Evaluation of the Pretransplantation Workup before Allogeneic Transplantation

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A B S T R A C T

An extensive workup is generally performed before allogeneic transplantation. The extent of this workup varies substantially between centers because of a lack of guidelines. We analyzed 157 consecutive allogeneic transplant candidates to understand the significance of components of the pretransplant evaluation. Workup consisted of chest computed tomography (CT); magnetic resonance imaging of the head; dental, ears-nose-throat (ENT), ophthalmology, and gynecology evaluations; pulmonary function tests; echocardiography; cytomegalovirus PCR; urine culture; clinical evaluation; and disease staging. Results were categorized as "normal or minor finding" or "major finding" (having significant consequences such as further testing or therapy). Major findings were classified as incidental or related to history and symptoms. Components of the pretransplant workup with the highest rate of major findings were CT (22%), dental evaluation (13%), and ENT (12%, mostly symptomatic). All other components had a low rate of major findings. Although 126 transplants were performed as scheduled, 24 were delayed and 7 canceled at short notice. The main reasons for delaying or canceling transplantation were active infection and unexpected disease progression. A prospective evaluation of a more restricted, symptom-guided pretransplant evaluation appears to be warranted.

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (HSCT) is standard of care for a number of hematologic diseases. The procedure is associated with a substantial risk of morbidity and mortality. Efforts to make transplantation safer include an optimal selection of transplant candidates and an extensive pretransplant workup. The aims of this workup are to ensure sufficient organ function, rule out infections, evaluate disease status, and generally exclude any contraindications to allogeneic transplantation. Although recommendations concerning the pretransplant evaluation have been published [1], the extent and logistics of the pretransplant workup vary substantially among centers.

Numerous studies have shown a correlation between pretransplant abnormalities and transplant outcome, either for individual parameters such as pulmonary function tests [2] and echocardiography [3] or in the form of comorbidity scores, such as the hematopoietic cell transplantation-specific comorbidity index [4]. However, only a few studies have analyzed whether performing an extensive pretransplant evaluation reduces transplant-related mortality by detecting latent infections or unapparent organ dysfunction. In an attempt to understand the significance of the different components of our pretransplant workup as well as reasons for delaying or canceling a transplant, we evaluated the workup of 157 consecutive patients scheduled for allogeneic HSCT at our center.

METHODS

Patients

Between May 2010 and October 2012, allogeneic transplants were planned in 100 men and 57 women with a median age of 51 years (range, 19 to 70). Patient characteristics are shown in Table 1.

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Study Design and Definitions

We performed a retrospective chart review of the results of our pretransplant workup. Data were collected from electronic and paper charts and from the institutional database. All patients gave written consent to the analysis of outcome data at the time of treatment, and the study was approved by the institutional board of ethics.

At the time of analysis, the pretransplant workup consisted of magnetic resonance imaging (MRI) of the head; computed tomography (CT) of the chest and upper abdomen; gynecology, ophthalmology, ears-nose-throat (ENT), and dental evaluations; pulmonary function tests (PFTs) and echocardiography; and quantitative PCR for cytomegalovirus (CMV) in whole blood and urine cultures. All patients received a history and thorough physical examination and disease staging by bone marrow aspirate and biopsy. Patients with extramedullary disease (mainly those with lymphoproliferative disorders) additionally received staging by fluorodeoxyglucose positron emission tomography-CT imaging. Some examinations were canceled in selected patients because of scheduling issues.

We assessed the results of the pretransplant workup, categorizing results as "normal or minor finding" if no abnormalities were found or if abnormalities were detected that did not lead to further diagnostic or therapeutic interventions or "major finding" if results had significant consequences such as further testing or therapy. Among major findings, we distinguished between those that did not interfere with the transplant schedule, those that led to delay of the transplant, and those that led to cancellation of the transplant. In case of a major finding, we also considered whether this was incidental or whether the patient had clinical symptoms or a previous history indicating the patient was at risk for the given finding.

Statistical Analysis

Nonrelapse mortality was defined as death without previous relapse or progression. The incidence of nonrelapse mortality was calculated using the cumulative incidence method, and Gray's test was used to compare among groups.

RESULTS

One hundred twenty-six transplants were performed as scheduled, whereas 31 transplants were either delayed once (n = 22) or twice (n = 2) for a median of 21 days (range, 4 to 146) or were canceled altogether (n = 7). The number of major findings including those leading to delay or cancellation of transplant are summarized in Table 2 for the respective examinations. Examinations in which major findings led to delaying or canceling a transplant are depicted in Figure 1A. The distribution of incidental and symptomatic diagnoses among major findings is depicted in

Table 1
Patient Characteristics (N = 157)

Characteristics	Value
Median age at transplant, yr (range)	51 (19-70)
Male	100
Female	57
Diagnosis	
Acute myeloid leukemia	54
Acute lymphoblastic leukemia	26
Myelodysplastic syndrome	19
Lymphoproliferative disorder	25
Myeloproliferative disease	14
Multiple myeloma	15
Aplastic anemia	4
Planned conditioning intensity	
Myeloablative	112
Reduced intensity	45
Donor	
Related	70
Unrelated	86
Cord blood	1
Patient origin	
Transplant center	54
External center	103

Figure 1B. The number of major findings did not differ between patients referred from other centers and our own patients (data not shown). None of the patients whose transplant was delayed for reasons unrelated to the underlying disease experienced relapse or progression before being able to proceed to transplant. The nonreapse mortality at day 100 for all patients that proceeded to transplant was 11.3%, with 7.7% versus 14.1% for patients with no versus at least one major finding, respectively ($P = .13$).

MRI of the Head

Five patients had major findings in the MRI, 1 of which resulted in delay of transplant. There were 2 cases of clinically relevant sinusitis, 1 of which was symptomatic; 1 unclear lesion in the thalamus; 1 case of perineural effusion of both optic nerves, both of which led to further testing but did not need specific therapy; and 1 case of progressive subdural hematoma, which required surgery and led to a delay of the transplant. The hematoma was asymptomatic at the time of the workup but was previously known and had been symptomatic at the time of first manifestation several weeks before transplant and was therefore not classified as incidental.

CT of the Chest and Upper Abdomen

Over 20% of CT scans revealed major findings, of which almost half were incidental. Most of these were pulmonary infiltrates or nodules (n = 29), whereas new liver lesions were found in 4 cases and pleural effusions in another 2. All pulmonary infiltrates not previously documented were investigated by bronchoalveolar lavage, and antifungal or antibacterial therapy was initiated if appropriate (n = 21). Transplant was delayed because of previously undocumented liver lesions (n = 2) or cavitary lesions of the lung (n = 2).

Dental Evaluation

Dental evaluation revealed a major finding in 13% of patients, with most of these being incidental. Most of these were severe caries or periodontitis. Of note is the fact that sanitation of dental foci before transplant was recommended in 3 patients but not performed because of time constraints. None of these 3 patients developed active dental infection post-transplant.

Table 2
Major Findings

Exam (no. patients evaluated)	Major Finding		
	No Delay in Transplant (n = 126)	Transplant Delayed (n = 26)*	Transplant Canceled (n = 7)
MRI (n = 150)	4 (3%)	1 (1%)	0 (0%)
CT scan (n = 156)	31 (20%)	4 (3%)	0 (0%)
ENT (n = 153)	18 (12%)	0 (0%)	0 (0%)
Dental evaluation (n = 145)	17 (12%)	2 (1%)	0 (0%)
Gynecology (n = 52)	2 (4%)	0 (0%)	0 (0%)
Ophthalmology (n = 154)	1 (1%)	0 (0%)	0 (0%)
Echocardiography (n = 153)	1 (1%)	0 (0%)	0 (0%)
PFT (n = 153)	5 (3%)	0 (0%)	0 (0%)
CMV PCR (n = 145)	3 (2%)	1 (1%)	0 (0%)
Urine cultures (n = 143)	3 (2%)	0 (0%)	0 (0%)
Clinical evaluation (n = 157)	24 (15%)	7 (4%)	0 (0%)
Disease staging (n = 157)	Not applicable	7 (4%)	6 (4%)
Other	Not applicable	4 (3%)	1 (1%)
Donor issues		3	
Toxicity		1	
Revision of diagnosis			1

* Transplant was delayed once in 22 patients and twice in 2 patients.

ENT Evaluation

A major finding was diagnosed in 12% of ENT evaluations, almost all of these being sinus or upper respiratory tract infections (n = 16); however, only 1 finding was incidental. In 1 case pretransplant sanitation of chronic sinusitis was recommended but was not performed because of scheduling issues. This patient developed a severe fungal sinus infection 3 months post-transplant that required surgical revision.

Gynecology and Ophthalmology Evaluation

Gynecology and ophthalmology evaluation revealed major findings in only 4% and 1% of patients, respectively. Gynecology findings were bacterial vaginosis treated with metronidazole in 2 patients, 1 of which was asymptomatic. The major ophthalmologic finding was idiopathic asymptomatic bilateral papilledema, which led to further testing but did not require treatment.

Echocardiography and PFTs

Echocardiography showed only 1 major finding, which was a case of previously unknown heart failure, for which treatment was initiated. Not classified as major findings were 2 other patients with known heart failure where the echocardiography showed a stable ejection fraction, and therapy was not adjusted. PFTs showed mild to moderate obstruction for which inhalation therapy was initiated in 5 patients (3%), 1 of whom had a previous diagnosis of chronic obstructive lung disease. Abnormal PFTs that did not lead to further testing or treatment were not classified as major findings.

CMV PCR and Urine Culture

Three patients were found by PCR to replicate CMV and were treated, but transplant was performed as planned. One patient had a very high CMV load of 586,472 copies/mL and was symptomatic with CMV colitis with severe diarrhea, and transplant was delayed for CMV treatment. One further patient had a low positive CMV PCR that resolved without treatment and was not classified as a major finding. Three patients received treatment for bacterial urinary tract infection, which was asymptomatic in 1 patient. Urine culture was positive in another 9 patients who were not treated, but these were not considered as major findings.