Cellular Therapy and Transplantation (CTT). Vol.5, No.4 (17), 2016
doi: 10.18620/ctt-1866-8836-2016-5-4-15-20
Submitted: 21 September 2016, accepted: 28 October 2016

Allogeneic transplantation of hematopoietic stem cells and solid organ in the same patient: an update

Tapani Ruutu

Tapani Ruutu, Helsinki University Hospital, Biomedicum 2C, POB 705, FIN-00029 HUS, Helsinki, Finland

Phone: +358 50 555 1279
Fax: +358 9 4717 1506
E-mail: tapani.ruutu@hus.fi

Summary

Solid organ transplantation (SOT) is widely used for the treatment of end-stage organ insufficiency. Meanwhile, allogeneic hematopoietic stem cell transplantation (HSCT), by itself, causes frequent organ injury, thus being a potential indication for SOT. Due to increasing numbers of these interventions worldwide, a probability of combined disorders requiring both SOT and HSCT in the same patient is increasing. These transplantation combinations represent some clinical problems. Appropriate risk factors that may affect subsequent SOT outcomes post-HSCT include toxicity of HSCT procedure, immunosuppressive treatment for HSCT patients which may not be optimal for the SOT, potential problems caused by tissue incompatibility between host tissues, hematopoietic graft, and the solid organ graft, and emerging infections. Vice versa, in SOT recipients, the immunosuppressive medication may affect the organ functions, and increase the risk of infections. Moreover, SOT can be associated with development of hematological disorders, such as aplastic anemia, post-transplant lymphoproliferative disease, acute leukemias, etc. This paper aims at updating recent clinical experience with HSCT and SOT in the same patients. Here we discuss the survey which enrolled patients from 107 EBMT centres and clinical data on 45 SOTs carried out in the patients who previously underwent allo-HSCT. Kidney transplantations were performed, mainly, because of the drug-induced organ affection, or radiotherapy, whereas liver transplantations were made either early, for severe VOD or aGvHD, or later, due to chronic liver GVHD or cirrhosis. Survival rates and clinical outcomes are analyzed for each clinical situation in the groups. A special attention is given to the patients who received lung transplants in cases of bronchiolitis obliterans following allo-HSCT, characterized by inferior clinical outcomes and shorter survival time.

Some recent data concern allo-HSCT carried out after SOT. The hematological relapse rate was 22 %, thus allowing long-term observations. The 5-year rate for the solid organ failure was about 30%, mostly, due to graft rejection.

In summary, SOT can represent a valuable treatment strategy in HSCT recipients who develop an organ failure. Infections, graft rejection and other complications are frequent but usually manageable. Also, selected SOT recipients developing hematological disorders may benefit from allo-HSCT.

Keywords

Hematopoietic stem cell transplantation, solid organ transplantation, sequential treatment, indications, clinical outcomes, organ function.

Introduction

Solid organ transplantation (SOT) is widely used for the treatment of end-stage organ insufficiency. About 32000 SOTs were performed in the European Union in 2014, comprising approximately 20000 kidney, 7400 liver, 2100 heart, 1800 lung and 900 other transplants [6]. Allogeneic hematopoietic stem cell transplantation (HSCT) is the only cure or the most effective treatment for a large number of malignant and non-malignant diseases of the lympho-hematopoietic system with an otherwise poor prognosis. At present, the number of allogeneic HSCTs in Europe is more than 15000 per year [17]. With these large numbers of patients, the like-

lihood of coincidental occurrence of disorders potentially indicating SOT and HSCT in the same patient is increasing. Such transplantation combinations can be problematic for many reasons.

Allogeneic HSCT is an intensive treatment which frequently causes organ injury and failure, resulting in a potential indication for a SOT. The mechanisms of organ injury include cytotoxic drugs and radiotherapy in the pre-transplant conditioning, organ-toxic agents in supportive care, and immunological mechanisms. The organs most often affected are kidney, liver, lung and heart. Factors that may complicate a SOT in this setting are the fragility of the patient as a consequence of the toxicity of HSCT, immunosuppressive treatment for the HSCT which may not be optimal for the SOT, potential immunological problems caused by tissue type differences between the recipient, the hematopoietic graft and the solid organ graft, and infections. In SOT recipients, the long-lasting immunosuppressive medication may affect the function of organs, and increase the risk of infections. SOT can be associated with the development of hematological disorders comprising aplastic anemia, post-transplant lymphoproliferative disease, acute myeloid leukemia and myelodysplastic syndromes which can form a potential indication for allogeneic HSCT.

As the clinical situation is often found to be complicated and the risk of treatment failure regarded as high, the numbers of SOTs to HSCT recipients and those of HSCTs to SOT recipients have been low as compared to the number of patients who would have a potential indication for such treatment. Until recent years the literature of such transplantations consisted mainly of case reports as reviewed elsewhere [1,3,13], with the obvious risk of publication bias. This paper aims at updating recent clinical experience with HSCT and SOT in the same patients.

Experience with organ transplantation in hematopoietic stem cell transplant recipients

There is a rather limited published experience available for the assessment of the indications for SOT in HSCT recipients. Koenecke et al [13] carried out a survey among 107 EBMT (European Society for Blood and Marrow Transplantation) centres, with 67000 allogeneic transplantations performed during the study period of 1984-2007. In 28 centres a total of 45 SOTs had been carried out in 40 patients who had previously undergone allogeneic HSCT, of them 15 renal, 15 liver, 13 lung, 1 heart and 1 skin transplantation. Hence, the approximate frequency of these interventions was 67 SOTs per 100 000 HSCTs. Moreover, seven additional SOTs were identified from case reports or from centres that decided not to participate, altogether bringing the total number to 52 SOTs. The median age of the patients was between 20 and 35 years, depending of the organ graft type. The liver transplant patients were the youngest ones. Most of the patients had leukaemia, but about 15% had aplastic anaemia and another 15% an inherited disorder. A large majority of the patients received myeloablative conditioning. The graft had been bone marrow in 60%, and the donor was a matched related donor in 54% of the cases. Approximately half of the patients developed acute and/or chronic graft-versus-host disease. The median time from the HSCT to the organ transplantation ranged from 34 (liver transplants) to 84 (kidney transplants) months.

In kidney transplantations, the most frequent cause of renal failure was drug treatment or radiotherapy. All patients were on dialysis at the time of the SOT. The donor was unrelated in four cases and related in nine cases; of the latter four were the same as in the blood stem cell donation.

Patients receiving a liver transplantation could be divided into two groups, early and late transplantations after HSCT. Early liver transplantation (before six months post-HSCT) was performed because of acute liver failure due to veno-occlusive disease (VOD) or acute GVHD, late transplantation (usually 2-5 years post-HSCT) mostly because of chronic liver-GVHD or cirrhosis. In 75% of the transplantations an unrelated deceased donor was used.

In all lung transplantations the cause of the respiratory failure was bronchiolitis obliterans. In ten of the twelve cases the donor was a deceased unrelated donor. One of the two related donors was the HSCT donor.

The overall 5-year survival after SOT was 78%, in renal transplantations 100%, in liver transplantations 71% and in lung transplantations 63%. None of the renal transplantation patients was on dialysis at the end of the follow-up. The 2-year incidence of SOT failure was overall 16%, 20% in patients with GVHD preceding the SOT and 7% in those with no GVHD. Graft rejection occurred in approximately 30% of the patients with each type of transplantation, but it could usually be treated. Two patients with renal transplantation, 2 with liver transplantation and 4 with lung transplantation experienced graft failure. The relapse incidence of the underlying malignant disease was 4% at 5 years after the SOT. Of the six patients who received the SOT from the original HSCT donor (4 renal, 1 liver, 1 lung transplantation), all but the lung transplantation patient were alive at the time of the analysis.

Bronchiolitis obliterans has been the main indication for lung transplantation after allogeneic HSCT. Holm et al [10] reported on 13 such patients from the Nordic countries. Their median age was 34 (range 16-55) years. The indication for the HSCT had been a malignant hematological disease in all but two patients. All suffered from chronic GvHD. The median time from the HSCT to the lung transplantation was 8.2 (range 0.7-16) years. All had a bilateral lung transplantation. With a median follow-up time of 4.2 years from the lung transplantation, the survival of the patients was 90% at one year and 75% at 5 years. Of the two patients who died, one died of relapse of the underlying disease and one of infection. These results were compared to data obtained from the Scandiatransplant registry and found not to be differ-

ent from the general population of lung transplant patients. Four patients developed BOS in the transplanted lung; in one case, a second transplantation was carried out. Vogl and coworkers [27] reported a cohort of seven patients who received lung transplantation for bronchiolitis obliterans after allogeneic HSCT. In this cohort there was a case fatality rate of 57% and the median survival was 24 months after the lung transplantation. In this group of patients the interval between the HSCT and the lung transplantation was much shorter than in the study of Holm et al, median 18 (6-120) months. Cheng et al [2] reported on the outcome of nine patients with lung transplantation after allogeneic HSCT with a survival of 89 and 37% at 1 and 5 years, respectively. Jung ad coworkers [11] published recently their experience with nine patients treated with lung transplantation for BOS. After a relatively short median follow-up of 17 months, six of the nine patients were in good health. Soubani et al [21] reviewed recently the literature and identified 79 recipients of lung transplantation after allogeneic HSCT, including the patients of most of the reports referred to above. The median time from the HSCT to the lung transplantation was 52 months, and at three years the survival was 79%. Thirty per cent of the patients had developed BOS after the transplantation. The risk of relapse of the underlying hematological disease did not seem to be increased.

Upadhyay and Fine [26] have presented a review on solid organ transplantation following end-organ failure in recipients of hematopoietic stem cell transplantation in children. The results have been dependent on various risk factors, but especially the kidney transplant patients have fared well, and the authors recommend transplantation of the failed organs to be considered as potential treatment in selected patients.

Experience with allogeneic HSCT in solid organ transplant recipients

Basak et al [1] reported a survey of allogeneic HSCT carried out after SOT at EBMT centres. Thirty-one HSCTs had been performed in 28 SOT recipients. Thirteen patients had a preceding liver transplantation, 12 kidney transplantation, and 3 heart transplantation. The indication for the HSCT was a malignant hematological disorder in 22/28 patients, mostly acute leukemia. The diagnosis leading to HSCT was known before the SOT in 8/28 patients. The median time from SOT to HSCT was 37 (range 1-315 months). Two thirds of the hematopoietic grafts were from peripheral blood. Approximately one half of the donors were HLA-identical siblings, the rest unrelated or haploidentical. Half of the patients received myeloablative, the other half reduced intensity conditioning. All evaluable patients except one showed engraftment, one graft was lost later. The incidence of acute and chronic GVHD was not clearly different from what could be expected in a general HSCT population. Despite the often advanced state of the underlying disease at the time of HSCT, the relapse rate was low, 22%. With a 5-year follow-up, solid organ graft failure occurred in 9 of 31 patients, in 5/13 (38%) of the renal transplantations, 3/15 (20%) of the liver transplantations, and in one of the three heart transplantations. Five of the nine failures were defined as graft rejection. The median time to graft failure was 1.8 months with a range of 0 to 131 months. The TRM at three months was 25%. Infection was the most common cause of death. The overall survival at five years after the allogeneic HSCT was 40% for all patients, 51% for liver transplant recipients and 42% for renal transplant recipients. There were no significant differences in the outcomes between different types of HSCT donors or grafts, or the conditioning intensity.

Doney et al [5] reported on eight patients who had received an allogeneic HSCT after SOT at their center. Four of the eight patients were alive after a median follow-up of 8.7 years post-transplantation. Schechter et al [20] published four pediatric patients, two of whom had been treated with HSCT for PTLD after heart transplantation, and two patients transplanted for aplastic anemia after liver transplantation. All four fared poorly and died within one year.

Discussion

Although a considerable number of reports describing SOT following HSCT have been published, the number of such transplantations has been small in relation to the frequent problems of organ injury and failure seen in clinical practice. There are apparently many reasons to this, including the often complicated clinical situation, poor general condition of the patient, and possibly a certain resistance of clinicians to consider such a treatment approach, but also insufficient information of the results of such transplantations. The described recent publications show that the outcomes can be quite good. In a previous survey [13], the 5-year survival of patients receiving a renal transplantation was 100 %, with no patient being on dialysis. The 5-year survival for liver transplantation was 71% and that for lung transplantation 63%. These figures are not markedly different from the outcomes in general SOT populations. It is clear that the patient populations in dual transplantations have been selected, with young patient age, benign diseases somewhat overrepresented, and underlying malignant disease under good control, but the results show that SOT carried out for organ failure after HSCT is a feasible treatment option in carefully selected patients. There is no indication that prolonged immunosuppressive treatment due to the SOT would significantly increase the risk of disease relapse. However, it has to be noted that in a large proportion of the patients in the survey [13], the SOTs following HSCT were carried out late, when the risk of relapse is already relatively low.

Bronchiolitis obliterans is a serious and problematic complication of allogeneic HSCT, for which there is no effective treatment. Therefore the good results of lung transplantations for this disorder, reported in some studies, are encouraging. In the report of Holm et al [10], the 5-year OS was 75%, in the report by Koenecke [13], 63%. In contrast, in the report of Vogl et al [27], the median survival in a group of seven patients was only 24 months and the case fatality rate 57%. As discussed by Holm et al [10], a major difference between the patient materials between their study and that of Vogl et al was the timing of the lung transplantation, the median time from the HSCT being 8.2 years in the Holm study vs. 18 months in the study by Vogl [27]. This proba-

bly reflects, at least in part, the general importance of patient selection; patients undergoing SOT early after HSCT being more likely to be at a high risk of failure because of a rapidly progressive complication and a more fragile general condition due to the recent HSCT.

The experience with dual transplantations including a cardiac transplantation published is small, consisting mainly of case reports [1,3,13,15,16,20]. Therefore, no general conclusions of heart transplantations in combination with HSCT can be drawn.

In a HSCT recipient treated with a SOT, the immunological conditions may be complicated. The immunosuppressive strategy applied in the two types of transplantations is somewhat different. These factors might affect the risk of solid organ graft rejection. In the survey [13], graft rejection was seen in renal transplantations in 4/13 cases, leading to kidney failure in two patients. These were treated with a second renal transplantation. In 2/14 liver transplantations rejection led to graft failure. In 2/10 lung transplantations rejection resulted in respiratory failure, in one case this was treated with retransplantation. Among the patients treated with lung transplantation in the study [10], no rejection leading to organ failure took place. Therefore, also given the small numbers of patients, the incidences of graft rejection were not markedly different from those that can be seen in non-HSCT SOT patients. The occurrence or absence of GVHD did not significantly affect the outcome.

The number of reports of HSCT in SOT recipients in the literature is rather limited. In such HSCTs the function and fate of the solid organ graft would be a concern. As shown in the survey [1], graft failure is a concrete risk; this was seen in 9/31 patients. There was a renal graft failure in 38%, liver graft failure in 20% and heart graft failure in 1/3 of the patients. In approximately half of the cases this was reported as being the result of rejection. There were no major problems with hematopoietic engraftment; with one exception, engraftment took place in all evaluable patients.

There are many possible mechanism of graft rejection in this transplant setting. An immune response can be directed against mismatched HLA molecules, because the hematopoietic graft is HLA-matched with the recipient rather than the solid organ. Conditioning prior to allogeneic HSCT and infection may increase the immunogenicity of the organ graft by enhancing antigen presentation, increasing costimulatory signals, changing the properties of the vascular endothelium, and suppressing regulatory T-cell function. Whereas the majority of solid organ grafts are matched with the recipient based on blood group, this is not required for HSCT donors. Thus, the majority of hematopoietic transplants are probably not matched with the solid organ graft, and this could affect the survival of the organ graft. Moreover, in most patients, the immunosuppressive regimen is changed after allogeneic HSCT from a regimen typical for SOT to an HSCT-specific regimen, which could be suboptimal in this situation.

Experience has been reported to show that tolerance to kidney transplant may occasionally occur after preceding HSCT, the organ graft surviving without any immunosuppression [4,9,18]. Some groups have worked for many years to develop methods to achieve tolerance to solid organ transplants by hematopoietic cell transplantation, aiming at mixed or complete chimerism [7,8,14,19,22-24,28,29]. The aim would be to avoid life-long immunosuppressive treatment with its adverse effects. After a long period of preclinical work some clinical experience is now available, mainly in kidney transplant patients [12,14,19]. It has been possible to discontinue immunosuppressive treatment permanently or for a long period of time in a significant proportion of organ transplant recipients after tolerance induction. The balance between the conditioning treatment, donor, chimerism, immunosuppressive treatment, organ rejection and graft-versus-host diseases is delicate, but this approach is of great importance with potentially major clinical consequences.

In summary, SOT can represent a valuable treatment strategy in HSCT recipients who develop an organ failure. In stringently selected young patients, the overall and organ survivals appear to be comparable to patients undergoing SOT for other causes. Complications, such as infections and graft rejection are frequent but usually manageable. Thus, SOT offers a viable therapeutic option for selected patients with single organ failure after HSCT. Also, selected SOT recipients suffering from hematologic disorders may benefit from allogeneic HSCT and experience long-term survival without loss of organ function.

Conflict of interests

No conflict of interests is declared.

References

1. Basak GW, Wiktor-Jedrzejczak W, Labopin M, Schoemans H, Ljungman P, Kobbe G, Beguin Y, Lang P, Koenecke C, Sykora KW, Te Boome L, van Biezen A, van der Werf S, Mohty M, de Witte T, Marsh J, Dreger P, Kröger N, Duarte R, Ruutu T. Allogeneic hematopoietic stem cell transplantation in solid organ transplant recipients: a retrospective, multicenter study of the EBMT. Am J Transplant. 2015; 15 (3): 705-714.

2. Cheng G-S, Edelman JD, Madts DK, Martin PJ, Flowers MED: Outcomes of lung transplantation after allogeneic hematopoietic stem cell transplantation. Biol Blood Marrow Transplant 2014; 20: 1169-1175.

3. Chiang KY, Lazarus HM. Should we be performing more combined hematopoietic stem cell plus solid organ transplants? Bone Marrow Transplant 2003; 31: 633-642.

4. Dey B, Sykes M, Spitzer T. Outcomes of recipients of both bone marrow and solid organ transplants: a review. Medicine 1998; 77: 355-369.

5. Doney KC, Mielcarek M, Stewart FM, Appelbaum FR. Hematopoietic cell transplantation after solid organ transplantation. Biol Blood Marrow Transplant 2015; 21 (12): 2123-2128.

6. EDQM, European Directorate for the Quality of Medicines & Health Care of the Council of Europe. Newsletter

Transplant. International figures on donation and transplantation 2014.

7. Fuchs EJ. Transplantation tolerance: from theory to clinic. Immunol Rev 2014; 258 (1): 64-79.

8. Granados JMM, Benichou G, Kawai T. Hematopoietic stem cell infusion/ transplantation. Curr Opin Organ Transplant 2015, 20: 49-56.

9. Helg C, Chapius B, Bolle JF, Morel P, Salomon D, Roux E, Antonioli V, Jeannet M, Leski M. Renal transplantation wihout immunosuppression in a shot with tolerance induced by allogeneic bone marrow transplantation. Transplantation 1994; 58: 1320-1421.

10. Holm AM, Riise GC, Hansson L, Brinch L, Bjørtuft O, Iversen M, Simonsen S, Fløisand Y. Lung transplantation for bronchiolitis obliterans syndrome after allo-SCT. Bone Marrow Transplant. 2013; 48 (5): 703-707.

11. Jung HS, Lee JG, Yu WS, Lee CY, Haam SJ, Paik HC. Early outcomes of lung transplantation for bronchiolitis obliterans syndrome after allogeneic haematopoietic stem cell transplantation; a single-centre experience. Interact CardioVasc Thorac Surg 2016; doi: 10.1093/icvts/ivw231

12. Kawai T, Sachs DH, Sprangers B, Spitzer TR, Saidman SL, Zorn E, Tolkoff-Rubin N, Preffer F, Crisalli K, Gao B, Wong W, Morris H, LoCascio SA, Sayre P, Shonts B, Williams WW Jr, Smith RN, Colvin RB, Sykes M, Cosimi AB. Long-term results in recipients of combined HLA-mismatched kidney and bone marrowtransplantation without maintenance immunosuppression. Am J Transplant. 2014; 14 (7): 1599-1611.

13. Koenecke C, Hertenstein B, Schetelig J, van Biezen A, Dammann E, Gratwohl A, Ganser A, Schleuning M, Bornhäuser M, Jacobsen N, Kröger N, Niederwieser D, de Witte T, Ruutu T. Solid organ transplantation after allogeneic hematopoietic stem cell transplantation: a retrospective, multicenter study of the EBMT. Am J Transplant. 2010; 10 (8): 1897-1906.

14. Leventhal JR, Elliott MJ, Yolcu ES, Bozulic LD, Tollerud DJ, Mathew JM, Konieczna I, Ison MG, Galcin J, Mehta J, BadderMD, Abecassis MMI, Miller J, Gallon L, Ildstad ST. Immune reconstitution/ Immunocompetence in recipients of kidney plus hematopoietic stem/ facilitating cell transplants. Transplantation 2015; 99: 288-298.

15. Lin RJ, Larson RA, van Besien K, Rich ES. Allogeneic hematopoietic cell transplantation for therapy-related myeloid leukemia following orthotopic cardiac transplantation. Case Reports in Hematology 2013; article ID 140138.

16. Lister J, Simpson JK, deMagalhaes-Silverman MM, Rybka WB, Donnenberg AD, Myers DJ, Ball ED. Allogeneic peripheral blood stem cell transplant for myelodysplasia after chemotherapy for post-transplant lymphoma in a cardiac transplant recipient at 10 years. Bone Marrow Transplant 1997; 19: 943-945.

17. Passweg JR, Baldomero H, Bader P, Bonini C, Cesaro S, Dreger P, Duarte RF, Dufour C, Kuball J, Farge-Bancel D, Gennery A, Kröger N, Lanza F, Nagler A, Sureda A, Mohty M for the European Society for Blood and Marrow Transplantation (EBMT). Bone Marrow Transplant 2016; 51: 786-792.

18. Sayegh MH, Fine NA, Smith JL, Rennke HG, Milford EL, Tilney NL. Immunological tolerance to renal allografts after bone marrow transplants from the same donors Ann Intern Med 1991; 114: 954-955.

19. Scandling JD, Busque S, Shizuru JA, Lowsky R, Hoppe R, Dejbakhsh-Jones S, Jensen K, Shore A, Strober JA, Lavori P, Turnbull BB, Engleman EG, Strober S. Chimerism, graft survival, and withdrawal of immunosuppressive drugs in HLA matched and mismatched patients after living donor kidney and hematopoietic cell transplantation. Am J Transplant 2015: 15: 695-704.

20. Schechter T, Gassas A, Weitzman S, Grant D, Pollock-BarZiv S, Dipchand A, Alexander S, Ali M, Avitzur Y, Doyle J. Hematopoietic stem-cell transplantation following solid-organ transplantation in children. Bone Marrow Transplant 2011; 46: 1321-1325.

21. Soubani AO, Kingah P, Alshabani K, Muma G, Haq A. Lung transplantation following hematopoietic stem cell transplantation: report of two cases and systematic review of literature. Clin Transplant 2014; 28: 772-782.

22. Spitzer TR: Intersection of hematopoietic cell and solid organ transplantation: lessons learned and unanswered questions. Biol Blood Marrow Transplant 2015; 21: 2037-2038.

23. Strober S. Use of hematopoietic cell transplants to achieve tolerance in patients with solid organ transplants. Blood 2016; 127 (12): 1539-1543.

24. Sykes M. Immune tolerance in recipients of combined haploidentical bone marrow and kidney transplantation. Bone Marrow Transplant 2015; 50: S82-S86.

25. Thomas SE, Hutchinson RJ, DebRoy M, Magee JC. Successful renal transplantation following prior bone marrow transplantation in pediatric patients. Pediatr Transplant. 2004; 8 (5): 507-512.

26. Upadhyay K, Fine RN. Solid organ transplantation following end-organ failure in recipients of hematopoietic stem cell transplantation in children. Pediatr Nephrol. 2014; 29 (8): 1337-1347.

27. Vogl UM, Nagayama K, Bojic M, Hoda MA, Klepetko W, Jaksch P, Dekan S, Siersch V, Mitterbauer M, Schellongowski P, Greinix HT, Petkov V, Schulenburg A, Kalhs P, Rabitsch W. Lung transplantation for bronchiolitis obliterans afer allogeneic hemaopoietic stem cell transplantation: a single-center experience. Transplantation 2013; 95:623-628.

28. Yolcu ES, Leventhal JR, Ildstad S. Facilitating cells in tolerance induction for kidney transplantation. Curr Opin Organ Transplant 2015; 20: 57-63.

29. Zakrzewski JL, van den Brink MRM, Hubbell JA. Overcoming immunological barriers in regenerative medicine. Nature Biotechnol 2014; 32 (8): 786-794.

Современные вопросы аллогенной трансплантации гемопоэтических стволовых клеток и солидных органов тому же пациенту

Тапани Рууту
Институт клинических исследований, Университетский госпиталь, Хельсинки, Финляндия

Резюме

Трансплантация органов (Тх) широко применяется для лечения тяжелой органной недостаточности. Аллогенная трансплантация гемопоэтических клеток (алло-ТГСК), как таковая, часто вызывает повреждение органов, что может быть показанием к Тх. В связи с возрастающим числом обоих видов лечения растет вероятность комбинированных состояний, требующих, как Тх, так и ТГСК у одного и того же пациента. Эти ситуации приводят к ряду клинических проблем. Так, факторами риска, способными повлиять на исходы Тх после ТГСК, могут быть: токсичность процедуры ТГСК, последующее иммуносупрессивное лечение, не адекватное режиму после Тх, возможные проблемы, связанные с тканевой несовместимостью больного, гемопоэтических клеток донора и органного трансплантата, а также развитие инфекций. В то же время иммуносупрессивная терапия больных после Тх может нарушать функции органа и повышать риск инфекций. Кроме того, Тх иногда ассоциирована с развитием гематологических заболеваний, как, например, апластической анемии, посттрансплантационных лимфопролиферативных заболеваний, острых лейкозов и др. Цель настоящей статьи состоит в анализе существующего клинического опыта в области алло-ТГСК и Тх у одних и тех же пациентов. В частности, рассматривается европейское исследование с участием 107 центров EBMT и клинические данные о 45 Тх, проведенных пациентам, которым ранее выполнялась ТГСК. Им проводили, главным образом трансплантацию почек из-за повреждений после химио- или радиотерапии, тогда как пересадки печени делали в ранние сроки после ТГСК в связи с тяжелой вено-окклюзионной болезнью или оРТПХб или позже, по поводу хронической РТПХ или цирроза. Выживаемость и клинические исходы анализировали для каждой клинической ситуации. Особое внимание уделяли больным, получавшим трансплантаты легких при облитерирующем альвеолите после алло-ТГСК, где наблюдались худшие клинические исходы и меньшие сроки выживания.

Ряд свежих работ касается алло-ТГСК, проведенных после Тх. Частота гематологических рецидивов составила 22%, что позволило длительно наблюдать пациентов. Пятилетняя выживаемость пересаженных органов была около 30%, в основном – из-за отторжения трансплантата.

Таким образом, Тх может быть ценной стратегией при лечении реципиентов гемопоэтических клеток в случае развития органной недостаточности. Инфекции, отторжение трансплантата и другие осложнения довольно часты, но обычно поддаются лечению. Кроме того, некоторые реципиенты органов, у которых развились гематологические заболевания, могут выиграть от алло-ТГСК.

Ключевые слова

Трансплантация гемопоэтических клеток, трансплантация органов, последовательное лечение, показания, клинические исходы, органная функция.