Transplant in Pediatric Hematology Oncology (TiP-HO)
Tumor Board Meeting Minutes (Thursday, September 1, 2022)

Discussion board during the last meeting (Alphabetical):

Name	Affiliation
Prof. Dr. Alaa Elhaddad	Clinical Director Pediatric Oncology and Stem cell transplant program Children's Cancer Hospital (CCHE-57357) National Cancer Institute, Cairo University, Egypt
Prof. Dr. Annapoorani R M	Consultant of Pediatric Hematology Oncology Meenakshi Mission Hospital, India
Prof. Dr. Hesham Eissa	Consultant of pediatric Hematology/Oncology and Stem cell transplant Children Hospital Colorado, United States
Prof. Dr. Ibrahim Abdelkader	Consultant of pediatric Hematology and Stem cell transplant Children's Mercy Hospital, Kansas City. University of Missouri-Kansas City School of Medicine. USA
Prof. Dr. Leslie Lehmann	Clinical director of the Stem Cell Transplantation Program Dana-Farber/Boston Children's Cancer and Blood Disorders Center, USA
Prof. Dr. Mahmoud Hammad	Consultant of pediatric Hematology/Oncology and Stem cell transplant Children's Cancer Hospital (CCHE-57357) National Cancer Institute, Cairo University, Egypt
Prof Dr. Sadaf Altaf	Consultant of Pediatric Hematology Oncology and Stem cell transplant Agha Khan University Hospital, Pakistan
Prof. Dr. Sajad Khazal	Consultant of pediatric Hematology/Oncology & stem cell transplant MD Anderson Cancer Center, University of Texas, United States
Prof. Dr. Yasser Elboraei	Consultant of pediatric Hematology/Oncology and Stem cell transplant Prince Sultan Military Medical City (PSMMC), Saudi Arabia
Dr. Zehra Fadoo	Professor, Chair and SLC, Department of Oncology, The Tajuddin Chatoor Family Endowed Chair, Medical College, Pakistan

List of participating Centers

1. Children’s Cancer Hospital (CCHE-57357), Egypt
2. Faculty of Medicine Ain Shams University, Egypt
3. Borg Alarab Hospital, Alexandria University, Egypt
4. South Egypt Cancer Institute, Assiut university, Egypt
5. Shefaa El-Orman Oncology Hospital (SOH), Luxor, Egypt
6. Dar el Salam Cancer Hospital, Egypt
7. Sheikh Zayed hospital, Cairo, Egypt
8. Faculty of Medicine Tanta University, Egypt
9. Dana-Farber/Boston Children's Cancer and Blood Disorders Center, USA
10. Children’s Mercy Hospital, Kansas City. University of Missouri-Kansas City School of Medicine. USA
11. MD Anderson Cancer Center, University of Texas, United States
12. Children Hospital Colorado, United States
12. Sultan Qaboos University Hospital, Muscat, Oman
13. Royal Hospital, Muscat, Oman
14. Prince Sultan Military Medical City, Saudi Arabia
15. Aga Khan University Hospital, Pakistan
16. Shaukat khanum hospital Lahore, Pakistan
17. University Hospital Ibn Rochd, Faculty of Medicine and Pharmacy of Casablanca. Casablanca Hassan II university, Morocco
18. Meenakshi Mission Hospital and Research Centre, Madurai, India

Case 1— Fanconi Anemia for Haplo Transplant

- Six years boy
- Asymptomatic
- Thrombocytopenia identified on a routine CBC 2 years ago
- Platelets ranging from 30 – 60 X E^9/L
- Hb and WBC normal but declining
- No transfusions yet
- F/H – brother diagnosed as FA with Myelodysplastic syndrome (EB-I) in November 2021 – passed away secondary to infection/bleeding
- 1 healthy sibling
- **On examination**
  - Well active, short stature
  - 10th percentile for both height and weight
  - Dysmorphic facies typical small chin and beaked nose
  - Otherwise normal
- **Work up at AKUH:**
  - Bone marrow biopsy hypoplastic trephine biopsy 35% cellularity, no abnormal cells (2021)
  - Negative MDS FISH panel (Monosomy 5,7 and trisomy 8)
  - Negative AML panel (FLT3/ITD, NPM, t(8;14), t(15;17), t(11q), inv16)
  - Genetic consult and testing sent for Fanconi
- **Proband:**
  - Positive with two pathogenic variants identified in FANCA (autosomal recessive Fanconi anemia)
  - One pathogenic variant identified in RUNX1 (RUNX1 is associated with autosomal dominant familial platelet disorder with associated myeloid malignancy
- **Parents & unaffected brother are carriers** with one pathogenic variant identified in FANCA
- **HLA typing:** No matched donor (both parents and brother: 5/10 mismatched locus: A, B, C, DRB1, DQB1)
- **Summary:**
  - 6-year-old male with FA not transfusion dependent
  - FANC-A gene when tested last year
  - Brother with FA FANC-A and RUNX1
- **Plan:**
  - Father or brother to be potential donor
  - PRA/DSA testing to be done
  - Consider conditioning regimen per Brazilian group (Flu/Cy/TBI 200cGy or Flu/ATG/TBI 200cGy)
  - Bone marrow as stem cells to reduce risk of GVHD
  - Post-transplant low dose cyclophosphamide PTCy
  - Cyclosporine +MMF for GVHD prophylaxis

Questions raised by presenter (Dr. Sadaf Altaf & Dr. Zehra Fadoo, Pakistan)

- HSCT with RIC haplo-identical donor transplant with sibling versus parents?
- Time to transplant for children with FA especially when not transfusion dependent?
- Significance of genetic mutation in prognosis

Tumor board recommendations:

- It is better to transplant patients when they are heading towards repeated transfusion however, you can wait as long as the patient is transfusion independent but still as per board it is recommended to transplant the patient soon due to dropping hemoglobin and platelets counts (HB 8, PLT 20,000)
- Repeat BM before transplant to asses cellularity and detect clonal evolution
- The recommended conditioning in the setting of haploidentical with is FLU/CY/low dose TBI + PTCy.

- Haploidentical transplant has been offered safely to patients with Fanconi anemia in the setting of T-cell depletion and CD34 selected grafts and recently an acceptable outcome has been observed with in other with PTCy
- Alemtuzumab is not recommended due to significant viral re-activation especially if you don't have access to proper antiviral therapy
- Low dose TBI improves the engraftment and it is better to be used with thymic shielding if available

Scientific materials:

1. Régis Peffault de Latour, Jean Soulier, How I treat MDS and AML in Fanconi anemia, Blood, 2016, https://doi.org/10.1182/blood-2016-01-583625
2. Carmem Bonfim, MD, Samantha Nichele, MD, Gisele Loth, MD, et al. Transplantation for Fanconi anaemia: lessons learned from Brazil, The Lancet hematology, 2022, https://doi.org/10.1016/S2352-3026(22)00032-1
3. ZunairahShah, IsrarKhan, Ali ShahbazBaloch, et al. Outcomes of Haploidentical Stem Cell Transplantation in Patients with Fanconi Anemia, Blood, 2021, https://doi.org/10.1182/blood-2021-152759
4. Ramya Uppuluri, Venkateswaran Vellaichamy Swaminathan, Kesavan Melarcode Ramanan, et al. Haploidentical Stem Cell Transplantation with Post-Transplant Cyclophosphamide in Fanconi Anemia: Improving Outcomes with Improved Supportive Care in India, Transplantation and cellular therapy, 2020, https://doi.org/10.1016/j.bbmt.2020.08.019

Case 2: Blastic Plasmacytoid Dendritic Cell Neoplasm, Indications and Timing of Transplant?

- 16-year-old male with no known medical problems
- March 2022: cervical lymphadenopathy and sore throat: 4 days of antibiotics and steroids
- April 2022: morbilliform rash, cervical lymphadenopathy and sore throat: 7 days course of antibiotics and steroids
- May 2022: rash, cervical and axillary lymphadenopathy, accompanied by bilateral periorbital ecchymosis
- Presented to an ER early June and found to be anemic and thrombocytopenic
- BM: Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN)
    - 87% blasts, 99% positive for CD123.
    - Additional markers show aberrant cells: positive for CD4, CD38, CD56, CD123, CD303 (decreased, partial), HLA-DR; they are negative for CD2, CD7, CD34, CD64.
- Involvement of cervical lymph nodes, sinuses, spleen, liver, skin
- Initially CNS Positive (WBC-0, blasts seen by cytology)
- Positive for JAK2, NF1 and NRAS mutations
- He completed 3 cycles Hyper-CVAD + Venetoclax + IT chemo
- CNS negative
- No comorbidities
- Family Hx: MSD identified (PBSC collected and cryopreserved)
- **Plan:** for CSI boost 10 Gy followed by TBI based myeloablative regimen (1320 cGy + cyclophosphamide)

Questions raised by presenter (Prof. Dr. Sajad Khazal, USA)

- Indication for SCT?: CR1 vs CR2 and beyond
- The ideal Conditioning regimen?

Tumor board recommendations:

- A rare disease with few publications to get a solid conclusion however, high-risk ALL therapy with central nervous system prophylaxis is recommended for upfront therapy
- Available publications observed longer remissions in BPDCN adult patients with allo-HCT in first complete remission and lower survival have been reported in patients transplanted in CR2

- Giving the patient age and CNS involvement at presentation, transplant in CR1 is recommended
- TBI based myeloablative regimen (1320 cGy + cyclophosphamide) preceded by CSI boost 10 Gy is a good option as a conditioning regimen
- The use of Tagraxofusp (anti-CD123) in the upfront therapy or as a maintenance therapy post-transplant is discouraged due to excessive toxicity

Scientific materials:

1. Marie Jeong-Min Kim, BHSc, Ahmed Nasr, MD, MSc, FRCSC, Bilaal Kabir, et al. Pediatric Blastic Plasmacytoid Dendritic Cell Neoplasm: A Systematic Literature Review, J Pediatr Hematol Oncol, 2017, DOI: 10.1097/MPH.0000000000000964
2. Qaiser Bashir, Denái R. Milton, Uday R. Popat, et al. Allogeneic hematopoietic cell transplantation for patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), Bone Marrow Transplantation, 2022, https://doi.org/10.1038/s41409-021-01478-5
3. Armin G. Jegalian, Nataliya P. Buxbaum, Fabio Facchetti, et al. Blastic plasmacytoid dendritic cell neoplasm in children: diagnostic features and clinical implications, Haematologica, 2010, https://doi.org/10.3324/haematol.2010.026179
4. Daniel Kerr II, MD, PhD1, Ling Zhang, MD, Lubomir Sokol, MD, PhD, Blastic Plasmacytoid Dendritic Cell Neoplasm, Curr. Treat. Options in Oncol., 2019, DOI 10.1007/s11864-019-0605-x
5. Naveen Pemmaraju, M.D., Andrew A. Lane, M.D., Ph.D., Kendra L. Sweet, M.D., et al, Tagraxofusp in Blastic Plasmacytoid Dendritic-Cell Neoplasm, The New England Journal of Medicine, 2019, DOI:10.1056/NEJMoa1815105
6. Naveen Pemmaraju, Branko Cuglievan, Joseph L Lasky, et al, Treatment of Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) in Pediatric Patients with Tagraxofusp, a CD123-Targeted Therapy, Blood, 2021, https://doi.org/10.1182/blood-2021-150393

Case 3: Relapsed Neuroblastoma Post Autologous HSCT

- 4 years old patient presented on June, 2018 with intermittent periumblical abdominal pain for 3 months, fever for 2 weeks and decreased intake with occasional vomiting for 1 month
- **On examination:**
  - Ill-defined 5x3 cm mass palpable in right paraumbilical area
  - Fixed and non-tender mass; no other palpable masses
  - No hepatomegaly
  - Systemic examination was normal
- LDH:539 high
- Ferritin - not done
- 24 hour Urine VMA : in normal range
- CT Abdomen and chest:
  - Calcified mass lesion 7.7 x3.5 x6.5 cm in right adrenal gland engulfing right renal artery, displacement of right kidney. lesion crossing midline.
  - Multiple enlarged lymph nodes in paraaortic area engulfing aorta and IVC. enlarged LN in celiac axis, left upper paraaortic region
  - No other metastasis
- CT guided Biopsy & Histopathology: Neuroblastoma, poorly differentiated, unfavorable histology
- **Staging work up:**
  - Bone marrow aspiration and biopsy: Infiltration by neuroblastoma
  - CT Chest: Normal
  - NMYC gene: not amplified
- **Final Diagnosis**:
  - 4 years old Stage IV, Unfavorable histology
  - NMYC : not amplified
  - High Risk Neuroblastoma
- **Treatment course:**
  - Rapid COJEC x 8 cycles (Pet CT: 40% reduction in size)

  - Subtotal excision done on 19. 9. 2018 (Histopathology: Neuroblastoma with necrosis calcification)
  - Auto HSCT with BUMEL conditioning on oct 2018
  - RT @ 21Gy followed by Cis-RA for 6 months
- Pet CT Day +195 post BMT and RT showed 70% reduction from the initial size of the mass
- **In January 2022 After 3.5 years from diagnosis:** He presented with decreased appetite/ intake and Pain abdomen for 1 week
- Pet CTs showed:
  - Stationary RT suprarenal mass 41.5 x34.5x53 mm (SUV 2.2)
  - Newly developed liver metastasis (SUV 4.8)
  - Newly developed enlarged retroperitoneal and periportal lymph nodes (SUV 4.6)
- Considering late metastatic relapse he is started on Vincristine, Irinotecan and Temozolomide Chemotherapy
- He is currently on 7th cycle of chemotherapy
- MIBG scan done after 3 cycles of chemotherapy showed Heterogenous MIBG uptake? uptake in Liver metastasis and minimal MIBG uptake in bone marrow metastatic lesions
- PET CT done after 6 cycles of VIT:
  - > 50% reduction in LIVER LESIONS
  - RESOLUTION OF BM LESIONS
  - RIGHT SUPRARENAL MASS - size slightly increased 41x49x53mm (SUV 1.85)
- **Final Diagnosis:**
  - 8 years old High-risk NB MYCN negative - post autologous HSCT
  - Metastatic recurrence after 3.5 years from initial diagnosis
  - Completed 7 cycles of VIT
  - No comorbidity, normal renal and cardiac function status

Questions raised by presenter (Dr. Annapoorani, India)

- Role of 177 -Lutetium DOTATATE therapy?
- Is second SCT - autologous or allogenic with be helpful in the scenario of non-affordability to Dinutuximab?

Tumor board recommendations:

- Haploidentical +/- NK cell infusion is under trial in relapsed NB with no solid conclusions yet
- Anti-GD2 is the recommended option for relapsed NB especially for patients who were not exposed to it before, yet if anti-GD2 is not available and you managed to get the patient into good or very good partial remission haplo-identical transplant is recommended
- MIBG therapy on palliative basis would be a more reasonable option than Lu 177 dotatate therapy

Scientific materials:

- ToniIllhardt, JacekToporski, TobiasFeuchtinger, et al. Haploidentical Stem Cell Transplantation for Refractory/Relapsed Neuroblastoma, Transplantation and cellular therapy, 2018, https://doi.org/10.1016/j.bbmt.2017.12.805
- Steven G. DuBois, MD; Margaret E. Macy, MD; and Tara O. Henderson, MD. High-Risk and Relapsed Neuroblastoma: Toward More Cures and Better Outcomes, ASCO EDUCATIONAL BOOK, 2022, https://doi.org/10.1200/EDBK_349783

P.S. Exceptionally, next month TiP-HO meeting will be postponed for 1 week and will be held on Thursday October 13, 2022 (3-4 PM Cairo local time (GTM+2)

Please send your cases one week before the due date of our next meeting.

For further inquiries please do not hesitate to contact us

Announcement

On behalf of the Egyptian Pediatric Hematology Oncology Society (EPHOS) organizing Committee we would like to invite you to attend the Hybrid EPHOS international Annual Conference about "**Debates & Updates in Hematological Malignancies**" on **6th-8th October, 2022** at *Sheraton Cairo Hotel* in Cairo, Egypt.

- A registration link and details of program will be sent this week in a separate email

Best Regards,

TiP-HO meeting coordinators

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