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Case Report

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Lyell-Like Acute Graft-Versus-Host-Disease

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ABSTRACT

Stage IV acute cutaneous graft-versus-host-disease (GVHD) is nowadays rarely seen due to tissue typing done before transplant. The first line treatment for acute GVHD grade II-IV is systemic corticosteroids. However, although there is no consensus for refractory cases, literature report diverse therapies to be effective. We report the case of a 34 year-old patient with refractory acute cutaneous graft-versus-host-disease stage IV successfully treated with etanercept.

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Case Report

A 34 year-old female patient presented erythematous papules of the neckline, 2 weeks after bone marrow transplantation for B-cell acute lymphoblastic leukemia. Histological analysis of a skin biopsy showed a lichenoid infiltrate with few necrotic keratinocytes, compatible with an engraftment syndrome . The evolution with methylprednisolone 2mg/kg/day (d) was good. One week after, a diagnosis of HHV6 hepatitis motivated tapering off steroids. Photophobia, mouth and genital pain appeared, associated with elevated fever. On lab examinations, there was no leukocytosis and the C reactive protein was slightly elevated (42 mg/ml). Imipenem antibiotherapy and ruxolitinib 10 mg 2x/d were introduced, methylprednisolone was increased to 125 mg/d. Over 72 hours, she presented diffuse skin pain, treated with paracetamol and fentanyl pump. Clinically, she presented an erythematous macular-papular exanthema involving up to 70% of the body surface area (BSA), with central dusky grey aspect, erythematous-violaceous palms (Fig 1) and soles (Fig 2) and tense bullae on both arms and back (Fig 3) with positive Nikolsky sign. We observed buccal and genital erosions, and a bilateral conjunctival hyperemia. Skin biopsies for frozen, and formalin-fixed, paraffin-embedded sections were done. The histological analysis revealed a complete epidermal necrosis with cleavage at the dermal-epidermal junction (DEJ) and necrotic keratinocytes along sweat ducts and hair follicules (Fig 4). Direct immunofluorescence showed colloid bodies at the DEJ. We concluded to a cutaneous stage IV GVH disease (toxic epidermal necrolysis (TEN)-like).

We stopped all unnecessary treatments, increased methylprednisolone to 500 mg/day, introduced immunoglobulins 1g/kg for 3 days, ciclosporine 60mg/day, and transferred the patient in intensive care unit for monitoring and local cares. A favorable evolution after 3 weeks of treatment motivated tapering off steroids. She presented few days after a recurrence of diffuse erythema involving up to 70% of BSA with focal dusky grey aspect but without Nikoslky sign. Histological analysis revealed basal keratinocytes necrosis, with lymphocytes exocytosis ("satellite-cell necrosis"), consistent with a recurrence of the GVHD. We increased methylprednisolone to 500mg/day, re-introduced immunoglobulins 1 g/kg for 3 days and added etanercept 50 mg sub cutaneous (SC) injection. After 2 days, we observed a dramatic improvement and initiated extracorporeal photopheresis for short and long-term control of the GVHD.

Acute GVHD (aGVH) is a common complication of hematopoietic stem cell transplantation. It is induced by the donor immunocompetent T cells that, following an enhanced expression of major-histocompatibility-antigen by actived host-presenting cells, secret IFN-γ, IL-2 and TNF-α, leading to activation of cytokines effector cells with Fas- and perforin-mediated killing mechanisms, and cells of the innate immune system [1]. During all the process, JAKs play an important role [3]. It results in an attack of fast proliferating tissues epithelia (liver, gastrointestinal tract and skin) [1].

The cutaneous aGVHD has a peak incidence around day 30 [1]. It may begin on the posterior auricular or acral skin and can evolve in a confluent maculopapular rash with acral erythema and/or folliculocentric blanching erythema with small macules and papules being suggestive [1]. Conjunctival and mucosal lesions can be associated. In severe cases, it can evolve in an erythroderma with bullae and positive Nikolsky sign, similar to a TEN and potentially fatal. [1, 2] Grading classification depends on the extent of skin lesions (from stage 1 involving 25% of BSA to stage 4 consisting in erythroderma with bullae), liver and intestinal tract involvement [1]. Differential diagnosis with TEN remains difficult [4].

Treatment of aGVHD depends on the severity of the disease. The recommended first line treatment for aGVHD grade II or

higher is systemic corticosteroids (methylprednisolone). For refractory cases, different therapies are described in the literature as mycophenolate mofetil, JAK 1/2 inhibitors (ruxolitinib 10 mg twice a day), anti-TNF alpha (etanercept) and extracorporeal photopheresis [1,3, 5-7].

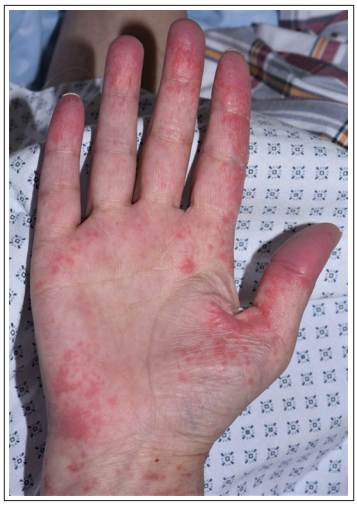

Figure 1: Erythematous-violaceous of the right palm

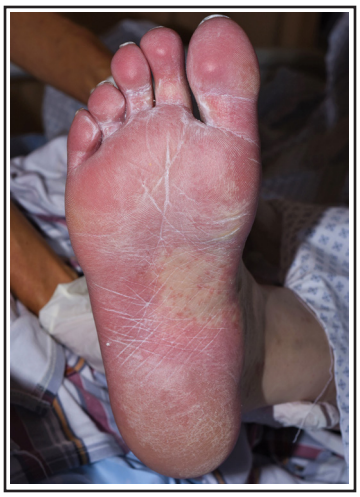

Figure 2: Erythematous-violaceous of the right sole

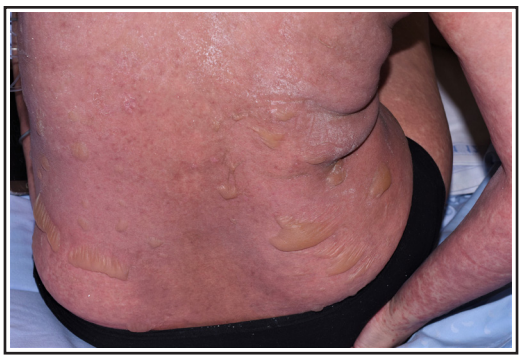

Figure 3: Confluent macular-papular exanthema with central grey aspect and tense bullae

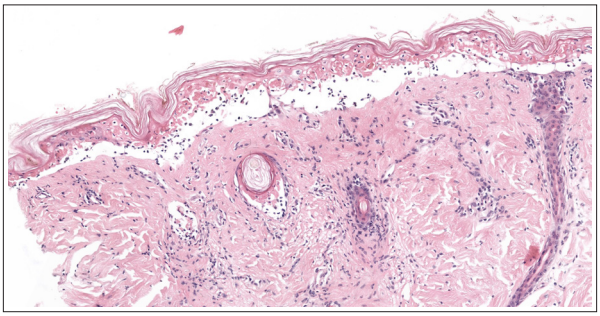

Figure 4: Complete epidermal necrosis with cleavage at the dermal-epidermal junction and necrotic keratinocytes along sweet ducts and hair follicles (haematoxylin and eosin ×50).

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Conflict of Interest: The authors have no conflicts of interest to disclose.

References

1. Häusermann P, Walter RB, Halter J, Biedermann BC, André Tichelli et.al.(2008) Cutaneous graft-versus-host disease: a guide for the dermatologist.216:287-304.
2. Itin P, Lautenschlager S, Orth B, Rufli T, Gratwohl A (1996) Skin manifestations of graft-versus-host reaction following bone marrow transplantation: 126:339-347.
3. Schroeder MA, Choi J, Staser K, John F DiPersio (2018) The Role of Janus Kinase Signaling in Graft-Versus-Host Disease and Graft Versus Leukemia 24: 1125-1134.
4. Rodríguez Tejero A, Badiola González J, Roldán Mateo L, Molina Leyva A (2020) Toxic Epidermal Necrolysis vs. Acute Cutaneous Graft Versus Host Disease after Hematopoietic Stem Cell Transplantation: A Diagnostic and Therapeutic Challenge 112: 81-82.
5. Wolff D, Roessler V, Steiner B, Wilhelm S, V Weirich et al. (2005) Treatment of steroid-resistant acute graft-versus-host disease with daclizumab and etanercept 35: 1003-1010.
6. Kennedy GA, Butler J, Western R, Morto J, S Durrant et.al (2006) Combination antithymocyte globulin and soluble TNFalpha inhibitor (etanercept) +/− mycophenolate mofetil for treatment of steroid refractory acute graft-versus-host disease 37: 1143-1147.
7. Zhang H, Chen R, Cheng J, Jin N, Baoan Chen (2015) Systematic review and meta-analysis of prospective studies for ECP treatment in patients with steroid-refractory acute GVHD 9: 105-111.