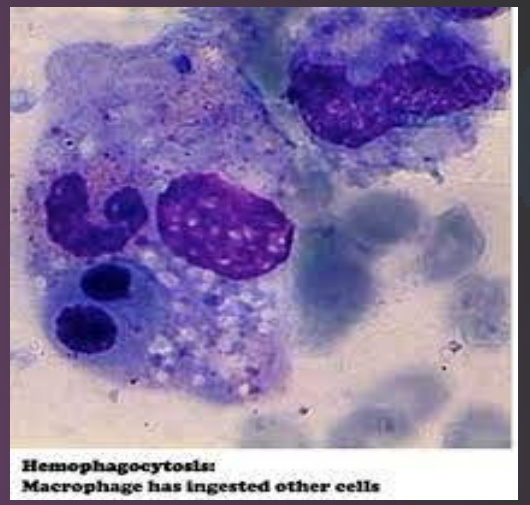
CORD BLOOD- HSCT IN GRISCELLI SYNDROME & HLH



Hemophagocytosis:
Macrophage has ingested other cells

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Mofid Children Hospital. HSCT ward.

Case Presentation
Griscelli syndrome & HLH

- An 8 years old girl , First child , No Sibling, Parents ; Second relation ship **BW: 35kg**
- Presentation : Since 5 y old , Fever ,splenomegaly , pancytopenia **& Silver gray Hair in PE**
- From birth – 5 Y old : No finding ?
- Evaluations in Mofid Children Hospital : BMA & BMB : Nl cellular + pos for hemophagocytic cell
- **Hair:(Large Clumped Melanosomes in hair shaft)** in favour of Griscelli syndrome
- **Gene analysis : RAB- 27a Gene mutation -Homozygote (AR)**
- EBV PCR : Neg CMV PCR : neg CMV IgG : 37 BG ;A neg
- MRI :NL CSF : NL
- **Diagnosis : Griscelli Syndrome & HLH**
- **Start Protocol: HLH 2004**

Case Presentation
Griscelli syndrome & HLH

- In March 2021/ In Remission HSCT , from 5/6 Match unrelated Cord Blood
- Donor : Male , BG;A neg TNC : 6.4 x 107/kg CD34 : 2 x105/kg
- Protocol (RIC) : Fludarabin 30mg /M2 / day /IV x 5 days + MEL 70 mg / m2 / day/ x 2 days /IV + ATG 2.5mg/kg/ days/IV x 3 days
- GVHD-Prophylaxis : Cyclospurine + MMF GCSF : Day + 5
- She Engrafted : Day +15
- Chimerism : 100%
- Complication : CMV reactivation (PCR level : 2000) , treatment : Val Gancyclovir/ po .
- Now :4 mo after HSCT: She is on cyclosporine & Last Chimerism :%100
- 2 days ago again CMV PCR was pos , that we start treatment.

Risk factors affecting outcome of unrelated cord blood HSCT for children with familial HLH.
British Journal of Haematology, 2019, 184, 397–404

- **Studies using UCBT for patients affected by FHLH are scarce and the results are variable, showing survival rates ranging from 25% to 85%**
- **Ogha etal(2010 - Japan);** 57 patients with FHLH & EBV associated HLH . 50% of patients UC –HSCT . 26%; RIC , survival of UCBT recipients >65% in both FHL and EBV group.
- **Patel et al (2017):** UCBT in 14 children / 1998 -2016.
- All children received standard HLH **chemotherapy before UCBT**
- Median follow-up of > 11 years
  - **OS 71 & EFS;64.3%**

Literature Review: UCBT and HLH

Study/First Author/Reference	Publication Year	n	Engraftment	OS
CIBMTR/Baker [10]	2008	9	100%	67%
AIEOP/Cesaro [11]	2008	6	-	83.3%
COBLT/Frangoul [19]	2010	5	60%	40%
Korean registry/Yoon [28]	2010	4	50%	25%
Japan/Ohga [27]	2010	28	-	71%
HLH94/Trottestam [14]	2011	10	-	80%
Japan/Nishi [17]	2012	13	69%	85%
Japan/Sawada [18]	2013	38	-	63%
Current study	2017	14	78.6%	71.4%

CIBMTR indicates Center for International Blood and Marrow Transplant Research; AIEOP, Italian Association of Pediatric Hematology and Oncology.

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- **Juliana Montibeller Furtado-Silva (2019)- Europe**

- **118 children** with /FHLH / **single-unit umbilical cord blood HSCT /1996 - 2014.**
- Myeloablative conditioning regimen(MAC) ;90% of the patients, and was mostly busulfan-based (n = 81,76%), including anti-thymocyte globulin or alemtuzumab (n = 102, 86%).
- Incidence of Day 60 neutrophil engraftment was 85%
- Non-relapse mortality (NRM)& acute -GvHD: 21% & 33% at 100 days, respectively.
- The 6-year cumulative incidence of chronic GvHD;17%
- **6-year probability of OS was 55%.**

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- Analysis result;
- Total nucleated cell (TNC) dose > than 9. 9x 107 /kg & Degree of (HLA) matching (5/6 vs. 6/6); improved disease-free survival
- **Umbilical cord blood HSCT with a high cell dose and good HLA match is a suitable alternative option to haematopoietic stem cell trans-plantation in children with FHLH who lack a HLA-matched donor.**

Successful Haploidentical Stem Cell Transplant With Posttransplant Cyclophosphamide for HLH .
Pediatr Hematol Oncol Volume 41, Number 3, April 2019

- Donor availability is an issue in patients with lymphohistiocytosis (HLH)
- **Haploidentical HSCT with posttransplant cyclophosphamide (PTCy)** has been investigated as a feasible option for various malignant and nonmalignant conditions with reduced incidence of acute (GVHD) and graft rejection.
- **Report : 2 boys who underwent successful haploidentical HSCT with PTCy.**
- **None had acute GVHD and 1 had limited chronic GVHD.**
- **Full Chimerism in both patients were seen**
- **Both are alive and disease-free at follow-up of 912 and 239 days, respectively.**
- **Haploidentical HSCT with PTCy is a feasible option for children with HLH lacking a matched sibling donor**

Question :

- IS unrelated cord blood ,an effective graft source for pediatric patients with HLH lacking conventional donors???
- Other Option???

THANK YOU