

A Patient Presentation:
Familial MPN, AML, LCH
and **MDS**

A story from 2021 and way before...

Presented by: **Howard S. Oster**, Tel Aviv, Israel

A Patient Presentation:

- Index patient:
 - **PA: January 2021**
 - High risk Myelodysplastic syndrome (MDS)
 - Preexisting hematologic
 - and other diseases
-
- Back in time... **Family history**

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- **Paternal grandmother:**
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- **Three other family members**
 - Hematologic disease (including AML)

Genetic Workup

1. **MPN Workup:**
 - **JAK-2** (V617, exons 12, 14): negative
 - **Cal-R**, type 1, 2: negative
 - **C-MPL**: negative
 - **ABL-BCR**: negative
2. Next generation sequencing (**NGS**):
 - TruSight panel (Illumina, **54 myeloid genes**)
 - Negative
3. Whole exome sequencing:
 - **ANKRD26 mutation**

ANKRD26 Mutation: Familial Thrombocytopenia (THC2)

- **Autosomal dominant** mutation
 - Chromosome 10, 5'-UTR region, ANKRD26 gene
- **Familial** thrombocytopenia
- Possible **hematologic complications:**
 - Polycythemia
 - Major bleed rare
 - Leukemic association, ~10% (CML, CLL, AML)
 - Bone marrow disease, **including MDS**

Management (MA, PA): Like MPN; Genetic counseling

PA: Disease course, January 2021

- **Perianal lesion (2 cm)**
 - Biopsy: **Langerhans Cell Histiocytosis (LCH)**
 - **BRAF+**
- Headaches, polyuria, weight loss (13kg/yr)
 - Low urine osmolarity
 - **Diabetes insipidus (DI)**
 - MRI: enhanced bone signals (diffuse); **lytic lesions** (skull, mandible)
- Skin (red-yellow papules): **Juvenile xanthogranuloma**
 - **BRAF+**
- **Bone Marrow:** normal at this time
- LCH is associated with myeloid diseases

PA: Disease course, 2021-2022

- **Treatment:**

- Desmopression (DDAVP) - Successful
- **Cytarabine** (100mg/dx5/m)
 - After 5 months: Improvement !

- **After 11 months: Relapse**

- Skin lesion: Perianal biopsy - identical
- Decreasing CBC
- **Bone marrow: dysplasia, 9% blasts! 46XY**
- **Dg: Myelodysplastic Syndrome (MDS)**
 - Treatment: Azacitidine + Venetoclax – **CR!**
 - **Platelets – normalized**
 - **Perianal lesion – resolved**

Questions for discussion:

1. LCH and Familial thrombocytopenia (THC2) - relation?
2. Relation to MDS?
3. Treatment of PA (now in CR):
 - Indication for BRAF inhibitors?
 - What's next?