Myelodysplastic Syndrome/Myeloproliferative Neoplasm Unclassifiable

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Abstract: MDS/MPN Unclassifiable is rare disease with mixed myelodysplastic and myeloproliferative features and cannot categorised into MDS OR MPN. WHO 2008 defined a MDS/MPN overlap category that includes:
1) MDS/MPN Unclassifiable, 2) CMML, 3) JMML, 4) Atypical CML, BCR-ABL 1 negative, 5) Refractory anemia with ring sideroblasts and thrombocytosis
MDS features with <20% blasts (not due to treatment), Prominent myeloproliferative features (leukocytosis, thrombocytosis, splenomegaly).
No recent cytotoxic / growth factors Treatment Ph1 negative, PDGFRA/PDGFRB negative, no del 5q, t(3;3) or inv 3 OR Denovo features of MDS/MPN that cant be assigned to another category

I. Introduction
MDS/MPN Unclassifiable is rare disease with mixed myelodysplastic and myeloproliferative features and cannot categorised into MDS OR MPN.

II. Objective
To review the clinical and pathological features of the disorder
To discuss the prognosis and potential treatment approach.
MDS and MPN have overlapping features
WHO 2008 defined a MDS/MPN overlap category that includes:
MDS/MPN Unclassifiable
CMML
JMML
Atypical CML, BCR-ABL 1 negative Refractory anemia with ring sideroblasts and thrombocytosis

III. Case Report
50 yr serviceman vegetarian nonalcoholic came with C/o generalised weakness since 1 month, Ecchymoses, petechiae since 15 days, swelling over right leg since 20 days, General Examination :- Pallor ++ Ecchymoses& petechiae on lower legs, Pulse :- 86/ min Systemic Examination :- CVS :- S 1 S 2 RS :- AEEBS PA :- moderate degree of hepatosplenomegaly On FNAC from swelling over right leg we found scattered large atypical cells ( ? blasts cells) with degenerated morphology that is suspicious of hematological malignancy. Patient further investigated

Investigation
1) CBC
Hb :- 7.4 gm%
TLC :- 130000 /cumm
DLC :- P-80% L-10% E-5% M-5%
Plat :- 57,000/cumm

2) Peripheral Smear
RBC :- Anisocytosis, Macrocytes, Microcytes, Moderate to severe degree of hypochromia
TLC :- Above normal

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Figure 1: Blast cells and hypolobated myeloid cells in 40x

Figure 2: Hypolobulated and vacuolated Blast cells in oil immersion

**DLC:** Blast like cells – 10 %, Myelocytes – 30 %, Metamyelocytes -20 %, Band Forms – 5 %, Mature polymorphs – 20 %, Lymphocytes – 10 %, Eosinophils – 5 %, Myeloid cells series shows hypolobulation with cytoplasmic vacuoles, 5-6 nucleated RBC /100 WBC Platelet severely depleted.

3) BM Aspiration

Figure 3: shows presence of blast cells, erythroid precursor, eosinophilic blast cells.

Figure 4: BM aspiration shows myeloblast and late erythroblasts. BM Aspiration: Shows hypercellular marrow with marked paucity of differentiation myeloid series noted. Erythroid series are decreased, Megakaryocytes are not identified. Hypercellular marrow with myeloid preponderance & 11% blasts

Suspect MDS/MPN

4) BM Biopsy

Figure 5 & 6: BM Biopsy: Presence of blast cells hypolobulated myeloid series. Consistent with AML.
Hyperplastic bone marrow shows presence of left shift of myeloid series, presence of pseudo pelgerhuet cells, blast cells. Erythroid series are decreased, megakaryocytes are not identified.

5) **Flow Cytometry**

Morphological and immunophenotyping are consistent with MDS/MPN Unclassifiable, MPO +ve, with dim expression of CD 45 +ve, CD 117 +ve compare to normal progenitors. CD 34 +ve, granulocytes are hypogranular in nature and show asynchronous maturation. These findings are consistent with MDS-MPN.

6) **Molecular Cytogenetics (FISH)**

No indication of deletion 5q (for RAEB, RARS), 7q (for JMML, CMML, RAEB, RARS), 20q, and Trisomy 8 (for CMML, MDS) along with no evidence of BCR/ABL fusion and negative for single round RT-PCR for b2a2 and b3a2 transcript. Also show no evidence of: t(8;21) (for AML M2), MLL translocation and inv (16)/t(16:16) for AML M4.

Karyotyping suggestive of no chromosomal abnormality.

IV. **Discussion**

Very rare disorder, 2% of cases in retrospective MDS series. The cases classified as MDS/MPN U do not meet the criteria for CMML, JMML, atypical CML.

**Clinical presentation**

Anemia, +/- Macrocystosis, Proliferation in one of the myeloid lineages with dysplasia in at least 1 cell line. Thrombocytosis > 450ac/mm, large and hypogranulated or Leucocytosis, WBC > 13000/ mm neutrophils may be dysplastic Blasts ≤ 20%. Cytochemical / immunophenotype findings similar to MPN and or MDS Males = Females, 60% symptomatic at diagnosis. Complication of cytopenia: fatigue, bleeding, infection, Infiltration of spleen/liver, early satiety. Constitutional symptoms.

V. **Diagnostic Criteria**

MDS features with <20% blasts (not due to treatment). Prominent myeloproliferative features (leukocytosis, thrombocytosis, splenomegaly). No recent cytotoxic / growth factors. Treatment. Ph1 negative. PDGFRA/PDGFRA negative, no del 5q, t(3;3) or inv 3. Or Denovo features of MDS/MPN that can’t be assigned to another category.

VI. **Conclusion**

MDS/MPN Unclassifiable clinically can present AML or CML morphologically immunophenotyping like FISH. Cytogenetics are needed for confirmation of diagnosis and further management of patients.

**References**

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