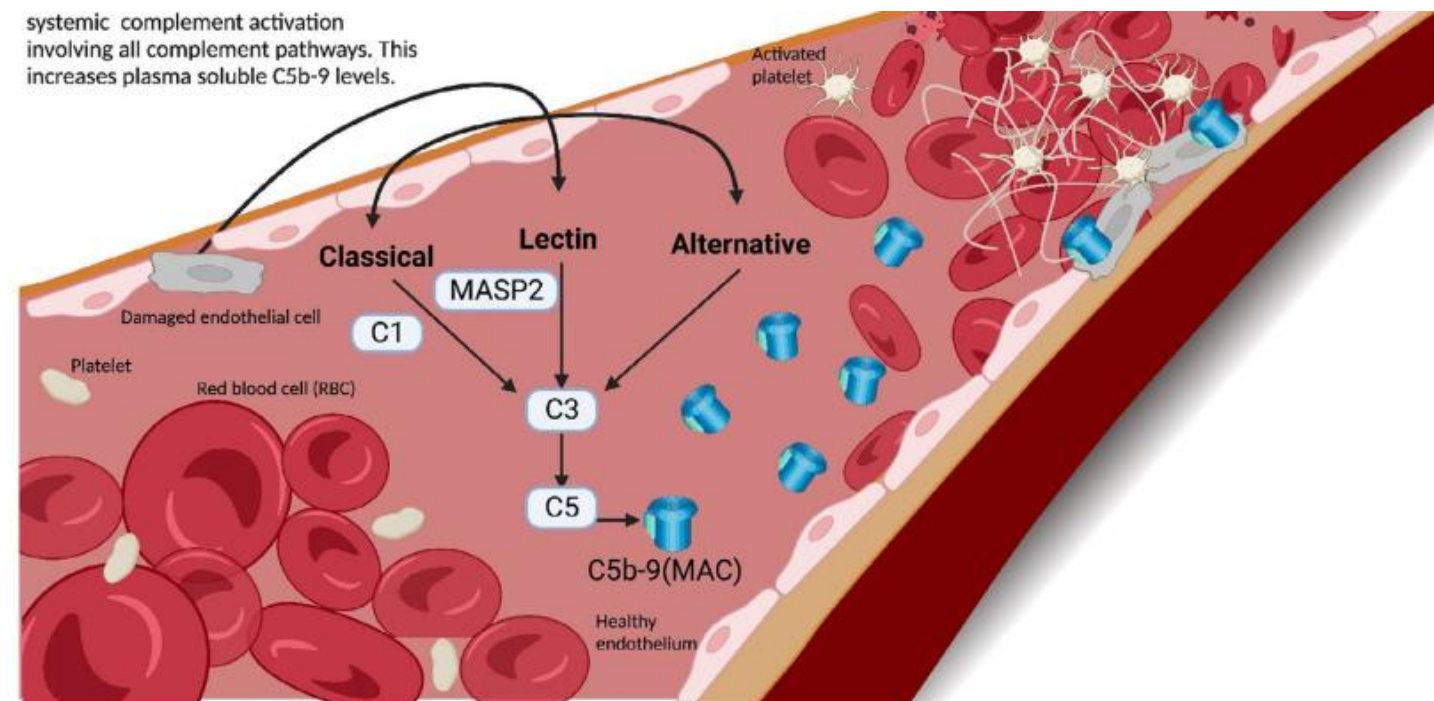


TMA in transplant- Who is the culprit?



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Background History

- A 63 year old female, hypertensive - Diagnosed as **Triple negative Right breast carcinoma**.
- Chemotherapy → surgery (BCS) → radiation → pembrolizumab maintenance (18th # on April'2024).
- Incidentally- CBC showed Blasts, BM evaluation s/o AML.
- Cytogenetics:- **46XX, t(9,11)**.
- NGS:- **KMT2A-MLL2 FUSION, KRAS**.
- Final diagnosis: **Therapy related AML**, ELN 2022 adverse risk.
- Post 1st cycle Azacitidine + venetoclax, BM- 84% blasts s/o refractory AML.
- Came to RGCI for further management.
- Re-induction FLAG+venetoclax based chemotherapy → BM in remission → Was then on Revumenib from D+24.

The Transplant

- **CONDITIONING REGIMEN - (FLU-TREO - TBI-PTCy35 -Cyclosporine-MMF)**
- Donor –haploidentical match daughter
- CMV IgG:- Donor + Receptient +
- Blood group: B+ to O+
- Stem cell dose -5 * 10⁶/kg
- **complications during transplant**
 - 1.Left subclavian vein DVT (Day+3).
 - 2.CR Klebsiella BSI (Day+7).
- **The Engraftment** : Neutrophil +10, Platelet +13.

CULPRIT ON RUN

- Day+14- Patient had altered sensorium, repetition of words, flapping tremors, headache, hypertension.
- **MRI brain s/o non territorial tiny infarcts and hemorrhagic foci.**
- Neurologist and ID physician consultation was taken , CSF evaluation done & Infective causes were ruled out.
- Indirect hyperbilirubinemia + 3% schistocytes in PS + raised LDH + Low haptoglobin was s/o ongoing **TMA**.
- In view of evidence of TMA, cyclosporine was withheld. But patient worsened clinically.
- Urine PCR was > 3mg/mg creatinine. Hence a provisional diagnosis of **TA-TMA** was made after excluding all possible causes of TMA.

New Consensus TA-TMA diagnostic criteria (Modified Jodele)

Srl No	Comment	Biopsy proven disease or meet ≥ 4 of criteria (1) to (7) concurrently for ≥ 2 times in 14 days
1	Schistocytes	Presence
2	Thrombocytopenia	>50% Plt reduction from baseline after engraftment or transfusion dependence
3	Anemia	$\geq 1g/dl$ Hb reduction from baseline after engraftment or transfusion dependence (rule out AIHA & PRCA)
4	Elevated LDH	LDH > ULN
5	Hypertension	1. >99 th percentile for age (<18 yr) 2. > 140/90 (≥ 18 yr)
6	Proteinuria	Spot rUPCR $\geq 1mg/mg$
7	Elevated sC5b9	sC5b9 > ULN

ASH Edu 2024

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CASE PRESENTATION

POLICE IN THE ACTION

- Patient was treated with low dose defibrotide and Ruxolitinib for TA-TMA.
- In view of worsening cytopenias with UGI bleed- defibrotide was withheld.
- Patient was started on Eculizumab weekly (3 doses) Patient improved symptomatically, TMA resolved, Proteinuria settled, schistocytes disappeared. Patient did well , kept on OPD follow up.
- **CURRENT STATUS:**
- Day +156.
- No TMA/ GVHD/VOD/ CMV reactivation(?blip – day+60).
- VNTR Chimerism on Day+72 is 100% for donor.
- Patient is on calcineurin inhibitor free GVHD prophylaxis (MMF till D+140, On ruxolitinib)
- BM- Remission, MRD negative on D+156
- Completed post transplant Azacytidine, venetoclax maintenance – 3 cycles till date.

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CASE PRESENTATION

SUGGESTIONS FROM THE EXPERTS!

- Any possible risk factors predisposing to TA-TMA in this case? Any predictors?
- What was your experience with low dose defibrotide for TA-TMA/ eculizumab?
- Experience with CNI- free GVHD prophylaxis in similar/ other post transplant cases?
- How long would you monitor for TMA post transplant? Any other markers for TA-TMA?