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CYTOMEGALOVIRUS REACTIVATION IN ALLOGENEIC STEM CELL TRANSPLANT RECIPIENTS: FREQUENCY, TIME TO REACTIVATION AND DYNAMIC OF VIREMIA IN DIFFERENT TYPES OF DONORS AND IN REPEATED EPISODES

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Background: Cytomegalovirus (CMV) remains leading to high morbidity and mortality in allogeneic stem cell transplant (Allo-SCT). High immunosuppression increases the risk of reactivation and allows repeated reactivation episodes. However, immunosuppression varies in accordance to donor types. In this study, we compared CMV reactivation in different Allo-SCT: Related (RD), unrelated (URD), and haploidentical (Haplo) donor SCT and analyzed the dynamic of repeated CMV episodes. **Methods:** Prospective cohorts of Allo SCT (from 2013 to 2019). Patients were screened by CMV quantitative PCR (Taqman Sistem – artus CMV Qiagen) in plasma. The screening started on the first week after SCT, repeated once a week until D+100, and after D+100 if immunosuppression was maintained. Repeated episode was defined if at least two negative CMV CRP results were obtained after the first episode. The following variables were analyzed: time after SCT to reactivation, initial viral load, highest viral load within the event, duration of viremia, and response to treatment. **Results:** There were 123 Allo-SCT performed. Median age was 47 years (ranging 1 to 70), and acute leukemia represented 63%. RD, URD, and Haplo were 72 (58%), 30 (24%), and 21 (17%), respectively. The median duration of follow-up was 251 days. CMV reactivation was documented in 84 (68%), with a median number of 2 (1 – 9) episodes per patient. RD, URD, and Haplo had similar frequencies of reactivation (64%, 70%, and 81%; p = 0.33). URD-SCT had earlier reactivation than others (median D+6, versus D+37 and D+ 21 in RD and Haplo, p < 0.001). A total of 192 CMV reactivation episodes were analyzed: 100 in RD, 55 in URD, and 37 in Haplo. Haplo-SCT reached the highest viral loads (median of 1070 copies/mL vs., 373 and 163 copies/mL in RD and URD-SCT; p = 0.036). First CMV reactivation episode reached higher viral load (median 1897 vs. 143 copies/mL; p < 0.001) and longer viremia (median 28 vs. 14 day; < 0.001), compared with repeated ones. **Conclusions:** Reactivation of CMV occurred with different dynamics by SCT donor type and in the first or repeated episode. Treatment and preventive strategies should be adapted, considering these different scenarios.

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DEFIBROTIDE TREATMENT IN PAEDIATRIC PATIENTS WITH SEVERE/VERY SEVERE VENO-OCCLUSIVE DISEASE/SINUSOIDAL OBSTRUCTION SYNDROME AFTER HAEMATOPOIETIC CELL TRANSPLANTATION: DEFIFRANCE INTERIM RESULTS

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Objectives: Veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a potentially fatal complication of haematopoietic cell transplantation (HCT) conditioning that may also develop after high-dose chemotherapy. Defibrotide is approved in Brasil and the US for adult and paediatric patients (aged >1 month in Brasil) with hepatic VOD/SOS with renal or pulmonary dysfunction post-HCT, and in the EU for patients aged >1 month with severe hepatic VOD/SOS post-HCT. The DEFIFrance study is collecting real-world data on outcomes in patients treated with defibrotide across France. This interim analysis evaluated a subgroup of paediatric patients (<18 years) with severe/very severe VOD/SOS post-HCT who were treated with defibrotide. **Material and methods:** DEFIFrance is a multicentre, post-marketing study collecting retrospective and prospective real-world data on patients receiving defibrotide at 53 HCT centres in France since July 2014; this analysis includes data collected from 36 active HCT centres. Criteria used for VOD/SOS diagnosis were at the discretion of the treating physician based on their clinical expertise; severity was adjudicated by an expert steering committee member according to EBMT criteria. Primary endpoints included Kaplan-Meier (KM)–estimated Day 100 survival rate post-HCT and Day 100 complete response (CR; total serum bilirubin <2 mg/dL and resolution of multiorgan failure [MOF] per investigators'assessment) in patients with severe/very severe VOD/SOS post-HCT. Secondary endpoints included evaluation of adverse events (AEs) of interest, irrespective of their relationship to treatment. **Results:** As of 8 November 2018, 324 patients were included in DEFIFrance. Of these, 41 paediatric patients had VOD/SOS post-HCT, of which 23 had severe/very severe VOD/SOS and were included in this analysis. Median age was 8.5 (range, 0.4–17.5) years. MOF occurred in 5 (22%) patients. The KM–estimated Day 100 post-HCT survival rate was 85% (severe [n = 14]: 100%; very severe [n = 9]: 53%); estimated survival rates were 68% and 55% at 6 and 12 months, respectively. The Day 100 post-HCT CR rate was 81% in patients with severe/very severe VOD/SOS. Among evaluable patients with severe (n = 14) and very severe (n = 7) VOD/SOS, Day 100 CR rates were 93% and 57%, respectively.

Day 100 VOD/SOS-related mortality was 15%; deaths after Day 100 resulted from causes other than VOD/SOS. AEs of interest occurred in 15/23 patients; common events included infection (n = 7/23) and respiratory symptoms (n = 6/23). **Discussion:** The DEFIFrance study represents the largest collection of real-world data on the use of defibrotide. This subgroup analysis focused on paediatric patients who received defibrotide for the treatment of severe or very severe VOD/SOS (per EBMT criteria) post-HCT. Limitations of DEFIFrance include some retrospective data collection and limited data at the time of this interim analysis. **Conclusion:** Prognosis is poor for patients with untreated, very severe VOD/SOS post-HCT. Among paediatric patients treated with defibrotide post-HCT for VOD/SOS, outcomes were better in severe versus very severe disease, highlighting the importance of early VOD/SOS diagnosis and treatment initiation. The incidence of AEs of interest was consistent with previous studies.

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DOENÇA LINFOPROLIFERATIVA RELACIONADA A EPSTEIN-BARR VÍRUS (EBV) PÓS TRANSPLANTE ALOGÊNICO: RELATO DE CASO

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Introdução: Dentre as complicações pós transplante de medula óssea (TMO) alogênico, as doenças linfoproliferativas pós-transplante relacionadas ao Epstein-Barr Vírus (EBV-PTLD) se destacam por serem potencialmente fatais. Apesar de raras, as EBV-PTLD são caracterizadas pela proliferação de células B previamente infectadas pelo EBV. Desta forma, no período pós TMO, diante da intensa imunodeficiência provocada com subsequente comprometimento da atividade celular T, o paciente fica susceptível à reativação e proliferação de células B infectadas por EBV. Dentre as apresentações clínicas, estão descritas linfadenomegalias, sintomas B (perda de peso, sudorese, febre e astenia) e massas extranodais. **Relato:** Relatamos o caso de uma jovem do sexo feminino de 16 anos com diagnóstico de anemia aplásica grave submetida a transplante alogênico haploidêntico. A doadora foi a mãe e a fonte medula óssea. A sorologia (IgG) para EBV da receptora era positiva e da doadora negativa. Foi realizado condicionamento de intensidade reduzida com fludarabina, ciclofosfamida, irradiação corporal total 4Gy e timoglobulina com ciclofosfamida no D+3 e D+4, micofenolato e ciclosporina para profilaxia da doença do enxerto contra o hospedeiro. Foram infundidas 4,2 x 10^8 de células nucleadas totais com enxertia neutrofílica no D+16 pós infusão. Não apresentou complicações ou intercorrências significativas até o D+65, quando apresentou quadro de febre, odinofagia discreta e exantema máculo-papular. Após alguns dias, evoluiu com aumento progressivo do volume cervical, piora da odinofagia, febre persistente e piora do exantema. Diante da suspeição clínica de PTLD foi suspensa a ciclosporina no D+68. Ao estudo tomográfico, apresentava múltiplas linfonodomegalias cervicais (a maior medindo 2,7 x 1,7 cm), axilares, peri-hilares esplênica e mesentérica. Foi realizado carga viral sérica para EBV com resultado de 6.406.010 cópias/mm^3 (log de 6,8). Foi iniciada terapia com rituximabe na dose de 375 mg/m^2 no D+70, totalizando 4 doses com intervalos semanais. A paciente evoluiu para insuficiência respiratória aguda grave devido a compressão em região cervical, com necessidade de intubação orotraqueal e cuidados em terapia intensiva (UTI), com melhora clínica gradual e extubação efetiva em 13 dias nos quais realizou antibioticoterapia empírica com ampla cobertura. Teve também uma suspeita de síndrome hemofagocítica tendo sido prescrita dexametasona 20 mg/m^2 associada a imunoglobulina humana EV. No período em que esteve internada na UTI, houve queda progressiva da viremia de EBV DNA, com negativação no D+97. A paciente atualmente está assintomática, com quimera completa, em acompanhamento ambulatorial, sem sinais de DECH crônica. **Discussão/Conclusão:** A EBV-PTLD pode ser uma complicação grave ou fatal do transplante. Tendo em vista a importância do diagnóstico precoce, discute-se a profilaxia primária com rituximabe ou a monitoração do EBV-DNA com tratamento preemptivo em pacientes de alto risco, como o caso descrito acima, permitindo a instituição da terapia mais precocemente. Atualmente, o uso do rituximabe associado à redução/suspensão da imunossupressão compõem o tratamento de primeira linha. No entanto novas terapias celulares, anticorpos monoclonais e drogas antivirais estão em estudo e podem modificar o cenário da terapia proposta em casos de EBV-PLTD.

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HIPERTRIGLICERIDEMIA GRAVE EM PACIENTE COM DOENÇA DO ENXERTO CONTRA HOSPEDEIRO EM TRATAMENTO COM RUXOLITINIBE, SIROLIMUS E CORTICOIDE

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Paciente do sexo feminino, 22 anos, diagnóstico de linfoma de Hodgkin refratário após TMO autólogo em dezembro de 2016 com protocolo Fludarabina, Ciclofosfamida e irradiação corporal total. Submetida a novo TMO, haploidêntico e tendo como doadora sua mãe, no dia 02/07/2017. Desenvolveu DECHc, síndrome de sobreposição em boca e pele decorrentes do primeiro transplante, iniciando corticosteróide em 12/06/2016. Não houve controle da DECH, sendo tratada inicialmente com Basiliximab, três doses, também sem resposta clínica. A ciclosporina foi suspensa por insuficiência renal e posteriormente substituída por Sirolimus. Ainda sem resposta a paciente iniciou tratamento com Ruxolitinibe com estabili-