ORAL GRAFT VERSUS HOST DISEASE: A REVIEW


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ABSTRACT:

Graft versus host disease (GVHD or GHz) is a pathological condition in which cells from the transplanted tissue of a donor initiate an immunologic attack on the cells and tissue of the recipient. Generally, transfer of tissues between normal individuals usually results in the recognition and destruction (rejection) of the foreign tissue in a host-versus-graft reaction but immunologically competent cells contained in the transplanted tissue or graft can result in immunologic recognition in the other direction, initiating a graft-versus-host (GVH) reaction. GVHD is a serious, life-threatening disease and it is major complication of bone marrow transplant. The bone marrow is the spongy tissue inside the large bones in the body that makes blood cells and platelets. GVHD may happen in the (short term) acute, or (later after transplantation) chronic, in which case a wider range of organs can be involved.

Key words: Graft versus host disease (GVHD OR GHz), Acute GVHD (aGVHD), Chronic GVHD (cGVHD), immunosuppression, ulceration, lichenoid reaction.

INTRODUCTION:

GVHD (GHz) encompasses most aspects of the human immune response. When a donor's and a recipient’s genetic composition are not identical, grafted organs stimulates an immune response. Lymphocytes, particularly T lymphocytes, are instrumental in transplantation failure and are stimulated during rejection. A donor’s major histocompatibility complex (MHC), a genetic region found on the short arm of chromosome number 6 of all mammalian cells, codes for products (antigens) that allow immune cells to identify self from non self. In human, the self antigens encoded by MHC include human leukocyte antigen (HLA) system. Although many other gene products can stimulate graft rejection, it is the HLA system that produces the strongest immunologic response that can be acute or chronic.1,2,3,4

Acute GVHD (aGVHD) generally occurs early post-transplant most commonly within the 100 days has relatively uniform clinical picture, classically manifested by erythematous rash, diarrhoea and /or liver involvement and is the major cause of early lethality.4 This acute process related to the

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primary activation of T cells and usually can be reversed by changing the immunosuppressive medications or the medication regimen.\textsuperscript{5} Chronic GVHD (cGVHD) is a distinct syndrome that can affect virtually every major organ system but most commonly involves skin, oral, vaginal, and conjunctival mucosa, salivary glands and lacrimal glands, and the liver. This type of rejection is slow and insidious and cannot be reversed. It probably occurs by continued, albeit muted, cell toxicity that results in vascular changes to the transplanted organ, leading ultimately to graft rejection. It is estimated that 40\% of engrafted patients surviving the initial transplants eventually develop cGVHD, which can persist for months to years and require long term management from multidisciplines.\textsuperscript{6} The clinical manifestation and histopathology of oral aGVHD and cGVHD also are very similar, although aGVHD changes tend to be less pronounced and distinct, and tends to be predominated more by erythema and atrophy, especially after 50 days of post transplant; however, LP-like hyperkeratotic changes can be noted but are less prominent than cGVHD.\textsuperscript{3,7} Another type of reaction is known as hyper acute rejection. This occurs within minutes to hours after a transplantation procedure. This type of reception occurs in who have undergone previous transplant, patient who had multiple pregnancies, and patient who have had multiple blood transfusions. It is caused by preformed antidonor antibodies that activate complement, resulting in a severe attack on graft, which often cannot be reversed.\textsuperscript{6} Hyper acute GVHD defined as unexplained fever in addition to skin rash, hepatic dysfunction, or diarrhoea, all occurring before neutrophil engraftment.\textsuperscript{7}

\textbf{PATHOPHYSIOLOGY OF ACUTE GRAFT VERSUS HOST DISEASE:}

Distinct clinical forms of GVHD including acute and chronic GVHD are, in large part, a consequence of damage to host tissues by activated donor derived T lymphocytes in response to the MHC disparities. However, the pathophysiological mechanisms of the different GVHD syndromes are not the same.\textsuperscript{8,9,10,11} Pathophysiology of acute GVHD is currently understood as a process consisting of afferent and efferent phases. First, recognition of host tissues activates donor T lymphocytes (afferent phase). Activated T-cell subsequently attack target tissue in transplanted recipients (efferent phases). The first phase involves tissue damage secondary to the conditioning regimen, while the second phase consists of donor T-cell activation, stimulation, and proliferation. Those two phases make the afferent phase of GVHD. Finally, the efferent phase comprises the third phase of GVHD pathophysiology.\textsuperscript{12, 13}

\textbf{PATHOPHYSIOLOGY OF CHRONIC GRAFT VERSUS HOST:}

The exact pathogenesis of cGVHD, however, remains ambiguous. In addition to donor-derived alloreactive T cells that are so important in aGVHD, post thymic CD41 T cells are thought to play an important role in cGVHD. The T-cell precursors may undergo aberrant “thymic education” after SCT that effectively makes them self-reactive or autoreactive. Additionally, the activation of different helper T-cell subsets (Th1 versus Th2) may be responsible for distinct manifestations of acute and chronic GVHD.\textsuperscript{14-18} The role of alloreactivity versus autoreactivity in the pathogenesis of cGVHD remains an area of intense debate. Alloreactivity to minor histocompatibility antigens is believed by some to explain cGVHD as a late phase of aGVHD. The importance of autoreactivity, however, is suggested by clinical manifestations of cGVHD that frequently mimic those of autoimmune diseases, the finding of autoantibodies in some patients with chronic GVHD, and experimental data suggesting the importance of thymic education in the pathogenesis of cGVHD.\textsuperscript{16-33}

\textbf{ORAL MANIFESTATION OF ACUTE AND CHRONIC GRAFT VERSUS HOST DISEASE:}

Graft versus host disease (GVHD) is a common complication in bone marrow transplant (BMT) patients. It is characterized by systemic and oral cavity alterations.
Depending on the timing of lesions, GVHD is classified as acute or chronic. Alterations in the oral cavity are lichenoid reticular lesions, erythema, ulcerations, and xerostomia. Sporadically, mucocele and pyogenic granulomas can be present. Clinically, acute and chronic oral GVHD are characterized by mucosal hyperkeratotic responses, erythema and inflammation, atrophy, pseudomembranous ulceration, fibrosis, and salivary gland dysfunction and taste disorders in patterns reminiscent of autoimmune disorders such as lichen planus, lupus, systemic sclerosis, and sjogren syndrome. Pseudomembrane ulceration is noted across the spectrum of aGVHD and cGVHD and is indicator of severity. Whether these variations are due to specially to different pathologic mechanism or a result of the effect of chronicity and severity of the attack is not known.

The choice of the donor is one of the most important variables for the prevention of GVHD. The use of a young related HLA-matched, sex-matched donor can minimize GVHD severity. With limitations of the donor pool it is often necessary to utilize HLA-matched unrelated donors. Post-transplant immunosuppressive therapy is the most common form of GVHD prevention.

MANAGEMENT OF GRAFT VERSUS HOST DISEASES:

Clinical factors that may influence the development of GVHD are related to donor-host factors, source of stem cells and types of preparative regimens given before transplant. Among donor-host variables, the most commonly recognized GVHD risk factors are HLA differences, female donor to male recipient, and donor and recipient age. Moreover, a sterile environment is mandatory to protect against GVHD.

ORAL MANAGEMENT OF GRAFT VERSUS HOST REACTION:

Multiple factors must be considered when treating a patient with oral GVHD. Even though oral GVHD may have serious health consequences, GVHD of the liver or lungs is life threatening.

Suggested local measures for oral lesions treatment are medications such as diphenhydramine with kaolin and pectin or magnesium sulfate mouth washes, which reduce pain, topical steroids or azathioprine, budesonide gargle and ultraviolet irradiation or systemic medication such as prednisone, Cyclosporine-A, azathioprine, thalidomide, mophetyl mycophenolate, and tacrolimus.

RECENT ADVANCES IN GVHD:

Recent advances in the understanding of the basic mechanisms involved in GVHD pathophysiology have led to new strategies designed to block GVHD. Although acute GVHD is a predictor for development of chronic GVHD, successful efforts to decrease acute GVHD have not resulted in decreased rates of chronic GVHD. Prevention of GVHD are discussed with respect to three areas: GVHD pathophysiology, Regimens in common clinical use, and Regimens under investigation.

CONCLUSION:

Graft-versus-host disease (GVHD) is a common but serious complication of allogeneic haematopoietic stem cell transplantation (HSCT). GVHD occurs when the transplanted donor immune cells (graft) react and try to destroy the host tissues. Although GVHD is not yet preventable, steps can be taken to reduce the incidence and severity of GVHD. Administration of immunosuppressive drugs such as cyclosporine (alone or in combination with steroids) and methotrexate prior to the transplant have proven effective in reducing the incidence and severity of GVHD.

REFERENCES:

5. Burkett’s Oral Medicine Diagnosis and Treatment; tenth edition;503-24.
19. LM Ball , RM Egeler,On behalf of the Pediatric Working Party of the EBMT; Bone Marrow Transplant. 2008; 41: S58–S64


34. F. Demarosi, G. Lodi, A. Carrassi, L. Moneghini, B. Sarina, A. Sardella clinical and histopathological features of the oral mucosa in allogeneic haematopoietic stem cell transplantation patients Experimental Oncology. 2007;29:304–308.


