Case report: Systemic mastocytosis with associated clonal hematological non-mast cell lineage disease; refractory anemia with ring sideroblasts associated with marked thrombocytosis.

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Background

- Systemic mastocytosis (SM) is a myeloproliferative neoplasm (MPN) characterized by infiltration of neoplastic mast cells into one or more organ systems.
- SM with associated clonal hematological non-mast cell lineage disease (SM-AHNMD) is diagnosed when criteria for SM and a second hematopoietic neoplasm are concurrently met.
- Myelodysplastic syndrome (MDS), MPN, Acute myeloid leukemia and Acute lymphoid leukemia are described in SM-AHNMD. A case of SM-AHNMD with refractory anemia with ring sideroblasts associated with marked thrombocytosis (RARS-T) has never been reported.
- RARS-T is currently a provisional diagnosis, described as having overlapping features of MDS and a BCR-ABL(-) MPN.
- In the next WHO update, RARS-T will be included as a subtype of MDS/MPN due to the strong association of SF3B1 mutation, present in 80% of cases.

Case presentation

- Otherwise healthy 64-year-old male with chronic thrombocytosis and 3 year history of pruritic rash.
- JAK2 V617F(+), BCR-ABL1(-)
- Nutritional deficiencies and liver disease were ruled out.
- Suspected MPN, MDS, or MDS/MPN

Case findings

Physical Exam:
- Widespread urticaria pigmentosa rash
- Mild splenomegaly

Laboratory results:
- Thrombocytosis
- Macrocytic anemia
- Elevated LDH and serum tryptase levels
- KIT D816V(+)

Histologic findings

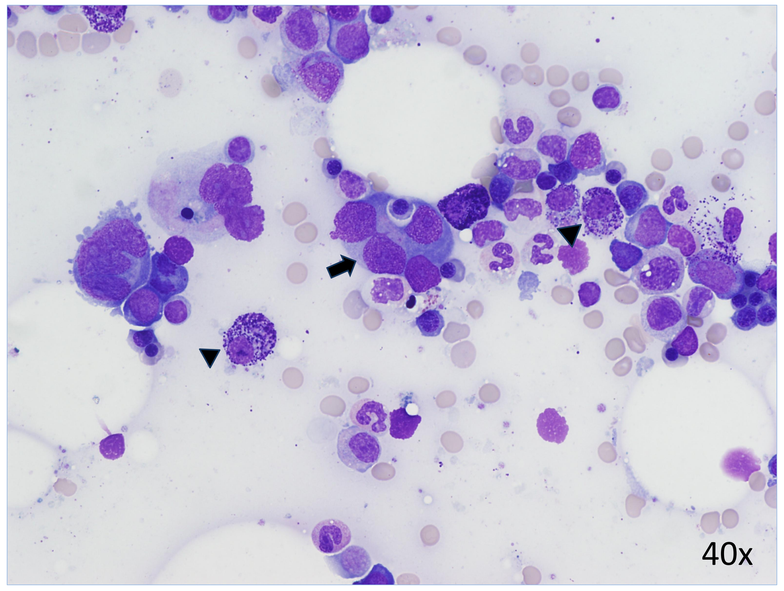

Figure 1. Giemsa-stained bone marrow aspirate showing prominent erythroid dysplasia (arrow), and marked mastocytosis with unusual hypogranulated morphology (arrowhead).

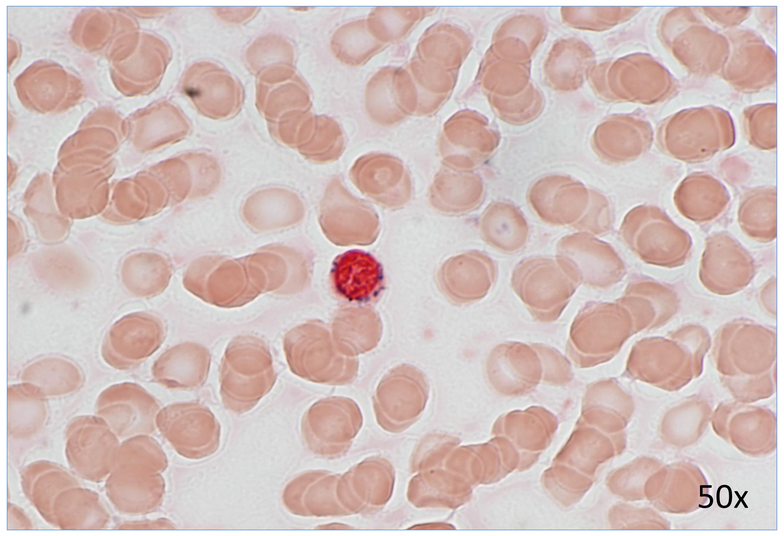

Figure 2. Bone marrow aspirate stained with Prussian blue demonstrates 15% ring sideroblasts.

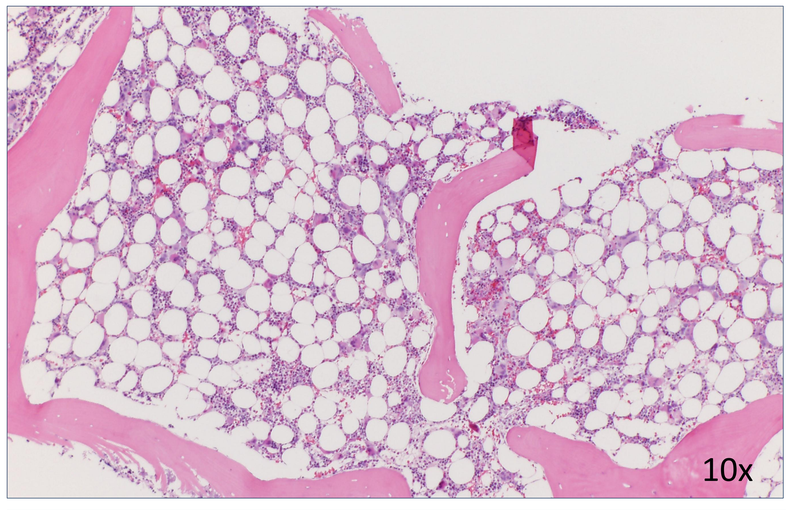

Figure 3. H&E stained trephine biopsy with increased numbers of large, clustered megakaryocytes.

Histologic findings

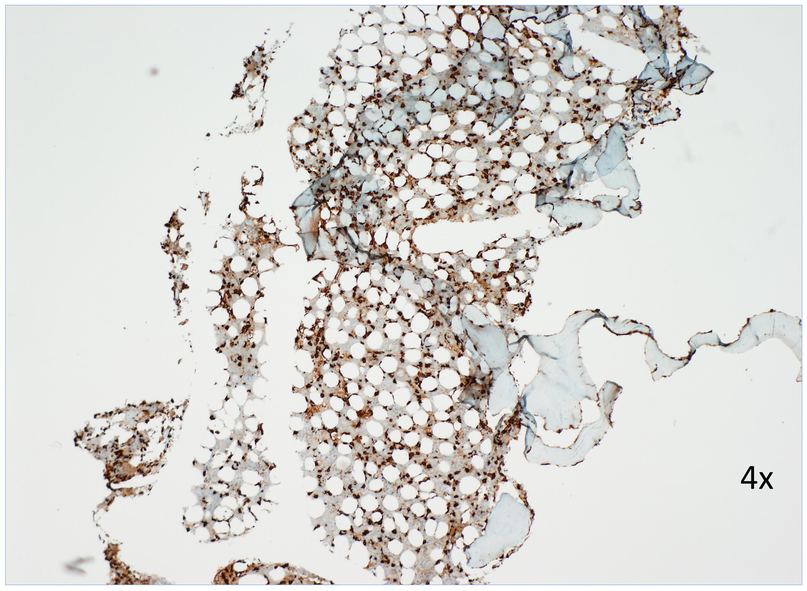

Figure 4. IHC for tryptase highlighting mast cell proliferation in bone marrow.

Next-generation sequencing

Data were aligned to the human reference genome and processed using best-practices guidelines. Only variants below a 1% allele frequency in any population, with an estimated somatic allele frequency above 2% and with a read depth greater than 500 bp, and with a functional impact on the protein or a known clinical association were kept in the analysis. Thirteen SF3B1 sequence variants were identified, including the Lys666Glu mutation with a somatic allele frequency of 2.8%.

Conclusion

- To our knowledge this is the first reported case of SM-AHNMD; RARS-T
- The upcoming edition of the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues places a greater emphasis on molecular testing.
- Our case lacks the major diagnostic criterion for SM, namely dense infiltrates of mast cells. The SM diagnosis was based on minor diagnostic criteria alone.
- Mutations in the JAK2, KIT, and SF3B1 genes supported the diagnosis.