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Autologous Graft Versus Host Disease: An Updated Review

*Kanfar S and Al-Anazi KA**

Department of Hematology and Hematopoietic Stem Cell Transplantation, King Fahad Specialist Hospital, Saudi Arabia

Abstract

Graft versus host disease is an increasingly recognized complication of autologous hematopoietic stem cell transplantation. It may occur spontaneously, but can be induced by a number of immunosuppressive agents. There are specific risk factors for the evolution of this complication. Clinically and histologically, it resembles graft versus host disease occurring after allografting. It varies in severity from mild and self limited illness to severe forms that may become life-threatening. Early recognition and prompt institution of immunosuppressive therapy are essential to prevent further complications.

Keywords: Graft versus host disease; Hematopoietic stem cell transplantation; Draft versus tumor effect; Engraftment syndrome; Immunosuppressive therapy

Introduction

Graft Versus Host Disease (GVHD), that has Graft Versus Tumor (GVT) effect, is a major complication of allogeneic Hematopoietic Stem Cell Transplantation (HSCT) which is associated with significant morbidity and mortality [1-5]. GVHD in allogeneic HSCT is attributed to donor T cell recognition of recipient alloantigens which results in the generation of cytotoxic effector cells and the production of proinflammatory cytokines [1,4]. The higher relapse rates encountered after autologous HSCT compared with allogeneic HSCT were previously attributed to the lack of GVT effect following autologous HSCT [6,7]. However, recent as well as old studies argue in favor of the existence of autologous GVT effect without the detrimental complications of GVHD that follow allogeneic HSCT [6,8,9-11].

GVHD is an autoimmune complication of HSCT [12]. The recent increase in the number of studies reporting the clinical manifestations and the histological appearances as well as the responses to immunosuppressive therapies prove the existence of GVHD in the setting of autologous HSCT [1,3,4,13-22].

Landmarks in the history of autologous GVHD

Autologous GVHD has also been called: secondary disease, Omenn syndrome and autoaggression syndrome [13,19,23-26]. In 1951, Lorenz first described secondary disease; manifested by diarrhea, weight loss and coat changes; in lethally-irradiated mice receiving Bone Marrow (BM) and spleen cell transplants [13]. In 1955, Main and Prehn reported secondary disease in mice, when BM and spleen cells from a parent were injected into unirradiated F1 hybrid but not in the converse [13]. In the late 1970s, Rappeport reported the occurrence of GVHD in humans following syngeneic BM transplantation which prompted exploration of the biological mechanisms underlying this phenomenon [2].

In 1987, Hood retrospectively noted the onset of spontaneous autologous GVHD in 7 out of 96 recipients of autologous HSCT between 1977 and 1984 [2,27]. Most of the cases reported were mild, self-limited and all were confined to the skin. A minority of patients required treatment with topical or systemic corticosteroids [2]. Glazier in 1983 and Geller in 1989 developed preclinical transplantation models of autologous HSCT using cyclosporine-A to induce GVHD in the autologous HSCT setting [2,12]. In 1988, Jenkins and Gao demonstrated that while cyclosporine-A greatly reduced the number of mature CD4+ and CD8+ T cells, cyclosporine-treated mice harbored CD8+ T cells with T cell receptor specific for Human Leukocyte Antigen (HLA) class II antigens concluding that cyclosporine therapy impaired central tolerance [2]. In the year 2000, Borrello demonstrated that additional tumor specific antigens may play a role in the development of autologous GVT mechanisms using a syngeneic transplantation model [2]. In 2009, Paczesny described a biomarker panel associated with the clinical and pathological diagnosis of acute GVHD in the setting of allogeneic HSCT that included elevation of serum concentrations of: interleukin

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Correspondence:
Al-Anazi KA, Department of Hematology and Hematopoietic Stem Cell Transplantation, Oncology Center, King Fahad Specialist Hospital, P.O. Box: 15215, Dammam 31444, Saudi Arabia, Fax: 966 -13- 8427420; Tel: 966 - 03- 8431111;
E-mail: kaa_alanazi@yahoo.com

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(IL)-2Rα, interferon-R1, hepatocyte growth factor and IL-8 [13]. Lastly in 2011, Brandon found that antibiotic therapy of mice before syngeneic transplants with cyclosporine prevented the development of clinical and pathological features of acute GVHD that occurred when antibiotics were administered [13].

Epidemiology and incidence of autologous GVHD

Studies have shown that: (1) the incidences of spontaneous and induced GVHD following autologous HSCT are 5%-20% and 20%-100% respectively, (2) the incidences of spontaneous intestinal and skin autologous GVHD are 13% and 5%-10% respectively, and (3) the frequency of autologous GVHD induced by cyclosporine or IL-2 ranges between 30% and 80% [2,3,14]. The incidence of autologous GVHD following peripheral stem cell transplantation is lower than that following BM transplantation and this lower incidence may be attributed to peripheral regulatory cells that are transferred to the stem cell inoculum [26].

Etiology and pathophysiology of autologous GVHD

After syngeneic or autologous HSCT, a GVHD-like syndrome which is clinically and histologically indistinguishable from allogeneic GHVD has been described in the skin, liver and gastrointestinal tract (GIT) [3]. Autologous GVHD is an autoimmune syndrome initiated by auto-reactive T cells that recognize self-major histocompatibility complex (MHC) class II antigens [5,28-30]. In autologous GVHD, autoreactive CD8+ T cells recognize MHC class II determinants in association with a peptide from the invariant chain [31]. Also, the discrete antigen-driven expansion of T cells is involved in autologous GVHD [32].

The etiology of syngeneic and autologous GVHD is not well understood, but there are two hypotheses: (1) dominance of autoreactive T cells post-transplantation, and (2) presence of microchimeric or allogeneic T cells [3]. However, microchimerism can be established in two ways: (1) women have higher frequency of microchimerism than men as a result of passage fetal cells into maternal circulation during pregnancy, and (2) blood transfusion [3]. Recent studies have indicated that 2 major factors are necessary for the induction of autologous GVHD: (1) disruption of thymic-dependent immune reconstitution, and (2) failure to reestablish peripheral self-tolerance [19].

In Multiple Myeloma (MM), the predisposing factors for autologous GVHD may include dysregulation of immune response resulting from either the disease, or the immunomodulatory drugs that are used in the treatment of MM or the HSCT conditioning therapy [33]. Polymorphisms in the IL-10 promoter region may explain differences in the susceptibility of patients to autologous GVHD. Additionally, IL-10 and interferon-γ may be critical mediators for the development of autologous GVHD [31]. The association between autograft absolute lymphocytic count (ALC) on day 15 following autologous HSCT and survival further supports the existence of GVHD following autologous HSCT [6]. Induction of autologous GVHD may also be beneficial to recipients of autologous HSCT by providing GVT effect thus aiding the elimination of minimal residual disease after autologous HSCT [30,34,35].

Types of Autologous GVHD

There are three types of autologous GVHD: (1) spontaneous autologous GVHD [15,16,36-38], (2) induced autologous GVHD; using cyclosporine, tacrolimus, interferon-α, interferon-γ and alemtuzumab; in order to induce GVT effect in diseases such as: Hodgkin lymphoma, Non-Hodgkin Lymphoma (NHL), chronic lymphocytic leukemia and acute myeloid leukemia [14,23,26,28-31,34,36,39-41], and (3) GVHD induced by transfusion of unirradiated blood products [36].

Risk factors for spontaneous autologous GVHD

The following factors predispose to the development of spontaneous GVHD following autologous HSCT: (1) primary disease such as MM, NHL and breast cancer, (2) second autologous HSCT, (3) heavily pre-treated patients, (4) female gender, (5) high CD34+ stem cell dose infused, (6) achievement of high levels of ALC after autologous HSCT, and (7) the use of bortezomib, lenalidomide, pomalidomide and alemtuzumab in the pre-transplantation therapies of hematological malignancies [1,3,4,8,9,15-18,20,24,27,33,35-38,42-44].

Clinical manifestations of autologous GVHD

Autologous GVHD may present with: fever, erythematous skin eruption, liver dysfunction, nausea, vomiting, diarrhea, non-cardiogenic pulmonary edema and clinical features consistent with bronchiolitis obliterans organizing pneumonia (BOOP) [9,15,16,27,36,42]. The clinical manifestations of autologous GVHD are very variable. They may be mild and self-limited, moderate requiring immunosuppressive therapies or severe and life-threatening with partial or total unresponsiveness to treatment leading ultimately to organ failure and death. Also, autologous GVHD can be limited to one organ or it may involve multiple organs in either a subsequent or simultaneous manner [8,16-18,24,43-45].

In autologous GVHD, the following body organs are particularly involved: skin, GIT, liver, lungs and kidneys [1,3,15,19,20,22,23, 27,34,36,37,42,43]. Autologous GVHD may be acute, chronic or recurrent, thus all forms of GVHD can occur following autografting [4,15,21,22,37,38,42,46]. Studies have shown that autologous GVHD may be: (1) limited to one body organ or can involve multiple organs simultaneously [1,8,16-18,22,38,42,43,47] and (2) variable in severity from mild and self-limited that requires no treatment or local therapy to severe, steroid-refractory and life-threatening forms [1,3,4,15-17,24,36,37,42,43,47].

Skin involvement can be in the form of maculopapular eruption, diffuse erythema, desquamation, sclerodermatous changes or chronic lichenoid eruptions [1,16,21,46,47]. The following histological changes have been reported: dermatitis, cell necrosis, intra-epidermal pustules, proliferation of collagen bundles in the dermis, infiltration by lymphocytes and eosinophils in addition to lichenoid skin changes [1,16,21,46,47]. The clinical manifestations of GIT involvement include: anorexia, nausea, vomiting, heartburn, dysphagia, abdominal pain and diarrhea [1,3,4,16-18,20,22,45]. Histologically, the following findings have been encountered in autologous GVHD: mucosal inflammation, ulcerations and hemorrhage; apoptotic crypt cells and crypt abscesses; infiltration by lymphocytes, eosinophils and mononuclear cells; and fibrotic changes [1,3,4,16-18,20,22].

Autologous GVHD of the liver causes liver dysfunction and abnormal hepatic profile with biochemical evidence of elevation of serum levels of alkaline phosphatase, gamma glutamyl transferase, alanine aminotransferase and bilirubin and histological evidence of non-specific infiltration by lymphocytes and neutrophils in the portal areas [1,16,17]. Although lung involvement is rare in autologous GVHD, clinical manifestations such as dyspnea, productive cough, increasing respiratory distress and even respiratory failure have

been reported [27,42]. The following radiological abnormalities have been encountered: bilateral interstitial pulmonary infiltrates, multiple nodular lesions, bronchiolitis, bronchiectasis and tree in bud radiological appearances. In patients with BOOP syndrome, pulmonary function tests usually show mixed obstructive and restrictive ventilator defects [27,42]. Lung biopsies in patients with autologous GHVD have shown: apoptosis, perivasculitis, T cell infiltration, perivascular lymphocytic cuffing and bronchiolar lymphocytic infiltration [27]. Kidney involvement by autologous GVHD may present with proteinuria and renal dysfunction. Histologically the following changes have been reported: immune-mediated glomerulonephritis, deposition of immune complexes and membranous nephropathy [19]. Other rare clinical and laboratory features that have been reported in patients with autologous GVHD include: fever, variable degrees of BM suppression, thinning and ridging of nails in addition to onycholysis [17,45].

Biomarkers of autologous GVHD

The following laboratory abnormalities, which can be used as biomarkers, have been reported in patients with autologous GVHD: (1) lower CD3 and CD8 cell counts, (2) peripheral eosinophilia associated with eosinophilic GIT involvement secondary to elevated serum levels of IL-2, IL-4 and IL-5, (3) enhanced expression of GATA-2, CD130 and CXCR4 on CD34+ hematopoietic progenitor cells on flow cytometry, (4) profound FOXP3 regulatory T cell defect coinciding with hyper inflammatory T cell responses that are reversible by rapamycin administration, and (5) expression of HLA-B55 [15,20,25,33].

Diagnosis and differential diagnosis of autologous GVHD

The diagnosis of autologous GVHD of the GIT can be established when the following criteria are met: (1) ongoing GIT symptoms consistent with GVHD, (2) macroscopic evidence of abnormal mucosa of stomach, duodenum or colon on upper or lower endoscopy, (3) histological evidence of apoptosis or lymphocytic infiltration, and (4) negative viral, bacterial and fungal cultures for pathogens in stools, mucosal brushings or tissue biopsies [3]. The differential diagnosis of autologous GVHD includes: (1) infections such as cytomegalovirus, herpes simplex virus, adenovirus and enteroviruses, (2) medications such as chemotherapeutic agents; immunosuppressive therapies such as cyclosporine, tacrolimus and mycophenolate mofetil; non-steroidal anti-inflammatory drugs and laxatives, (3) engraftment syndrome, (4) transfusion-associated GVHD, and (5) pre-existing inflammatory bowel disease or coeliac disease in patients with GIT manifestations [4,36]. Thus, the diagnosis of autologous GVHD requires: (1) clinical suspicion, (2) ruling out other differentials such as infections, drug effect and engraftment syndrome, (3) performance of biopsies of skin, liver, GIT and lungs, and (5) having biomarkers of GVHD [1,4,13,48].

Management of autologous GVHD

The main lines of therapy of autologous GVHD are: (1) symptomatic treatment, (2) corticosteroids, and (3) other immunosuppressive therapies [1,4,15,20]. However, autologous GVHD can occasionally be severe and refractory to steroid treatment and may eventually cause death [1,4].

In most cases of autologous GVHD, spontaneous resolution occurs as the condition is mostly mild and self-limited [14,17,46]. In some cases topical or local therapy such as topical steroids for skin involvement or non-absorbable steroids for lower GIT involvement may be required [15,36,37,42]. In moderately severe cases, systemic corticosteroids in the form of oral prednisolone 1 mg/kilogram (kg) body weight/day or intravenous methylprednisolone 2 mg/kg/day in 2 divided doses may be needed for one week or even longer period of time then steroid therapy can be gradually tapered once clinical improvement is encountered [15,22,28,42-44,47]. Occasionally, prolonged corticosteroid therapy may be needed for patients who are not totally refractory to steroid therapy [24]. Also, autologous GVHD in some patients may be refractory to corticosteroids and such patients may develop organ dysfunction or failure and may eventually die [1,4,16,17]. However, other lines of therapy have been reported and these include: infliximab, alemtuzumab, rituximab, etanercept, rapamycin and hemicolectomy for refractory GIT forms of autologous GVHD [4,19,25].

Course and prognosis of autologous GVHD

The course of the disease is very variable and ranges from mild and self-limiting illness to severe forms which may require prolonged corticosteroid therapy or other more aggressive lines of treatment and the illness may even become life-threatening [1,4,14-17,19,22,24,25,28,36,37,42-44,46,47]. So, the prognosis largely depends on the: (1) severity of the illness, (2) grade of the GVHD, (3) number of organs involved, and (4) rapidity of initiation of therapy [1,4,20,45]. Prompt recognition of autologous GVHD is essential in order to prevent further complications [15,20,22,45].

Conclusions and Future Directions

GVHD is a well established complication of autologous HSCT. It resembles GVHD which is encountered following allogeneic HSCT clinically, biochemically, radiologically and even histologically. Also, it responds to corticosteroids and other immunosuppressive therapies. It is essential to establish its existence clinically and histologically, have biomarker panels taken at presentation, and to document not only its severity scores but also its response criteria.

As this complication has certain risk factors and favorable response to immunosuppressive therapies, it is vital to have early recognition of autologous GVHD and prompt institution of treatment in order to prevent further complications.

References

1. Drobyski WR, Hari P, Keever-Taylor C, Komorowski R, Grossman W. Severe autologous GVHD after hematopoietic progenitor cell transplantation for multiple myeloma. Bone Marrow Transplant. 2009;43(2):169-77.

2. Kline J, Subbiah S, Lazarus HM, van Besien K. Autologous graft-versus-host disease: harnessing anti-tumor immunity through impaired self-tolerance. Bone Marrow Transplant. 2008;41(6):505-13.

3. Holmberg L, Kikuchi K, Gooley TA, Adams KM, Hockenbery DM, Flowers ME, et al. Gastrointestinal graft-versus-host disease in recipients of autologous hematopoietic stem cells: incidence, risk factors, and outcome. Biol Blood Marrow Transplant. 2006;12(2):226-34.

4. Cogbill CH, Drobyski WR, Komorowski RA. Gastrointestinal pathology of autologous graft-versus-host disease following hematopoietic stem cell transplantation: a clinicopathological study of 17 cases. Mod Pathol. 2011;24(1):117-5.

5. Zalom M, Lill M, Lukic D, Balzer BL, Lim S. Autologous graft-versus-host disease after denileukin diftitox and autologous stem cell transplantation for refractory T-cell lymphoma. Leuk Lymphoma. 2009;50(1):124-6.

6. Porrata LF. Autologous graft-versus-tumor effect: reality or fiction? Adv Hematol. 2016;2016(2016):5385972.

7. Maloney DG. Graft-vs.-lymphoma effect in various histologies of non-Hodgkin's lymphoma. Leuk Lymphoma. 2003;44(Suppl 3):S 99-105.
8. Byrne JL, Carter GI, Ellis I, Haynes AP, Russell NH. Autologous GVHD following PBSCT, with evidence for a graft-versus-myeloma effect. Bone Marrow Transplant. 1997;20(6):517-20.
9. Al-Anazi KA. Autologous hematopoietic stem cell transplantation for multiple myeloma without cryopreservation. Bone Marrow Res. 2012;2012:917361-7.
10. Cornell RF, Hari P, Drobyski WR. Engraftment syndrome after autologous stem cell transplantation: an update unifying the definition and management approach. Biol Blood Marrow Transplant. 2015;21(12):2061-8.
11. Mutahar E, Al-Anazi KA. Engraftment syndrome: an updated review. J Stem Cell Biol Transplant. 2017;1(2):16.
12. Holbro A, Abinun M, Daikeler T. Management of autoimmune diseases after haematopoietic stem cell transplantation. Br J Haematol. 2012;157(3):281-90.
13. Otegbeye F, Gale RP, Lazarus HM. Autologous GVHD? Bone Marrow Transplant. 2014;49(11):1349-51.
14. Streetly M, Kazmi M, Radia D, Hoyle C, Schey SA. Second autologous transplant with cyclosporin/interferon alpha-induced graft versus host disease for patients who have failed first-line consolidation. Bone Marrow Transplant. 2004;33(11):1131-5.
15. Lazarus HM, Sommers SR, Arfons LM, Fu P, Ataergin SA, Kaye NM, et al. Spontaneous autologous graft-versus-host disease in plasma cell myeloma autograft recipients: flow cytometric analysis of hematopoietic progenitor cell grafts. Biol Blood Marrow Transplant. 2011;17(7):970-8.
16. Fidler C, Klumpp T, Mangan K, Martin M, Sharma M, Emmons R, et al. Spontaneous graft versus host disease occurring in a patient with multiple myeloma after autologous stem cell transplant. Am J Hematol. 2012;87(2):219-21.
17. Goddard DS, Ruben BS, Mathes ED, Nixon M, Wolf J, Fox LP. A case of severe cutaneous, GI and liver GVHD in a patient with multiple myeloma, status-post-second auto-SCT. Bone Marrow Transplant. 2010;45(2):409-11.
18. Garg A, Nityanand S. Isolated gastrointestinal graft versus host disease after autologous hematopoietic stem cell transplantation in a patient of multiple myeloma. Ann Hematol Oncol. 2017;4(4):1146.
19. Abudayyeh A, Truong LD, Beck LH, Weber DM, Rezvani K, Abdelrahim M. Membranous nephropathy in autologous hematopoietic stem cell transplant: autologous graft-versus-host disease or autoimmunity induction? Clin Kidney J. 2015;8(4):440-4.
20. Chen M, Olson K. Colonic graft-versus-host disease (GVHD) manifesting as eosinophilic colitis following autologous hematopoietic stem cell transplantation. Blood. 2013;121(20):4020.
21. Nakamura K, Kawakami Y, Oyama N, Kaneko F, Abe H, Sagara H, et al. A case of sclerodermatous graft-versus-host disease following autologous peripheral blood stem cell transplantation. J Dermatol. 2006;33(2):135-8.
22. Barbash B, Kramer S, Tzimas D, Saitta P. Graft-versus-host disease of the upper gastrointestinal tract after an autologous stem cell transplant. ACG Case Rep J. 2014;2(1):55-7.
23. Park J, Lee MH, Lee HR, Park SH, Lee SH, Lee KE, et al. Autologous peripheral blood stem cell transplantation with induction of autologous graft-versus-host disease in acute myeloid leukemia. Bone Marrow Transplant. 2003;32(9):889-95.
24. Lee SE, Yoon JH, Shin SH, Park G, Min CK. Skin graft-versus-host disease following autologous stem cell transplantation for multiple myeloma. Immune Netw. 2013;13(3):107-10.
25. Vinh DC, Bin Dhuban K, Mason H, Lejtenyi D, Jung S, Sheppard DC, et al. Acquired Omenn-like syndrome, a novel posttransplant autoaggression syndrome reversed by rapamycin. Clin Vaccine Immunol. 2012;19(1):109-12.
26. Miura Y, Ueda M, Takami A, Shiobara S, Nakao S, Hess AD. Enhancement of cyclosporin A-induced autologous graft-versus-host disease after peripheral blood stem cell transplantation by utilizing selected CD34 (+) cells. Bone Marrow Transplant. 2003;32(8):785-90.
27. Choi SI, Lee EJ, Kang DO, Lee SY, In KH, Kim HK, et al. Pulmonary graft-versus-host disease after autologous hematopoietic stem cell transplantation. Korean J Intern Med. 2016;31(6):1181-3.
28. Zenz T, Ritgen M, Dreger P, Kröber A, Barth TF, Schlenk R, et al. Autologous graft-versus-host disease-like syndrome after an alemtuzumab-containing conditioning regimen and autologous stem cell transplantation for chronic lymphocytic leukemia. Blood. 2006;108(6):2127-30.
29. Hess AD, Jones RC, Santos GW. Autologous graft-vs-host disease: mechanisms and potential therapeutic effect. Bone Marrow Transplant. 1993;12(Suppl 3):S65-9.
30. Karasuno T. Autologous graft-versus-host disease. Int J Hematol. 1997;65(2):105-113.
31. Miura Y, Thoburn CJ, Bright EC, Chen W, Nakao S, Hess AD. Cytokine and chemokine profiles in autologous graft-versus-host disease (GVHD): interleukin 10 and interferon gamma may be critical mediators for the development of autologous GVHD. Blood. 2002;100(7):2650-8.
32. Miura Y, Thoburn CJ, Bright EC, Sommer M, Lefell S, Ueda M, et al. Characterization of the T-cell repertoire in autologous graft-versus-host disease (GVHD): evidence for the involvement of antigen-driven T-cell response in the development of autologous GVHD. Blood. 2001;98(3):868-76.
33. Batra A, Cottler-Fox M, Harville T, Rhodes-Clark BS, Makhoul I, Nakagawa M. Autologous graft versus host disease: an emerging complication in patients with multiple myeloma. Bone Marrow Res. 2014;2014:891427.
34. Marin GH, Porto A, Prates V, Napal J, Etchegogen O, Rubens L, et al. Graft versus host disease in autologous stem cell transplantation. J Exp Clin Cancer Res. 1999;18(2):201-8.
35. Kennedy MJ, Jones RJ. Autologous graft-versus-host disease: immunotherapy of breast cancer after bone marrow transplantation. Breast Cancer Res Treat. 1993;26(Suppl):S31-40.
36. Moors I, Noens L, Kerre T. Occurrence of mild spontaneous graft-versus-host disease after autologous stem cell transplantation for multiple myeloma: a case report and review of the literature. Belg J Hematol. 2016;7(2):83-86.
37. Krishna SG, Barlogie B, Lamps LW, Krishna K, Aduli F, Anaissie E. Recurrent spontaneous gastrointestinal graft-versus-host disease in autologous hematopoietic stem cell transplantation. Clin Lymphoma Myeloma Leuk. 2010;10(1):E17-21.
38. Sica S, Chiusolo P, Salutari P, Piccirillo N, Laurenti L, Sora F, et al. Autologousgraft-versus-host disease after CD34+-purified autologous peripheral blood progenitor cell transplantation. J Hematother Stem Cell Res. 2000;9(3):375-9.
39. Bolaños-Meade J, Garrett-Mayer E, Luznik L, Anders V, Webb J, Fuchs EJ, et al. Induction of autologous graft-versus-host disease: results of a randomized prospective clinical trial in patients with poor risk lymphoma. Biol Blood Marrow Transplant. 2007;13(10):1185-91.
40. Nakamura H, Nakao T, Ujiie H, Karasuno T, Teshima H, Komatsu K, et al. Induction of autologous graft-versus-host disease after autologous peripheral blood stem cell transplantation. J Allergy Clin Immunol. 1999;103(5 Pt 2):S457-61.
41. Niederwieser D, Eibl B, Nachbaur D. Graft-versus-host disease after autologous bone marrow transplantation: a realistic expectation? Wien Med Wochenschr. 1995;145(2-3):25-27.

42. Alonso S, Cabrero M, Caballero JC, Dávila J, de la Calle VG, López-Godino O, et al. Acute graft-versus-host disease and bronchiolitis obliterans after autologous stem cell transplantation in a patient with multiple myeloma. Clin Case Rep. 2015;3(6):370-5.

43. Kline J, van Besien K, Nathanson J, Noffsinger A, Artz A. Severe intestinal graft-versus-host disease following autologous stem cell transplantation. Bone Marrow Transplant. 2006;38(5):391-2.

44. Baker M. Graft-versus-host disease following autologous transplantation. Oncol Nurs Forum. 2010;37(3):269-73.

45. Oberlin K, Ledon J, Villada G, Romanelli P. Delay of the diagnosis of Graft versus host disease in an autologous stem cell transplant recipient: a case report and literature review. CellR4. 2016;4 (2): e1814.

46. Martin RW, Farmer ER, Altomonte VL, Vogelsang GB, Santos GW. Lichenoid graft-vs-host disease in an autologous bone marrow transplant recipient. Arch Dermatol. 1995;131(3):333-5.

47. Tokime K, Isoda K, Yamanaka K, Mizutani H. A case of acute graft-versus-host disease following autologous peripheral blood stem cell transplantation. J Dermatol. 2000;27(7):446-9.

48. Oyama Y, Cohen B, Traynor A, Brush M, Rodriguez J, Burt RK. Engraftment syndrome: a common cause for rash and fever following autologous hematopoietic stem cell transplantation for multiple sclerosis. Bone Marrow Transplant. 2002;29(1):81-5.