High-Risk MDS Patient

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• 39 Y/O M
• Pancytopenia and fever for a year
• BM biopsy: MDS, 3% blasts, complex karyotype: -5q, del p53
• High risk MDS, IPSSR: 6
• Patient with somewhat intellectual disability, “funny” looking facial features, glaucoma, ataxia. No definite neurological diagnosis

• Family history:
• Mother and father are related (fourth-degree kinship)
• 2 sisters (1 sister had breast cancer, BRCA neg)
• Multiple malignancies (mostly breast) in the family
Should we proceed for allo-BMT? Yes

Who are the potential allo-BMT donors of this patient?
Should we transplant one of his sisters in case of a match?
Or Search for MUD from the beginning?
Genetic analysis

• Triple whole exome sequencing was sent for analysis

• Pediatric Hemato-oncologist also suspected syndromic appearance and advised against MSD for allo-BMT, our BMT team supported MUD

• Whole exome results: JAK2 positive heterozygote (maternal), TDP2 homozygote
What is TDP2?

• Topoisomerase2 participate in the unwinding of DNA during replication – causing transient breaks in DNA
• Topo 2 poisons like Etoposide prevents re-ligation if DNA
• TDP2 - Tyrosyl-DNA phosphodiesterase 2
• DNA strand break repair protein
• It is required to repair the accidental double-strand breaks produced by the abortive activity of Topoisomerase II
TDP2

• *TDP2* mutation in humans has been associated with intellectual disability, seizures, and ataxia.

• An ultra rare disease now denoted as spinocerebellar ataxia, autosomal recessive 23 (SCAR23) in children (5 patients described).

• Neutropenia was reported in 1 case.

• MDS or other hematological malignancies not described.
Discussion

• Back to basics: history taking, family history and Physical examination!
• When to perform whole exome?
• Donor selection? MSD? MUD?
• Conditioning regimen? Is he chemo-sensitive as Fanconi anemia?
• What is the impact of JAK2 heterozygote in this case?
• Is MDS a feature in older patients with SCAR23 disease not yet described?