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Graft-versus-host disease (GVHD): General review

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ABSTRACT

Graft-versus-host disease (GVHD) is one of the major complications and source of morbidity and mortality after allogeneic hematopoietic cell transplantation (HCT) procedure. GVHD divided into two types, acute GVHD, and chronic GVHD. Traditionally as is known, acute GVHD accruing 3 months (100 days) after HCT, and the chronic GVHD accruing after 3 months (over 100 days) after HCT.

Generally, the most common symptoms of GVHD development: skin can be presented with rare rush, biopsies can show dyskeratotic keratinocytes. Liver presented with damage to the bile ducts and elevation of bilirubin levels. Lung's damage, bronchiolitis. Endoscopy of the anterointernal can show damage to the cecum, ileum, and colon. In addition, damage to the upper intestinal system.

Traditionally GVHD prophylaxis protocol consisted immunosuppression agents as calcineurin inhibitors such as Tacrolimus or Cyclosporine. In case of GVHD development, the standard first-line therapy of GVHD is corticosteroids (systemic and topical) including immunosuppression agent.

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KEYWORDS: GVHD, donor, host, hematopoietic cell, cytokine, inflammation, transplantation, immune system

INTRODUCTION

Graft-versus-host disease (GVHD) is one of the major complications and source of morbidity and mortality after allogeneic hematopoietic cell transplantation (HCT) procedure. GVHD divided into two types, acute GVHD, and chronic GVHD. The difference between acute and chronic GVHD is the timing of the onset of symptoms. Traditionally as is known, acute GVHD accruing 3 months (100 days) after HCT, and the chronic GVHD accruing after 3 months (over 100 days) after HCT.

The frequency of GVHD increasing with use of unrelated hematopoietic cells (HC) donors, the graft source of the HC as mismatched donors, bone marrow, peripheral blood, cord blood, haplo-identical related donors, the number of the HC CD34, female after several pregnancies and births older age of donors and HC recipients. In addition, the conditioning regimens treatment as myeloablative and reduced intensity regiments. [1][2]

Conditioning regimens in some cases include total body irradiation (TBI), TBI increases the tissues damage, which increases the risk of GVHD. [3]

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Diagnosis of GVHD based on the patient's clinical presentation. In addition, biopsy used to confirm the diagnosis in case of organ involvement. As mentioned above, GVHD divided into two types, acute GVHD defined by sequential cascade of inflammatory cytokines, and chronic GVHD is a potentially devastating late complication of HCT defined by chronic inflammation leading to issue damage.[4]

THE PATHOPHYSIOLOGY AND SYMPTOMS

The likelihood of GVHD accruing and severity is directly related to the matching degree of human-leukocyte-antigens (HLA) between the donor and the recipient. HLA-class1 antigens are found on all our body cells. HLA-class2 antigens are found on our body immune cells. [5][6]

GVHD caused by the donor T-lymphocyte cells by targeting and caused damage to host body-tissues. T-cell recognized the host body as "stranger" and start attacking and causing damage for the host body-tissues. [6]

Minor histocompatibility antigen (miHA) are peptides presented on the cellular surface of donated organs, the critical role of miHA in development acute GVHD is immunological response in some organ and tissues in the host. [6]

Antin and Ferrara described the immunobiology of GVHD, they presented sequential cascade into the recipient of the HC (table 1). [7]

Table 1: the immunobiology of GVHD.

THE IMMUNOBIOLOGY OF GVHD	
PHASE 1	Secretion of inflammatory cytokines, resulting host tissue damage
PHASE 2	Overactivation of T-lymphocytes cells
PHASE 3	Cytokine storm causing tissue damage and cytotoxicity

Generally, the most common symptoms of GVHD development (table 2): skin can be presented with rare rush, biopsies can show dyskeratotic keratinocytes. Liver presented with damage to the bile ducts and elevation of bilirubin levels. Lung's damage, bronchiolitis. Endoscopy of the anterointernal can show damage to the cecum, ileum, and colon. In addition, damage to the upper intestinal system. [8][6]

Table 2: symptoms of GVHD development. [8][6]

SYMPTOMS OF GVHD DEVELOPMENT	
SKIN	Dermatitis, rush, cutaneous blisters
GASTROINTESTINAL	Xerostomia, esophagus, abdominal pain, diarrhea, nausea and vomiting
LIVER	Elevation of bilirubin and liver enzymes, Hepatitis, VOD.
EYES	Xerophthalmia
LUNG AND HART	Bronchiolitis obliterans, serositis, pleural effusions,
KIDNEYS	Nephrotic syndrome
OTHERS	Fasciitis of Pericard, serositis, fibrosis of the affected organ

TREATMENT

Traditionally GVHD prophylaxis protocol consisted immunosuppression agents as calcineurin inhibitors such as Tacrolimus or Cyclosporine. In some conditions, another immunosuppression agent's treatment is added such as Methotrexate, Mycophenolate, or ant-thymocyte globulin (ATG), it depends on the HC source and patients' condition, and the high-risk of GVHD developments. the treatment begins before receiving the HC, and continues as long as there is no indication of GVHD development.

Approximately 30-60% of patients after allogenic HCT develop acute GVHD. In case of GVHD development, the standard first-line therapy of GVHD is corticosteroids (systemic and topical) including immunosuppression agent. [8]

Corticosteroids considered in an inflammatory inhibit. In case of acute GVHD development, the recommended treatment with corticosteroids depending on the severity and staging of the GVHD (table 3+4). For example, stage 1 of liver involvement can usually be treated with topical corticosteroids. The recommended in stage 2-3 with corticosteroids is 2 mg\kg\day systemic. [8][9][10][11][12]

Recent clinical trellis defined corticosteroids failure as:

1- No improvement after 3 days of treatments.
2- Progression after one week of treatment.
3- Lack of response and more progression after 14 days of treatment.[10][13]

GVHD STAGING BY ORGAN INVOLVEMENT

Table 3: GVHD staging by liver involvment.

STAGE	LIVER INVOLVEMENT (BILIRUBIN)
0	< 2mg \dl
1	2-3 mg\dl
2	3-6mg\dl
3	6-15mg\dl
4	>15mg\dl
GRADE	
1	Normal
2	Stage 1
3	Stage 2-3
4	Stage 4

Table 4: GVHD by skin involvment.

STAGE	SKIN INVOLVEMENT
0	Normal, no rash
1	<25% body surface
2	25%-50% body surface
3	>50% body surface
4	General body surface cutaneous involvement
GRADE	
1	Stage 1
2	Stage
3	Stage 3-4
4	Stage 4

SUMMARY

HCT is a potentially curative treatment option for several hematologic malignancies and nonmalignant blood disorders. Despite, GVHD is one of the major factors of morbidity and mortality after allogeneic HCT.

GVHD can be defined as a whole complex of immune response that cause serious complications, but yet, the kye mechanisms that can lead to contain development remain uncompleted.

REFERENCES

1. Pidala, J., Sarwal, M., Roedder, S. et al. Biologic markers of chronic GVHD. Bone Marrow Transplant 49, 324–331 (2014).

https://doi.org/10.1038/bmt.2013.97

2. Madan Jagasia, Mukta Arora, et al. Risk factors for acute GVHD and survival after hematopoietic cell transplantation. Blood 2012; 119 (1): 296–307. doi: https://doi.org/10.1182/blood-2011-06-364265
3. Rima M. Saliba, Marcos de Lima, Sergio Giralt, et al. Hyperacute GVHD: risk factors, outcomes, and clinical implications. Blood 2007; 109 (7): 2751–2758. doi: https://doi.org/10.1182/blood-2006-07-034348
4. Mahasweta Gooptu, Joseph Harry Antin. GVHD Prophylaxis 2020. ront. Immunol., 07 April 2021. Volume 12 –2. https://doi.org/10.3389/fimmu.2021.605726
5. Harris, A.C., Ferrara, J.L.M. and Levine, J.E. (2013), Advances in predicting acute GVHD. Br J Haematol, 160: 288-302. https://doi.org/10.1111/bjh.12142
6. Toubai, T., Sun, Y., & Reddy, P. (2008). GVHD pathophysiology: is acute different from chronic. Best Practice & Research Clinical Haematology, 21(2), 101-117. https://doi.org/10.1016/j.beha.2008.02.005
7. Ball, L., Egeler, R. & on behalf of the EBMT Paediatric Working Party. Acute GvHD: pathogenesis and classification. Bone Marrow Transplant 41 (Suppl 2), S58–S64 (2008). https://doi.org/10.1038/bmt.2008.56
8. Jacobsohn, D.A., Vogelsang, G.B. Acute graft versus host disease. Orphanet J Rare Dis 2, 35 (2007). https://doi.org/10.1186/1750-1172-2-35
9. Holtan, S.G., Yu, J., Choe, H.K. et al. Disease progression, treatments, hospitalization, and clinical outcomes in acute GVHD: a multicenter chart review. Bone Marrow Transplant 57, 1581–1585 (2022). https://doi.org/10.1038/s41409-022-01764-w
10. Ho, Vincent T., and Corey Cutler. "Current and novel therapies in acute GVHD." Best Practice & Research Clinical Haematology 21.2 (2008): 223-237. https://doi.org/10.1016/j.beha.2008.02.009
11. Corey S. Cutler, John Koreth, Jerome Ritz; Mechanistic approaches for the prevention and treatment of chronic GVHD. Blood 2017; 129 (1): 22–29. doi: https://doi.org/10.1182/blood-2016-08-686659
12. Laura F. Newell, Shernan G. Holtan; Acute GVHD: think before you treat. Hematology Am Soc Hematol Educ Program 2021; 2021 (1): 642–647. doi: https://doi.org/10.1182/hematology.202100030
13. Messina, C., Faraci, M., de Fazio, V. et al. Prevention and treatment of acute GvHD. Bone Marrow Transplant 41 (Suppl 2), S65–S70 (2008). https://doi.org/10.1038/bmt.2008.57