Acute graft-versus-host disease outcome during a 6-year period: a retrospective analysis

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Objectives: Acute graft-versus-host disease (aGVHD) remains one of the main causes of morbidity and mortality following allogeneic stem cell transplantation (SCT). Patients(pts) who failed to respond to steroids as first-line treatment of aGVHD have usually poor outcomes. There is no standard therapy uniformly accepted for refractory aGvHD.

Methods: We retrospectively reviewed our experience analyzing 22 pts (13 males, 9 females) treated for aGVHD between August 2005 and September 2010.

Results: The median age was 34 years (range 5-62) and grafts were from HLA matched siblings (8), matched (5) or mismatched unrelated donors (7), haploidentical (1) or cord blood donors (1).

Indications for SCT were acute leukemia (14), CML (1), myelodysplasia (2), myelofibrosis (1), lymphoma (2), thalassemia (1) and SCID (1) in early (9) or advanced status of disease (13). Stem cell source was peripheral blood in 5 pts, bone marrow in 15, both in 1 and cord blood in 1. The conditioning regimen was myeloablative in 20 pts and reduced intensity in 2 pts. Most pts received cyclosporine (CSA) and MTX with (19) or without (1) methylprednisolone (MP) and 2 pts received CSA + MP as initial GVHD prophylaxis. ATG was part of the preparative regimen for 53% of pts. The diagnosis of aGVHD was established at a median of 37 days (range 11-201) after transplantation and confirmed by biopsy in 42% of the cases. AGVHD grade I-II was 32%. Grade III-IV occurred in 68% of pts and was more frequent in unrelated recipients (11) compared to related siblings (3). Initial treatment consisted of MP up to 2 mg/kg in 10 pts and 3 to 5 mg/kg in the remaining The overall complete response (CR) to first-line was observed in 5 pts (22%). Second-line treatment was pentostatin alone or plus other in 9 pts, cyclophosphamide, mycophenolate, infliximab in the others. Overall 5 pts (23%) responded to the second-line (CR 14%, PR 9%). The pts who failed to respond received further salvage therapies including infliximab, rituximab, pentostatin or extracorporeal photopheresis. All refractory pts died without response. Fifty% of the responding versus 0% of the non-responders survived (4 pts died from relapsed or progressive disease, 9 from GVHD, 4 from infections, and 1 from organ failure).

Conclusions: Systemic steroids are the main therapy for aGVHD, but treatment failure is common and the outcomes remain very poor. It is still very important to find new methods of GVHD treatment. Our retrospective analysis confirms this need.

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Can we recognize clinical parameters which are associated with occurrence and severity of graft-versus-host disease?

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The application of allogeneic hematopoetic stem cell transplantation (HSCT) is limited by life-threatening complications such as severe or acute graft-versus-host disease (GVHD). Despite intensive prophylaxis with immunosuppressive agents, the incidence of GVHD occurs in 9-50% of patients undergoing transplant with an identical HLA sibling matched donor and 75% of patients undergoing unrelated HLA donors.

Aim of study: To evaluate our experiences in GVHD prophylaxis and treatment after alloTHSC, GVHD incidence and prognostic factors and administration of new immunosuppressive regiments. Patients and methods: Starting from September 2000 till September 2009, 63 patients (36 males and 27 females) at the age of 16-56 (median range 33 years) with hematological malignances were treated with alloTHSC on Department of Hematology, Clinical Centre, and Skopje. For 55 patients donors were HLA identical siblings and the rest 8 patients were transplanted from HLA unrelated donors. In 10 patients bone marrow was used as source of stem cells and in 53 patients stem cells were obtained from peripheral blood. From the group of 63 patients, 26 patients have active disease at the time of transplantation. GVHD prophylaxis was accomplished with combination of cyclosporine and metothrexate (Seattle regimen) or more intensive immunosupression regiments.

Results: GVHD was noticed in 30 patients (47,6%) and at 33 patients (52,4%) was not noticed a manifestation of GVHD. Acute GVHD was noticed in 24 patients (38%) and chronic GVHD in 20 patients (31,7%) The remaining 32 patients (45%) achieved complete clinical and hematological remission. Lethal outcome was confirmed in 31(49%) patients (9 from chrGVHD,6 from acute GVHD, 16 from disease relapse).

Conclusion: The incidence of acute GVHD in our study was 38% and 31% of chronic GVHD. The most common GVHD reaction was registered in female donors and male recipients, with higher GVHD incidence in elderly patients. In all patients stem cells were obtained from peripheral blood. Active disease, sex, source of hematopoetic cells, age and conditional regiments are the most significant predictive factors with the higest influence of incidence of GVHD.

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Graft-versus-host disease management

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Graft versus host disease (GVHD), donor stem cells in patients with an immunological reaction caused by the healthy T-lymphocytes. Risk factors for GVHD, HLA mismatch, age, sex mismatch, underlying disease, type and stage, and is used in prophylaxis. GVHD allo BMT (bone marrow transplantation), after the most serious complication that can occur. The disease is usually the skin, gastrointestinal tract and liver effects, however, lungs, eyes, muscle-skeletal system, also affect the vagina and vulva. Acute GVHD and chronic GVHD graft versus host disease is divided into two.

- 1 Acute GVHD.
- 2 Chronic GVHD:
 - Skin: erythema, dryness, itching
 - Nail: Fracture
 - Hair: alopecia and premature bleaching
 - Eye: Dryness, Itching
 - · Vulva and vagina: vaginal dryness and atrophy
 - Liver: impaired liver function tests
 - Lung: Pulmonary function tests impaired
 - Mouth: Dryness, mucositis
 - · Gastrointestinal System: Nausea, vomiting, diarrhea
 - Musculoskeletal system: joint pain
 - · Hematological findings: severe thrombocytopenia
 - · Immune deficiency: recurrent infections, sinusitis.

As a result of GVHD to treatment-related or patients: skin, hair, nail problems, skin care, because, mucositis assessment and oral care, nutrition because of the lower and upper gastrointestinal problems, fluid-electrolyte balance is important. Immune insufficiency due to the risk of infection due to symptom control and prevention measures must be taken. Need to follow through due to dryness and itching eyes. According to laboratory tests, and symptom control organs is required. Vulva and vagina can occur due to problems of change seksüalitede. Cortisone is used in treatment of diabetic patients may develop due care, such as osteoporosis exercise programs due to be established. Physical integrity because of the disease and the treatment of patients with body image distortion and shock may develop psychological problems should be addressed. Our