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Review Article

Understanding basic steps to hematopoietic stem cell transplantation evaluation

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Abstract: We are celebrating one millionth transplant in year 2013! With continued improvement in hematopoietic cell transplantation (HCT) outcome, the indications for HCT continue to grow. Furthermore the sources of stem cells and the number of suitable matches are expanding. At the same time, modified transplantation regimens have facilitated safer procedures despite increase in patient's age and comorbidies. In the current era, any patient indicated for HCT has a stem cell source and therefore steps to HCT and coordinated pre-transplant care is an integral part of management to improve transplant outcome. This review discusses our approach to the transplant evaluation process and this article will serve as a valuable tool for primary care physicians and referring hematologists/oncologists.

Keywords: Transplantation, hematological malignancies, preparation, evaluation

Introduction

Hematologic malignancies account for approximately 10% of new cancer diagnoses in the United States [1]. For some, chemotherapy alone gives a high chance of cure. However, those diseases that cannot be cured with chemotherapy alone must often proceed to a hematopoietic stem cell transplantation (HCT). HCT provides curative therapy for a variety of diseases. Over the past several decades, significant advances have been made in the field of HCT and now allo-HCT has become an integral part of treatment modality for a variety of hematological malignancies and non-malignant diseases [2, 3]. Advances in transplantation technology and supportive care measures have resulted in significant decrease in early mortality resulting in continued growth in the number of long-term HCT survivors [3-6].

Since the first 3 cases of successful allo-HCT in 1968, the number of allo-HCTs performed annually has increased steadily over the past 3 decades [3]. It is estimated that by 2015 more than 100,000 patients will receive HCT (combined allogeneic and autologous) annually throughout the world, and numbers are increasing rapidly. Long-term survival after HCT has improved significantly since its inception over 40 years ago due to improved supportive care and early recognition of long-term complications [7, 8]. With broadening indications, more options for HCT and improvement in survival, by 2020 there may be up to a million long term survivors after HCT worldwide. In order to offer the curative allo-HCT treatment option in most patients, safer regimens with acceptable GVHD associated morbidity and TRM are preferred. A recently published MDACC study showed an excellent overall survival and progression-free survival (85% and 83%, respectively after median follow-up of 60 months) for relapsed follicular lymphoma after FCR RIC allo-HCT [9]. Similarly, many disease specific transplant regimens are in development to improve transplant outcome after HCT.

In this era, a stem cell source can be found for virtually all patients who have an indication to receive allo-HCT. Since 2007, more allo-HCT procedures have been performed using alternative donor stem cell sources, such as volunteer unrelated donors or cord blood than related donors [4]. Reduced intensity conditioning (RIC) haploidentical-related donor or cord blood

Table 1. Data review during different stages of transplant evaluations process

Discussion/Testing	Initial transplant center (pre-evaluation) visit	Pre-transplant Evaluation	Per referring hematologist/ oncologist
Diagnosis			x
Confirm Diagnosis, review pathology	x		
PMH review for consults needed (for clearance)	x	x	x
Question regarding potential related donors	x		x
Initial HLA typing	x		
Confirmatory HLA typing		x	
Question regarding substance use	x	x	x
Obtain negative substance screens	x	x	x
Review transplant goals	x	x	x
Review transplant complications (ie: infection, GVHD)	x	x	
Review transplant long-term follow up	x	x	
Review dental requirements	x	x	
Review organ function requirements	x		
Review time required near transplant center	x	x	
Review need for 24 hour caregiver during transplant	x	x	
Final disease testing		x	
Final organ function testing & lab work	x	x	
Donor testing (if applicable)		x	
Psychosocial evaluation		x	
Outside department referrals for transplant clearance	x	x	

PMH- past medical history; HLA- human leukocyte antigen; GVHD- graft-versus host disease.

transplantations have emerged as alternatives to fill the gap for those patients who do not have matched related donor or unrelated donor [10-12] and the outcome of these types of transplantations are expected to be better than chemotherapy alone or even better than auto-HCT for selected indications.

Being a most effective therapy for many hematological diseases creates an obligation to educate referring physicians on timely referral for HCT and co-ordination of pre-transplantation care to improve further transplant outcome. Many physicians are not aware of procedures to the transplant process after an initial referral discussion with transplant physician and our goal in this article is to walk through the basic steps to HCT.

Initial steps

Once it is determined that a patient should consider a HCT, there are several key steps to move toward this therapy. A patient should be referred to a transplant center to undergo a detailed evaluation for such. It is optimal to refer early as some pre-transplant treatments could alter a patient's anticipated transplant course.

Once a patient is referred to a transplant center, many internal steps begin. Prior to the patient's first visit, the clinic staff will obtain outside records (**Table 1**). These would include baseline and cumulative labs, clinic notes, hospital admission and discharge notes, chemotherapy infusion records, radiation records, and scan reports. Pathology will also be requested for review at the transplant center. If there is question regarding the exact disease process, discs of the scans will also be requested for radiological review.

Preparation for transplant center evaluation

Generally a referral appointment with transplant center occurs within one to two weeks of initial request. At the first visit the physician team will review patient's history. This review will include diagnostic workup, treatment completed, and tolerance to the treatment. They will also ask the patient numerous other questions to determine their eligibility for transplant. Key information to obtain will be past medical history, past surgical history, family history, substance use (prior and current), and social support.

Patients being considered for allogeneic stem cell transplant will also be asked about potential family donors. Potential donors would primarily include full siblings, but may not be limited to this. They would also be questioned about children, parents, and double first cousins. It is important for patients to know healthcare concerns about their family members that might preclude them from donation, such as

heart disease or oncologic history. If it is determined that there is a suitable candidate or candidates, the physician team will request HLA typing from the financial team on the patient and the family member(s). HLA typing results are typically available within a week's time.

During the initial visit, patients are also counseled regarding the transplant procedure. For patients who will be proceeding to an autologous HCT, the discussion will focus on the process for stem cell collection followed by high dose chemotherapy and stem cell rescue. They will be asked to stay near the transplant center for approximately one month after the transplant. For patients who will be proceeding to an allogeneic HCT, they will be counseled on high dose chemotherapy followed by stem cell rescue from an allogeneic donor. They will be asked to stay near the transplant center for approximately three months after the transplant. These patients are at risk for graft versus host disease (GVHD). Discussions regarding GVHD begin at this visit. Patients will also be told at this visit of their dental requirements and the need for a 24 hour caregiver during the acute transplant course.

After the initial visit, the patient is instructed to follow up with their local oncologist. Any recommendations for further treatment prior to transplant will be communicated by the staff at transplant center. Treatment recommendations may focus on disease debulking or maintenance therapy while a donor is selected (for allogeneic HCT patients). The local oncologist is asked to communicate with the transplant center once the requested disease control is obtained or if there is difficulty achieving this goal. More treatment may be recommended for the latter scenario. The transplant center, in turn, will also communicate with the referring oncologist once the patient and family members' HLA typing is complete. If no suitable donor is found, an unrelated donor search may be initiated.

Also, after the patient's initial visit with the transplant center, their primary hematologist will present the patient's case to the transplant board. This board consists of both transplant physicians and non-transplant physicians. Each case is discussed in detail with a recommendation to follow. If a patient is approved to proceed with either an autologous or allogeneic HCT, the patient is placed on the physician's hold list until all identified pending criteria are met. The results of this discussion are reviewed with the patient and referring physician along with what criteria must be met before proceeding to transplant.

Transplant center evaluation

Once a patient has met the criteria to move ahead with transplant and a donor has been identified (self, related, or unrelated), they are referred internally from their transplant center's hematologist into the actual transplant program. The patient's insurance company is contacted to gain initial clearance to proceed with further testing to ensure eligibility. The patient will be contacted by the transplant nurse practitioner to set up a two day transplant evaluation.

During the two days of evaluation, patients will undergo disease and organ function testing as well as a teaching session [13]. Disease testing may include bone marrow biopsy, radiological scans, and possibly a lumbar puncture. For some diseases, testing will also include blood and urine studies. Organ function testing will include electrocardiogram, chest x-ray, echocardiogram, and a pulmonary function test. Other blood work beyond disease testing will include a complete blood count with differential, comprehensive metabolic panel, cholesterol and triglyceride levels, viral testing, a urinalysis, drug and nicotine screens. Women will have hormone levels tested along with a pregnancy test. Men will have a prostate specific antigen checked. For allogeneic HCT patients, they will also see physical therapy and have a baseline bone density scan performed. If any of the evaluation workup is abnormal or if a patient is known to have health concerns, additional referrals will be made at this time. Referrals may include cardiology, urology, pulmonology, or infectious disease, for example. These referrals may require additional visits to the transplant center.

During the transplant evaluation, patients will be counseled further about the need for a 24 hour caregiver during transplant. They will be asked to submit their dental clearance and must have a tuberculosis skin test completed. Patients will have a visit with the financial counselor during the two day evaluation as well as

meet with a research team member if they are eligible for any current transplant related studies. Patients will also meet with a social worker. The social worker will assist with securing local housing for the transplant, but will also screen for any psychosocial concerns that may complicate transplant. The social workers also help inform patients of charities and programs that can assist the patients throughout the transplant.

Transplant teaching is a significant portion of the two day evaluation. A nurse practitioner will meet with the patient and caregiver(s) to not only review his/her in depth history, but also to inform the patient of the anticipated course along with the risks and benefits from the transplant. Items discussed will be proposed treatment dates, central line placement, treatment regimen (chemotherapy and/or radiation), nutrition, need for transfusions, infection risk, graft versus host disease, and long term complications. Patients will also be informed of transplant related mortality along with other alternatives to transplant management.

Post-evaluation review and final pre-transplant process

For patients proceeding directly to transplant, a calendar will be reviewed with them. For patients awaiting dates from an unrelated donor (through the National Marrow Donor Program), they will be asked to continue routine follow up with their referring physician and possibly receive interim therapy. After the evaluation, it typically takes one week for all results to become available. Once this data is obtained, the patient's insurance company is again contacted, this time for final approval to proceed. Insurance approval typically occurs within a week's time. Therefore, most patients will begin transplant about two weeks after initial evaluation, provided no additional workup is needed. Patients undergoing transplants from unrelated donors usually wait about six weeks between evaluation and transplant.

For those patients with related donors, the donor will undergo simultaneous workup. Donors will be asked to come to the transplant center for a half day of evaluation. Their evaluation will include blood work, tuberculosis testing, electrocardiogram, and chest x-ray. They will also undergo questioning regarding medical history and potential exposures which might present a risk to the recipient. Physical exam, along with the above mentioned studies, will help determine any risks to the donor themselves. Donors will also be counseled regarding the procedure and their individual risk.

After all testing is complete and insurance approval has been obtained, the recipient will undergo a final day of evaluation just prior to the start date for the transplant. This is to ensure no significant changes have occurred since evaluation that might place a patient at greater risk post-transplant. This evaluation includes a physical exam, blood work, and questioning regarding current health status. Two physicians will review all of the patient (and donor if applicable) information to approve them. If all data is unchanged and no heightened risk is identified, patient will then proceed to central line placement and chemotherapy in preparation for the transplant. A handover procedure is in place to ensure smooth transition to the post-transplant team that will then assume care. Referring physicians will be sent weekly updates as well as end of treatment notifications and recommendations.

Declaration of commercial interest

None.

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References

[1] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012; 62: 10-29.

[2] Thomas ED. A history of bone marrow transplantation. In: Appelbaum FR, Forman SJ, Negrin RS, Blume KG, editors. Thomas' Hematopoietic Cell Transplantation. West Sussex, UK: Wiley-Blackwell 2009; pp: 3-7.

[3] Horowitz MM. Uses and growth of hematopoietic cell transplantation. In: Appelbaum FR, Forman SJ, Negrin RS, Blume KG, editors. Thomas' Hematopoietic Cell Transplantation. West Sussex, UK: Wiley-Blackwell 2009; pp: 15-21.

[4] Pasquini MC, Wang Z. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR Summary Slides, 2010 at: http: //www.cibmtr.org. http: //www.cibmtr.org.
[5] Majhail NS, Rizzo JD, Lee SJ, Aljurf M, Atsuta Y, Bonfim C, Burns LJ, Chaudhri N, Davies S, Okamoto S, Seber A, Socie G, Szer J, Van Lint MT, Wingard JR, Tichelli A. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. Bone Marrow Transplant 2012; 47: 337-341.
[6] Majhail NS, Douglas RJ. Surviving the cure: long term followup of hematopoietic cell transplant recipients. Bone Marrow Transplant 2013; [Epub ahead of print].
[7] Savani BN. How can we improve life expectancy and quality of life in long-term survivors after allogeneic stem cell transplantation? Semin Hematol 2012; 49: 1-3.
[8] Savani BN, Griffith ML, Jagasia S, Lee SJ. How I treat late effects in adults after allogeneic stem cell transplantation. Blood 2011; 117: 3002-3009.
[9] Khouri IF, McLaughlin P, Saliba RM, Hosing C, Korbling M, Lee MS, Medeiros LJ, Fayad L, Samaniego F, Alousi A, Anderlini P, Couriel D, de LM, Giralt S, Neelapu SS, Ueno NT, Samuels BI, Hagemeister F, Kwak LW, Champlin RE. Eight-year experience with allogeneic stem cell transplantation for relapsed follicular lymphoma after nonmyeloablative conditioning with fludarabine, cyclophosphamide, and rituximab. Blood 2008; 111: 5530-5536.
[10] Savani BN. Transplantation in AML CR1. Blood 2010; 116: 1822-1823.
[11] Nishiwaki S, Atsuta Y, Tanaka J. Allogeneic hematopoietic cell transplantation from alternative sources for adult Philadelphia chromosome-negative ALL: what should we choose when no HLA-matched related donor is available? Bone Marrow Transplant 2013; [Epub ahead of print].
[12] Bacigalupo A, Marsh JC. Unrelated donor search and unrelated donor transplantation in the adult aplastic anaemia patient aged 18-40 years without an HLA-identical sibling and failing immunosuppression. Bone Marrow Transplant 2013; 48: 198-200.
[13] Hamadani M, Craig M, Awan FT, Devine SM. How we approach patient evaluation for hematopoietic stem cell transplantation. Bone Marrow Transplant 2010; 45: 1259-1268.