Impact of Second-Generation Antipsychotic Use in Pediatric Bone Marrow Transplant Engraftment: A Case Series

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Background

- Bone marrow transplantation (BMT) is an increasingly utilized treatment modality for multiple hematological, autoimmune, and genetic conditions.[1]
- Optimal engraftment is expected 15-30 days following peripheral BMT.
- Second-generation antipsychotics (SGA) may be used during the BMT course to manage comorbid psychiatric disorders or neuropsychiatric complications.
- SGA treatment in pediatric cancer patients for symptomatic management during BMT has shown efficacy and tolerability.[2-3]
- However, there is limited research on SGAs impact on the BMT process, considering their association with anemia, neutropenia, thrombocytopenia, and even agranulocytosis. [4-7]
- Risk factors for SGA related blood dyscrasia include extreme ages, African American race, and male gender.[5-6]
- In this case series, we present four pediatric BMT patients in which SGAs were used for a variety of clinical presentations.

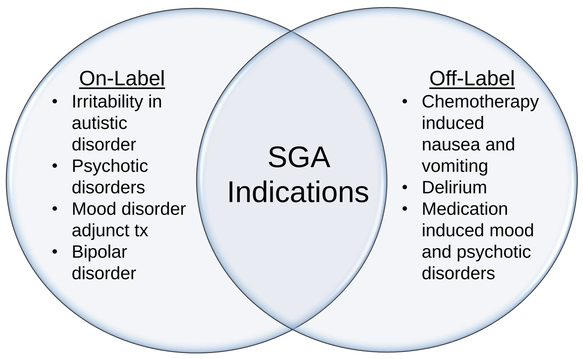

Figure 1: Second-Generation Antipsychotics (SGA) Indications

Aim

- To determine if SGA treatment impacts time to engraftment following pediatric BMT and at one-year follow up

Methods

- Four pediatric patients undergoing BMT whose clinical course included the use of SGAs were described.
- Patients were prospectively followed by the Consultation Liaison (CL) psychiatry team.
- Events described include patients' initial evaluation and neuropsychiatric symptoms, onset and duration of SGA treatment, time to engraftment, and engraftment status one-year post-transplant.

Timeline

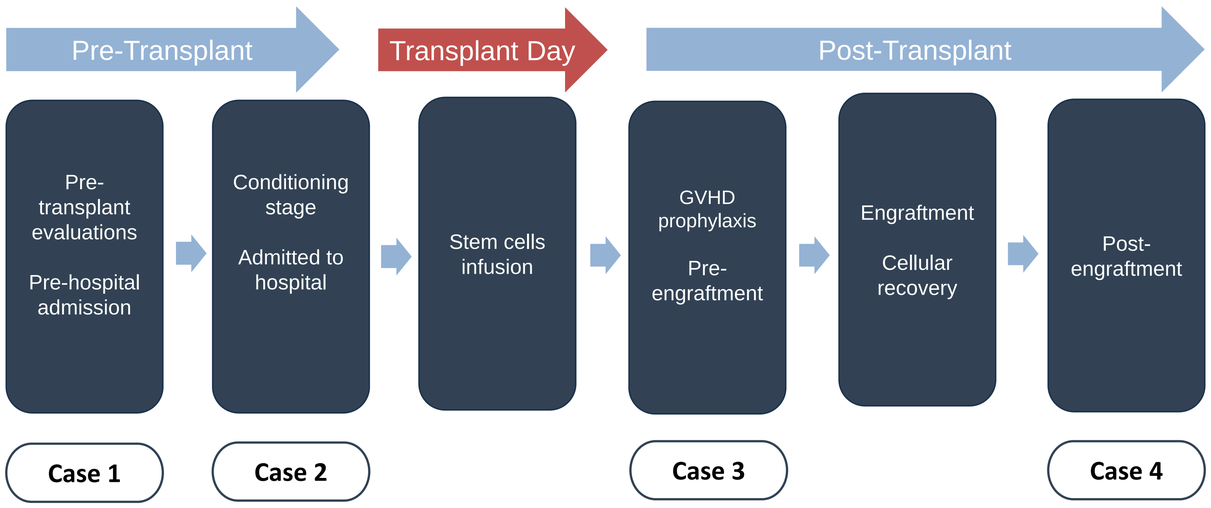

Figure 2: Stages of Peripheral Bone Marrow Transplant

Case Presentations

Patient	Case Description	SGA Treatment	Duration of SGA Treatment	Engraftment Outcome	
				Time to Engraftment (within 30 Days)	Graft Maintained at 1 Year
1	12-year-old boy with Evan's Syndrome and autism spectrum disorder experiencing disruptive and aggressive behavior, irritability, and anxiety.	• Risperidone 1mg twice a day • 1 year follow up: risperidone 0.5mg daily	19 months	Yes	TBD
2	8-year-old boy with GATA2 haploinsufficiency who developed dexamethasone induced severe mood and behavior disturbances.	• Olanzapine 2.5mg at bedtime and 2.5mg as needed • 1 year follow up: aripiprazole 7.5mg	14 months	Yes	Yes
3	15-year-old boy with Jobs syndrome who developed acute onset hypomanic symptoms (rapid and pressured speech, lack of sleep, increase physical activity, distractibility, and racing thought) following cyclophosphamide infusion.	• Olanzapine 5mg single dose • 2.5mg at bedtime for 1 week • Changed to 2.5mg as needed then discontinued after 1 week	2 weeks	Yes	Yes
4	13-year-old boy with Wiskott-Aldrich syndrome who experienced chemotherapy induced nausea and vomiting refractory to metoclopramide and ondansetron. He was subsequently admitted to the ICU for respiratory failure due to pneumonia and delirium.	• Olanzapine 5mg at bedtime for 1 week • Increased to olanzapine 7.5mg at bedtime for 1 week then discontinued	2 weeks	Yes	Yes

Discussion

- To our knowledge, this is the first pediatric case series that describes the use of SGAs and their impact on BMT engraftment outcomes.
- SGA use did not impact the time to engraftment or maintenance of the graft at one-year follow up regardless of duration of treatment.
- SGA treatments demonstrated efficacy and tolerability, with minimal adverse effects, which is consistent with previous findings.[2]
- Initiation and duration of SGA therapy can vary among patients depending on clinical presentation.
- Engraftment status should be monitored when SGAs are administered.
- Further research is required to understand:
  - Cellular mechanisms of SGA-related blood dyscrasias
  - Impact of SGAs in pediatric populations undergoing the BMT process
  - Mechanisms of how SGAs impact the extended engraftment process

Limitations

- Inclusion of only males and small sample size limits generalizability.
- SGA indications and dosages varied among patients.

Conclusion

- CL psychiatrists can play an important role in managing SGA therapy and consulting with transplant teams during the pediatric BMT process.
- Despite limited data on safety and efficacy, SGAs may provide benefit for both medical and psychiatric symptoms experienced during the clinical course of pediatric BMT.

References

1. Phelan R., et al. Updated Trends in Hematopoietic Cell Transplantation in the United States with an Additional Focus on Adolescent and Young Adult Transplantation Activity and Outcomes. Transplantation and cellular therapy, 2022;28(7):409e1–10.
2. Peled O, Lavan O, Stein J, Vinograd I, Yahel A, Valevski A, Weizman A, Kimmel-Tamir E, Apter A, Fennig S, Yaniv I, Bernfeld Y, Benaroya-Milshtein N. Psychopharmacology in the Pediatric Oncology and Bone Marrow Transplant Units: Antipsychotic Medications Palliate Symptoms in Children with Cancer. J Child Adolesc Psychopharmacol. 2020 Oct;30(8):486-494. doi: 10.1089/cap.2019.0164. Epub 2020 Aug 25. PMID: 32845729
3. Blom JMC, et al. The Use of Psychotropic Medication in Pediatric Oncology for Acute Psychological and Psychiatric Problems: Balancing Risks and Benefits. Children (Basel). 2022 Nov 30;9(12):1878.
4. Stroup, T. S., & Gray, N. (2018). Management of common adverse effects of antipsychotic medications. *World psychiatry: official journal of the World Psychiatric Association (WPA)*, *17*(3), 341–356. https://doi.org/10.1002/wps.20567
5. Atolagbe, A., Nkemjika, S., Popoola, O., Oladeji, O., Kogan, I., Saeed, H., & Olupona, T. (2021). Risperidone-Induced Neutropenia in a Schizophrenic Patient: A Case Report and Literature Review. *Case reports in psychiatry*, *2021*, 3980872. https://doi.org/10.1155/2021/3980872
6. Malik YK, Sahoo S, Avasthi A. Olanzapine-induced leucopaenia and thrombocytopaenia in an elderly patient: a case report and review of the evidence. Gen Psychiatr. 2018 Oct 25;31(2):e000013. doi: 10.1136/gpsych-2018-000013. PMID: 30582126; PMCID: PMC6234971.
7. Felin T, Naveed S, Chaudhary AM. Aripiprazole-Induced Neutropenia: Case Report and Literature Review. J Psychosoc Nurs Ment Health Serv. 2018 May 1;56(5):21-24. doi: 10.3928/02793695-20180419-02. PMID: 29715374.

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