Morphologic Changes in Myelodysplastic Syndrome Treated with Hypomethylating Agents

SK Rathke, MD, H Olteanu, MD, PhD, SH Kroft, MD, AM Harrington, MD
Department of Pathology, Medical College of Wisconsin, Milwaukee, WI, United States

Abstract

Background: Hypomethylating agents (HMAs) are frequently used as myelodysplastic syndrome (MDS) therapy. As little data exists on the morphologic changes observed with this treatment in peripheral blood (PB) and bone marrow (BM), we chose to study this in an MDS cohort.

Design: PBs and BMs from MDS patients were evaluated before (PTx) and after (FU) HMA treatment. Cell counts, lineage dysplasia, blast percentages, BM cellularity, stromal changes, lymphoid aggregates, bone changes, and hemosiderin deposition were recorded. The MDS diagnosis was made according to WHO 2008 criteria. Dysplasia was defined as morphologic abnormalities present in >10% of a lineage.

Results: 13 MDSs were included: 6 therapy-related MDSs, 4 MDS-unclassified; 2 refractory anemia with excess blasts (RAEB) and 1 refractory cytopenia with multilineage dysplasia (RCMD). 7 males, 6 females; aged 35-79. Median PTx CBC data was 2.6/kL (1.1-5.8) WBCs, 9.2/μL (7.2-12.4) RBCs and 105/μL (25-250) PLTs; compared to 2.3/kL (0.57-6.6) WBCs (p=0.012), 109/μL (8.8-13.1) RBCs (p=0.114), and 108/μL (15-588) PLTs (p=0.872) in FUs. Median time between PTxs and FU was 115 (44-507) days. 4 PTx cases had PB blasts, which were not present at FU, but 1 case acquired PB blasts. PB blasts were 3% (1-12%) PTx vs. 1.6% (0-14%) at F/U (p=0.06). BM cellularity decreased with HMA therapy. BM blasts were 3% (1-12%) PTx vs. 29% (≥5-75%) in F/U (p=0.009). BM granulocyte dysplasia persisted in 5/6 cases at F/U; erythroid dysplasia resolved in 5/7 cases, and platelet dysplasia resolved in 4/5 cases. One case acquired PB blasts at F/U. PB granulocyte dysplasia persisted in 5/5 cases and resolved in 3/5 at F/U. Erythroid dysplasia resolved in 5/7 cases, and platelet dysplasia resolved in 4/5 cases. One case acquired PB blasts at F/U. BM blasts were 3% (1-12%) PTx vs. 1.6% (0-14%) at F/U (p=0.06). Average cellularity was 61% (≥5-100%) in PTx vs. 29% (≥5-75%) in F/U (p=0.009). BM granulocyte dysplasia persisted in 5/6 cases at F/U. Erythroid dysplasia persisted in 5/6 cases and resolved in 4/5 at F/U. Megakaryocyte dysplasia persisted in 5/5 cases at F/U; and resolved in 3/5 at F/U. Erythroid dysplasia was present in 5/13 PTx cases; persisted in 5/5 cases; and resolved in 2/5 at F/U. Erythroid dysplasia was present in 7/13 PTx cases; resolved in 5/7 cases and persisted in 2/7 at F/U. Platelet dysplasia resolved in 4/5 cases at F/U.

Conclusion: Blast percentages decreased in both the PB and BM following HMA therapy. BM cellularity decreased with HMA therapy. There was no statistically significant difference in WBCs, PLTs, or Hgb, pre- or post HMA therapy. The most common morphologic changes observed were loss of erythroid and platelet dysplasia in the PB.

Materials and Methods

Patients: 13 cases of MDS treated with HMAs with pre-treatment (PTx) and follow-up (FU). PB and BM blast counts were identified from 1/2006 to 7/2011 at our institution. The MDS diagnosis was made according to 2001 or 2008 WHO criteria.

Peripheral blood morphologic analysis:
- Blast % (based on 100 cell differential of Wright-stained PB) was recorded.
- Erythroid, granulocytic and megakaryocytic morphologies were evaluated.
- Erythroid, granulocyte and megakaryocyte dysplasia were defined.
- BM blasts were 3% (1-12%) PTx vs. 1.6% (0-14%) at F/U (p=0.06). Average cellularity was 61% (≥5-100%) in PTx vs. 29% (≥5-75%) in F/U (p=0.009). BM granulocyte dysplasia persisted in 5/6 cases at F/U. Erythroid dysplasia persisted in 5/7 cases, and platelet dysplasia resolved in 4/5 cases. One case acquired PB blasts at F/U.

Results:

Patients: 13 cases of MDS treated with HMAs with pre-treatment (PTx) and follow-up (FU). PB and BM blast counts were identified from 1/2006 to 7/2011 at our institution. The MDS diagnosis was made according to 2001 or 2008 WHO criteria.

Peripheral blood morphologic analysis:
- Blast % (based on 100 cell differential of Wright-stained PB) was recorded.
- Erythroid, granulocytic and megakaryocytic morphologies were evaluated.
- Erythroid, granulocyte and megakaryocyte dysplasia were defined.
- BM blasts were 3% (1-12%) PTx vs. 1.6% (0-14%) at F/U (p=0.06). Average cellularity was 61% (≥5-100%) in PTx vs. 29% (≥5-75%) in F/U (p=0.009). BM granulocyte dysplasia persisted in 5/6 cases at F/U. Erythroid dysplasia persisted in 5/7 cases, and platelet dysplasia resolved in 4/5 cases. One case acquired PB blasts at F/U.

Conclusions:

- Blast percentage decreased in both the PB and BM after treatment with HMAs.
- BM cellularity decreased with HMA therapy.
- There was no statistically significant difference in WBCs, PLTs, or Hgb, pre- or post HMA therapy.
- The most common morphologic changes observed were loss of erythroid and platelet dysplasia in the PB.

Data Collection:

WBC, RBC, and PLT values at PTx and FU were collected.

Clinical Characteristics:

- 13 MDS patients (7 women) aged 35-79 yrs met inclusion criteria.
- The types of MDS represented were: 6 therapy-related MDSs, 4 MDS-unclassified, 2 RAEBs, and 1 RCMD.
- Median PTx and FU CBC data is provided in Table 1. Median time between PTx and FU analysis was 115 (44-507) days. Median time between completion of HMA therapy and FU analysis was 30 (9-257) days. 4 patients were still on therapy at time of FU.

Morphologic changes observed in Table 1:

- Peripheral blood:
  - PB blasts were present in 4/13 cases at PTx (≥4%, median 1%) and resolved in 4/5 cases at F/U.
  - Granulocyte dysplasia was present in 5/13 PTx cases; persisted in 5/5 cases and resolved in 2/5 at F/U.
  - Erythroid dysplasia was present in 7/13 PTx cases; resolved in 5/7 cases and persisted in 2/7 at F/U.
  - Platelet dysplasia resolved in 4/5 cases at F/U.
- Bone marrow:
  - BM blasts were 3% (1-12%) PTx vs. 1.6% (0-14%) at F/U (p=0.06).
  - Average BM cellularity was 61% (≥5-100%) in PTx and 29% (≥5-75%) in F/U (p=0.009) (Figure 1A-B).
  - Granulocyte dysplasia persisted in 5/6 cases at F/U.
  - Erythroid dysplasia persisted in 5/6 cases at F/U (Figure 1C).
  - Megakaryocyte dysplasia persisted in 5/6 cases at F/U (Figure 1D).
  - BM blasts were 3% (1-12%) PTx vs. 1.6% (0-14%) at F/U (p=0.06).
- BM cellularity decreased with HMA therapy.
- There was no statistically significant difference in WBCs, PLTs, or Hgb, pre- or post HMA therapy.
- The most common morphologic changes observed were loss of erythroid and platelet dysplasia in the PB.
- Despite overall decreased blast counts and BM cellularity, granulocyte, megakaryocyte, and erythroid dysplasia persisted in the marrow in the majority of cases.
- Stromal degeneration and fibrosis can occur, but are uncommon findings post-therapy.