Sinonasal Evaluation Preceding Hematopoietic Transplantation

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Abstract

Objective. To determine the efficacy of sinonasal evaluation preceding hematopoietic cell transplant (HCT) and to correlate pretransplant findings with subsequent risk of post-HCT complications based on radiographic, endoscopic, and microbiologic findings.

Study Design. Case series with chart review.

Setting. Academic tertiary care center.

Subjects and Methods. Seventy-one patients underwent pre-HCT sinonasal evaluation. Pre-HCT imaging and endoscopic exams were evaluated via standardized scales. Middle meatus culture results were also recorded. Pre-HCT intervention was noted, as was any post-HCT evaluation and intervention.

Results. Seventy-one patients underwent pre-HCT evaluation. Sixty-five percent of patients were asymptomatic at the time of evaluation. On computed tomography (CT) imaging, the average Lund-Mackay score was 2.2 ± 3.7. Mean endoscopic grading score was 0.6 ± 1.6. The majority of cultures grew commensal organisms only. Four of 71 patients (6%) had evidence of chronic rhinosinusitis pre-HCT; 3 patients underwent endoscopic sinus surgery, and 1 patient was treated medically. None developed rhinosinusitis following HCT. Four different patients were evaluated for sinonasal symptoms post-HCT. Two were diagnosed with acute rhinosinusitis; 1 was treated medically, and 1 was treated surgically. No patient developed invasive fungal sinusitis.

Conclusions. All patients who required pre-HCT medical or surgical intervention had symptoms of rhinosinusitis and positive endoscopy and/or CT imaging. Two patients who developed acute rhinosinusitis post-HCT had no evidence of rhinosinusitis during pre-HCT evaluation. Evaluation and studies are costly, time-consuming, and not found to be predictive in this study.

Keywords

sinus surgery, hematopoietic transplantation, acute rhinosinusitis, complications

Received September 10, 2010; revised November 2, 2010; accepted December 7, 2010.

Approximately 60,000 hematopoietic cell transplants (HCTs) are performed each year worldwide for hematologic malignancies and immunodeficiencies.1 Hematologic malignancies sensitive to chemotherapy are treated with autologous transplantation, whereas patients with recalcitrant malignancies undergo allogenic transplantation. Because these patients are treated with myeloablative immunosuppressive therapy, they are put at high risk for opportunistic infection. Infections involving the paranasal sinuses in these immunocompromised patients have potentially devastating consequences, and the most concerning among them is acute invasive fungal sinusitis (AIFS). Acute invasive fungal sinusitis is a severe fungal infection involving the sinuses that has the potential for rapidly spreading and causing multisystem failure and leading to death unless treated aggressively.

It is estimated that 1% to 38%2-6 of HCT patients suffer from rhinosinusitis during the posttransplant period, of whom approximately 0.5% to 3.8%7-9 develop AIFS. Because of this, some2,3 have recommended aggressive therapy for patients with pre-HCT clinical or radiographic evidence of rhinosinusitis. However, it is not clear whether the presence or absence of rhinosinusitis prior to HCT has any predictive value on whether rhinosinusitis or complications thereof develop in patients following HCT. Studies3,5,6 have sought to correlate the incidence of pre-HCT disease with the incidence of post-HCT disease in attempts to identify any predictive features. When compared, these studies present mixed results.

Shaw et al3 prospectively followed 26 patients with pre-HCT computed tomography (CT) and found an incidence
Parameters recorded included the degree of polyposis, edema, scarring, crusting, and discharge for a total score of 10 per side.

Computed tomography was performed on all patients beginning in 2008. Lund-Mackay scores were obtained in all subsequent pre-HCT patients, and the degrees of sinus obstruction were graded on a 0 to 2 scale for each sinus group. Osteoimatal central (OMC) obstruction was scored as 0 or 2, based on whether it was patent or occluded. A cutoff of ≥4 was used to indicate a positive CT in this retrospective review. Mucous retention cysts were not included in the grading system.

When cultures were performed in pre-HCT patients, they were obtained using calcium alginate swabs placed alongside the endoscope into the middle meatus.

Pre-HCT intervention, either medical or surgical, was documented. The medical records were reviewed for the diagnosis and treatment of rhinosinusitis (any form) and for any post-HCT inpatient or outpatient otolaryngology intervention (ie, medical or surgical).

Results

Seventy-one consecutive patients were evaluated pre-HCT from July 2006 to October 2009. All patients underwent allogenic HCT. Thirty-nine women (55%) and 32 men (45%), with a mean age of 48 ± 13 years, were evaluated. Indications for HCT included acute myelogenous leukemia (34%), non-Hodgkin lymphoma (17%), myelodysplastic syndrome (14%), acute lymphocytic leukemia (13%), chronic lymphocytic leukemia (8%), Hodgkin lymphoma (6%), chronic myelogenous leukemia (6%), multiple myeloma (1%), and myelofibrosis (1%). Ten patients (14%) developed GVHD. The patients were followed for an average of 31 ± 8 months.

Of the 71 patients evaluated, 46 (65%) denied the presence of any sinonasal symptoms consistent with acute, recurrent acute, or chronic rhinosinusitis. In the remaining 25 patients, approximately 20% complained of discolored rhinorrhea, 8% complained of nasal obstruction/congestion, and 6% complained of facial pain/facial pressure. Ten patients reported a subjective history of chronic rhinosinusitis or recurrent acute rhinosinusitis; however, only 3 of these 25 patients (12%) had symptoms of chronic rhinosinusitis corroborated by endoscopy ± CT imaging. Two patients had undergone prior endoscopic sinus surgery (ESS) but did not have symptoms or evidence of disease.

All 71 patients underwent pre-HCT nasal endoscopy. Mean endoscopic grading score was 0.6 ± 1.6. The highest endoscopic score (12) was noted in a patient presenting with symptoms of chronic rhinosinusitis. Fifty-five (77%) patients presented with an endoscopic score of 0, whereas 67 (94%) patients presented with a score of ≤2.

Nineteen consecutive patients (27% of 71 patients) underwent pre-HCT CT imaging of the sinuses. Mean Lund-Mackay score was 2.2 ± 3.7 in these patients. There were 3 patients (14%) with a Lund-Mackay score ≥4, the highest of which was 16 (endoscopic grade 12). Seventy-nine percent of patients presented with a Lund-Mackay score ≤3.
Cultures were obtained from 33 of 71 patients (46%) prior to undergoing HCT. There was no growth from 2 of 33 (6%) of culture samples. The remainder included coagulase-negative staphylococcus (CNS) (25/33 or 76%), Staphylococcus aureus (7/33 or 21%), Corynebacterium (5/33 or 15%), Streptococcus viridans (3/33 or 12%), Moraxella catarrhalis (2/33 or 6%), and Haemophilus influenzae (1/33 or 3%). Penicillium was cultured in 1 patient.

Four of 71 patients (6%) required pre-HCT intervention (Table 1). One patient with chronic rhinosinusitis (history, endoscopy, and CT) was managed medically prior to HCT. There were no post-HCT treatments related to rhinosinusitis in this patient. The remaining 3 patients were managed surgically. One patient underwent a maxillary antrostomy for recurrent acute maxillary rhinosinusitis, and the post-HCT period was unremarkable. Another patient with chronic rhinosinusitis underwent a Caldwell-Luc procedure for a calcified maxillary sinus mass noted on CT imaging. The endoscopic score was 0. A maxillary sinus polyp with calcification was noted; there was no evidence of malignancy, bacteria, or fungal disease. There were no post-HCT treatments in this patient. The final patient presented with chronic rhinosinusitis, with elevated Lund-Mackay (16/24) and elevated endoscopic grading (12/20) scores. The patient underwent bilateral ESS prior to transplant. This patient’s post-HCT course was unremarkable from a rhinologic perspective.

Following HCT, 4 (different) patients (6%) were diagnosed with “sinusitis” by the primary treating service (Table 2). One of the 4 patients complained of rhinorrhea during pre-HCT evaluation, but was noted to have no endoscopic or CT evidence of rhinosinusitis. One patient was found to have symptoms consistent with dental pathology and had no endoscopic or CT evidence of rhinosinusitis. A third patient was diagnosed with uncomplicated acute maxillary rhinosinusitis and was treated with antibiotics. The final patient evaluated presented with pain, periorbital edema, and acute vision loss. The Lund-Mackay score was 5, and the endoscopic grading score was 4/10 (right side). He underwent emergent ESS and was found to have purulent sphenoid fluid and a dehiscent optic nerve. Cultures were negative for fungal organisms. His vision improved following surgery.

No patient developing GVHD was diagnosed with acute or chronic rhinosinusitis or a complication related to rhinosinusitis or required otolaryngology intervention following HCT.

Discussion

Rhinosinusitis in the post-HCT population can be difficult to treat, and given the immunosuppression patients experience, physicians seek means of predicting which patients will experience complications. The ideal manner in which to screen HCT patients has yet to be determined, and existing data regarding screening are few.

Patients referred to otolaryngologists for pre-HCT workup often undergo a physical examination and in many cases are evaluated with nasal endoscopy and imaging (eg, CT, magnetic resonance imaging, plain films) and may even have...
cultures. Were all patients to undergo this sort of evaluation, the direct medical costs could exceed $56,000,000 annually. Controlling medical care expenditures is increasingly necessary, and the costs associated with an uncertain pre-HCT workup need to be considered.

In our review, we sought to identify whether pre-HCT sinonasal evaluation could predict or influence the outcome of patients following HCT. Of the 71 patients evaluated, only 4 (6%) were considered to have symptoms or radiological findings significant enough to undergo either medical or surgical intervention prior to undergoing HCT. Following transplantation, 4 different patients were evaluated for sinonasal complaints; 2 were treated medically or surgically for diagnosed acute rhinosinusitis. The data in all 4 post-HCT patients were reviewed to see if there were pre-HCT factors that correlated with post-HCT findings. The mean pre-HCT endoscopic score in these patients was low (0.5). Cultures either grew nothing or were CNS. Despite the development of symptoms post-HCT, these 2 patients were asymptomatic and had negative endoscopies pre-HCT. As for the remainder of patients, 67 of 71, including 12 with pre-HCT radiographic abnormalities and 14 with pre-HCT endoscopic abnormalities, did not develop any post-HCT rhinosinusitis or complications. Because some patients with normal pre-HCT evaluations developed disease and some patients with pre-HCT abnormalities failed to develop disease, we fail to see any relationship between evaluation and outcome in our group.

The Value of Endoscopic Cultures

This study is the only one to our knowledge that attempted to look at middle meatus flora prior to HCT. Cultures were obtained in 33 of 71 (46%) patients prior to HCT. In the majority of patients, CNS, *S aureus*, and *Corynebacterium* were isolated. Of the 4 patients with post-HCT “sinusitis,” the 2 patients with definitive acute rhinosinusitis had pre-HCT cultures that did not correlate with post-HCT cultures. Although performing cultures is useful for guiding antibiotic therapy in patients with purulent drainage, they do not appear to be useful in helping predict outcome following HCT because only 1 of 33 patients with cultures actually developed acute rhinosinusitis post-HCT.

The Value of CT Imaging

Radiographic abnormalities can be found in 10% to 67% of patients undergoing HCT. Frequently, these patients are asymptomatic. The average Lund-Mackay score in our patient population was 2.2 ± 3.7. No patient with a positive pre-HCT sinus CT developed post-HCT rhinosinusitis. The pre-HCT sinus CTs in our study did not help us predict the rhinologic course in HCT patients. Rather, they confirmed the endoscopic findings in the 4 symptomatic patients prior to HCT. Because only 19 of 71 patients underwent pre-HCT imaging, more evidence needs to be acquired prior to recommending against pre-HCT imaging in the asymptomatic patient.

As with our study, Thompson et al were unable to find any relationship between pre-HCT CT imaging and post-HCT outcomes. Shaw et al identified 10 patients with pre-HCT CT abnormalities who developed acute rhinosinusitis following HCT; there were patients with multi-sinus abnormalities, however, who did not develop acute rhinosinusitis following HCT. This suggests that the CT findings may not accurately predict post-HCT outcomes. Both Kasow et al and Billings et al show that children undergoing HCT show sinus abnormalities 52% to 67% of the time; however, neither review discusses the extent of the disease or whether treatment prior to HCT would have possibly predicted or altered the outcome.

Computed tomography findings may appear in both asymptomatic and symptomatic patients undergoing HCT, and in this study, we found no relationship between pre-HCT findings and the outcome of patients undergoing HCT and may simply corroborate endoscopic findings.

The Value of Endoscopic Grading

Nasal endoscopy is recommended in the evaluation of patients with symptoms of chronic rhinosinusitis because it offers a more in-depth examination of the nasal cavity and sinuses. Endoscopic grading can be used to standardize the amount of purulent discharge, scarring, crusting, edema, and polyps in patients with nasal symptoms. In our study, all 71 patients underwent endoscopic grading, the mean of which was 0.6 ± 1.6; 94% of patients (67/71) had a score of ≤2. Of the 4 patients who required a post-HCT evaluation, 3 had pre-HCT endoscopic scores of 0, and 1 patient had a score of 2. Coupled with the 14 of 71 pre-HCT patients with endoscopic abnormalities who did not develop post-HCT rhinosinusitis, it is not clear to us as to whether pre-HCT endoscopic grading had any ability to predict post-HCT course.

Although Shaw et al performed endoscopy in the 26 patients undergoing HCT, there was no specific delineation of the endoscopic findings but rather physical exam findings that included septal deflection, “mucosal disease,” drainage, turbinate enlarge-ment, and tenderness. We observed a low incidence of mucosal inflammation based on endoscopy. Shibuya et al recommend endoscopic examination in addition to CT imaging, but it was not made clear how endoscopy might aid in guiding treatment. Similarly, it is not clear how endoscopy guided treatment in our population because the rate of positivity was very low.

The role of endoscopy in the diagnosis of rhinosinusitis has been studied before, especially in relationship to symptoms and CT imaging. In a review of 78 patients, Stankiewicz demonstrated that a negative nasal endoscopy predicted a normal CT in 78% of patients. The authors also suggested that if endoscopy is positive, a CT is not necessary to initiate medical treatment; however, if nasal endoscopy is negative, treatment may not be necessary despite symptoms. In our study, the percentage of pre-HCT patients with positive endoscopic findings was low (6%). The rate of positive CT findings in pre-HCT patients was also low (14%); however, the population studied with CT imaging was low as well (19/71). Although we cannot attest to the true rate of CT positivity, we can attest to the fact that endoscopic evaluations were by and large negative in this group.

The rate of positive endoscopy in our population was low. However, the question is not really whether endoscopy correlated...
with CT findings or symptoms but rather the post-HCT course. No factors in our pre-HCT nasal endoscopy were capable of predicting sinonasal outcomes in patients post-HCT. Therefore, although useful in the evaluation of patients in general, nasal endoscopy does not appear to be useful as a screening tool in patients undergoing HCT.

Limitations

There are a number of limitations to this study. Foremost, the study is retrospective in nature, and although we review the course and outcomes of consecutive patients undergoing HCT at our institution, the manner in which each patient was evaluated and followed was not uniform. Not all patients had pre-HCT cultures performed. Only selected patients with evidence of rhinosinusitis underwent pre-HCT imaging until imaging was made standard in 2008. Only patients with clinical evidence of disease underwent CT imaging following HCT, and the timing was based not on standardized interval but rather on symptoms during an evaluation. The retrospective nature of the study and the absence of certain pre-HCT evaluation parameters lessen our ability to find factors in pre-HCT patients that predict post-HCT disease. However, all patients were evaluated by an otolaryngologist, and all underwent nasal endoscopy, which has the distinct advantage of correlating with CT when negative.10

Follow-up averaged 31 ± 8 months; more recent patients have not been followed as long as patients earlier in the review. It is not known whether some of these patients went on to develop acute or chronic rhinosinusitis or complications related to rhinosinusitis. It is possible that some have developed GVHD, which has been shown to correlate with post-HCT rhinosinusitis.5

Patients who developed post-HCT rhinosinusitis originally presented with symptoms of rhinosinusitis; however, the number of patients (2/71 or 2.8%) was too small to draw statistical analysis. Ongoing collection of data will allow us to determine the significance of this finding.

Conclusions

All patients underwent physical examination and nasal endoscopy, and with adjunctive evaluation, we were unable to find a significant incidence of rhinosinusitis in the pre-HCT population and were not able to find any pre-HCT patient characteristics that would predict the incidence and outcome of post-HCT disease. All patients who required pretransplant medical or surgical intervention had symptoms of rhinosinusitis elicited during the medical interview. The 2 patients who did develop significant rhinosinusitis following transplantation had no evidence of disease during pre-HCT evaluation; however, at this time, we are unable to determine the significance of this finding. The pre-HCT evaluation is often costly and time-consuming. The findings in this review suggest that pre-HCT examination may have limited utility; however, continued study is necessary.

Author Contributions

Carl W. Moeller, project conception, data collection, data interpretation, manuscript writing and revising, final approval; James Martin, data collection and interpretation, contribution to manuscript writing, final approval; Kevin C. Welch, project conception, data interpretation, revising and rewriting, final approval.

Disclosures

Competing interests: None.

Sponsorships: None.

Funding source: None.

References
