0.012$) and correlated the choice of management option in acute and chronic sinus immunocompromised patients ($p = 0.006$). There is no standardized method of treating the vulnerable patient population of immunocompromised patients with noninvasive acute and chronic sinusitis and this survey shows the wide range of practice. Clinical research is needed to standardize and optimize treatment for these patients.

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The immunocompromised and immunosuppressed populations are growing, as once fatal diseases such as human immunodeficiency virus (HIV) have become chronic, more patients have been able to benefit from organ transplantation, and the growing epidemic of diabetes in this country has led to new more fulminant presentations of immunocompromise within those who are unable to control their glucose levels. These patients are considered to have "secondary" or "acquired" immunodeficiency, as opposed to those with "primary" immunodeficiency (PID) syndromes. Those PID syndromes make up a much smaller group of patients, and the correction of deficiencies in symptomatic patients with intravenous immunoglobulin (IVIG) or more specific replacement strategies is well documented, albeit not conclusive. The focus of this study was on those patients with secondary immunocompromise and how we manage noninvasive rhinosinusitis in this setting. In stark contrast to the standardized and well-accepted protocol for invasive fungal sinusitis, the way we treat noninvasive chronic and acute sinusitis in this vulnerable patient population is completely empiric, despite rhinologists' improving focus on evidence-based practice.

Because these patients are often complex in their presentation and comorbidities, it is possible that a purely individualized approach is our only option. However, it is just as likely that the reason we do not have a clear protocol for treatment and management is that we have never studied the topic to establish one.

Several studies have identified that these patients tend to present with different bacteria than immunocompetent patients, as well as viruses that may be active in the disease process.[1–8] However, there is no study in the literature as to the appropriate management despite obvious differences in pathogenesis.

METHODS

This author set out to identify any possible practice patterns that she herself had not been exposed to during the process of her training. After living in three separate geographic regions during the training process and having exposure to experts in rhinology at each step, there did not appear to be any set protocol for managing these patients.

Therefore, an internet-based survey was sent to the membership list serve of the American Rhinologic Society. Twelve questions were asked. Four demographic questions were asked about the physicians and their practices. Four questions were asked about the type of immunocompromised or immunosuppressed patients they saw, restricted to secondary immunosuppression

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and not including PID syndromes. Two questions were asked about management in the setting of significant acute and chronic sinusitis. The responses were collected and analyzed using Pearson independent chi-square testing. Institutional Review Board waiver was obtained for this study.

RESULTS

Of the 871 members on the list serve only 89 physicians responded. The majority of responders were sinus and skull base surgeons practicing in an academic setting, but almost one-third were general otolaryngologists. There was a large range of geographic locations, years in practice, and patient population (Fig. 1). Most responders saw <20 patients in a given year that fit into our category of immunocompromised or immunosuppressed with acute or chronic sinusitis, respectively, although approximately one-quarter of the respondents saw up to 50 of each. The majority of responders noted that if they were seeing these patients in the hospital setting, <25% of these cases had been admitted to the hospital for sinus-related disease. A clear majority of responders chose i.v. antibiotics without surgery as their treatment option in immunocompromised patients with acute sinusitis impacting their health status, at 58.4%. However, 28% of our responders chose to treat this same population with i.v. antibiotics and surgery. Conversely, in the patient population of immunocompromised with chronic sinusitis impacting their health status, the field was much more divided, with 36% choosing i.v. antibiotics with surgery, 28.1% choosing i.v. antibiotics without surgery, 21.3% choosing oral antibiotics without surgery, and 14.6% choosing oral antibiotics with surgery. The only two significant findings when looking for patterns related years in practice to management of chronic sinus immunocompromised patients ($p = 0.012$) and the correlation between choice of management option in both acute and chronic sinus immunocompromised patients ($p = .006$).

DISCUSSION

Prominent rhinologists across the country have answered very differently to the questions asked on the survey above, some being very aggressive with regard to surgery and others very cautious. There is no evidence at this point to suggest which may be the better path.

This survey was performed to elucidate if there were any treatment patterns existing, and the results bear out that no such pattern exists. Unfortunately the response rate was poor, but varied enough in geographic range and years in practice to prove this point. The answer options were certainly overly simplified, and usually management of these patients occurs in a stepwise approach including more than one of the treatment options, although not always. This oversimplification was done purposely, to try and find trends when grouping these very complex patients into broader groups, thereby increasing statistical power of any one management choice. However, despite this, as the results show, no one option for any larger category of patient clearly won out. Interestingly, the two significant findings relating years in practice to management of immunocompromised patients with chronic sinusitis and choice of management option in chronic sinusitis correlating to choice in acute sinusitis suggest that certain rhinologists do have a set method of management, although these methods appear to be based on experience.

As far back as 1984, Fried *et al.* noted *Psuedomonas* to be an organism more likely found in the immunocompromised patient than the immunocompetent.[1] A publication in 1993 again called for heightened suspicion for this organism in HIV patients,[2] and in 1994 Milgrim *et al.* showed the presence of the usual pathogens mixed in with *Pseudomonas aeruginosa* as well as *Listeria monocytogenes* and *Candida albicans* in antral cultures from HIV patients.[3] In 1996 for the first time cytomegalovirus was implicated in sinusitis in HIV patients by Marks *et al.*[4] These organisms were again highlighted in1997, alongside fungi and mycobacteria as important and different pathogens in the HIV patient.[5] In 1999, Porter *et al.* showed that 66% of HIV patients surveyed acknowledged sinonasal disease in the prior 6 months, and in a separate article Decker noted that the clinician could reverse the course of rhinosinusitis by treating the underlying neutropenia or diabetic ketoacidosis that had led to the immunocompromise.[6,7] In 2001, Tarp *et al.* published an article on the presence and possible reactivation of herpesvirus type 1–8 in sinus aspirates of HIV-infected individuals.[8]

Despite these myriad reports on difference of pathogen and disease process in the immunocompromised population, the treatments used were only elucidated in a few and ranged from "aggressive debridement and topical therapy" to parenteral antibiotics followed by surgery to surgery alone. Not one of them outlined a guide or protocol for treatment options in that patient population. Indeed, the first report in the literature for suggesting how these patients should be appropriately managed has come in 2009, with an article published on balloon sinuplasty in five critically ill patients with acute rhinosinusitis. There was no control group, and only two of the five patients had follow-up after discharge from the hospital, but the authors suggested this to be a safe and effective method in treating this patient population.[9] Even in a meticulously researched review such as the European Position Paper on Rhinosinusitis and Nasal Polyps 2012, the amount of space dedicated to discussing the immunosuppressed patient

1. What is your primary focus of practice?

	Response Percent	Response Count
a. Sinus and/or Skull Base Surgery	68.5%	61
b. Allergy	2.2%	2
c. Plastic Surgery	0.0%	0
d. General ENT	29.2%	26

2. How many years have you been in practice?

	Response Percent	Response Count
a. 1-5 years	24.7%	22
b. 5-10 years	15.7%	14
c. 10-20 years	23.6%	21
d. 20-30 years	22.5%	20
e. 30+ years	13.5%	12

3. What is your type of practice?

	Response Percent	Response Count
a. Academic	55.1%	49
b. Single specialty	27.0%	24
c. Multi-specialty	5.6%	5
d. Solo practice	12.4%	11

4. What is the geographic location of your practice?

	Response Percent	Response Count
a. New England (Maine, Vermont, New Hampshire, Massachusetts, Connecticut, Rhode Island)	11.2%	10
b. Mid-Atlantic (New York, New Jersey, Pennsylvania)	16.9%	15
c. Southeast (Maryland, Delaware, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida)	21.3%	19
d. South central (Texas, Oklahoma, Arkansas, Kentucky, Tennessee, Mississippi, Alabama, Louisiana)	11.2%	10
e. Midwest (North Dakota, South Dakota, Nebraska, Kansas, Missouri, Iowa, Minnesota, Wisconsin, Illinois, Michigan, Indiana, Ohio)	22.5%	20
f. Mountain (Wyoming, Idaho, Montana, Nevada, Utah, Colorado, New Mexico, Arizona)	6.7%	6
g. West coast (Washington, Oregon, California, Alaska, Hawaii)	10.1%	9
h. Outside of United States	0.0%	0

5. During a typical year, how many immunosuppressed patients (patients with HIV/AIDS, poorly controlled diabetes, transplant patients, etc.) do you see with non-invasive acute sinusitis?

	Response Percent	Response Count
a. 0-20	71.9%	64
b. 21-50	23.6%	21
c. 51-75	3.4%	3
d. 76-100	1.1%	1
e. >100	0.0%	0

6. During a typical year, how many immunosuppressed patients do you see with non-invasive chronic sinusitis?

	Response Percent	Response Count
a. 0-20	58.4%	52
b. 21-50	28.1%	25
c. 51-75	6.7%	6
d. 76-100	2.2%	2
e. >100	4.5%	4

7. Do you see immunosuppressed patients with non-invasive sinusitis in consultation in the in-patient, hospital based setting?

	Response Percent	Response Count
a. Yes	85.4%	76
b. No	14.6%	13

8. If you see these types of patients, what percentage have acute sinusitis?

	Response Percent	Response Count
a. 0-25%	44.9%	40
b. 26-50%	29.2%	26
c. 51-75%	16.9%	15
d. 76-100%	9.0%	8

9. If you see these types of patients, what percentage have chronic sinusitis?

	Response Percent	Response Count
a. 0-25%	42.7%	38
b. 26-50%	30.3%	27
c. 51-75%	22.5%	20
d. 76-100%	4.5%	4

10. If you see these types of patients, what percentage have been admitted to the hospital due to sinus related issues?

	Response Percent	Response Count
a. 0-25%	77.5%	69
b. 26-50%	20.2%	18
c. 51-75%	2.2%	2
d. 76-100%	0.0%	0

11. If an immunosuppressed patient in the hospital has symptoms/signs consistent with non-invasive acute sinusitis, and is hemodynamically stable but sinus issues are complicating overall health status, your treatment plan would consist of:

	Response Percent	Response Count
a. Oral antibiotics without surgery	12.4%	11
b. Intravenous antibiotics without surgery	58.4%	52
c. Oral antibiotics and surgical intervention	1.1%	1
d. Intravenous antibiotics and surgical intervention	28.1%	25

12. If an immunosuppressed patient in the hospital has symptoms/signs consistent with non-invasive chronic sinusitis, and is hemodynamically stable but sinus issues are complicating overall health status, your treatment plan would consist of:

	Response Percent	Response Count
a. Oral antibiotics without surgery	21.3%	19
b. Intravenous antibiotics without surgery	28.1%	25
c. Oral antibiotics and surgical intervention	14.6%	13
d. Intravenous antibiotics and surgical intervention	36.0%	32

Figure 1. *Survey questions and responses to questions 1–12.*

Statement	Grade of Recommendation
Among tertiary CRS patients who undergo immune evaluation, a variety of PIDs are common	C
Among PID patients, clinical symptoms of CRS are found in approximately half	C
PID patients often have CT findings consistent with CRS	C
IVIG therapies improve survival and decrease serious infections in PID patients, but do not provide clinical benefit, prevent radiographic development of CRS or decrease bacterial culture rate from the sinuses	C
Screening CTs in asymptomatic patients prior to solid organ transplant or HSCT are not indicated	C
Successful treatment of AIFRS involves surgery, antifungal therapy and reversal of the immune compromised state	C

Figure 2. *European Position Paper on Rhinosinusitis and Nasal Polyps 2012 evidence-based recommendations regarding the immunosuppressed patient population.*

population with rhinosinusitis was a mere 3 pages, out of close to 300 pages. The evidence-based recommendations from this section can be seen in Fig. 2 and clearly do not discuss what a proper treatment protocol may be in these patients except in regard to invasive fungal sinusitis. Four of the six recommendations pertain to patients with PID. Only one of the six recommendations pertain to the group of patients we are discussing in this article, and that recommendation has to do with diagnostic screening, not management.[10]

Clearly, clinical research is needed to standardize and optimize treatment for this patient population. We are currently performing a retrospective review at our own institution to look for differences in treatment and outcomes and plan to use our findings as a basis for a prospective clinical trial.

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