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Acute Myelomonocytic Leukemia with Tetrasomy 8: Histologic and Immunophenotypic Features Mimicking Acute Promyelocytic Leukemia

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Introduction
The acute myeloid leukemias (AMLs) are a group of diseases representing clonal proliferations of hematopoietic precursors which typically involve the bone marrow and peripheral blood. Acute myelomonocytic leukemia (AMML) is a type of leukemia in which the sum of myeloblasts, monoblasts, and promonocytes is 20% or more. Trisomy 8 is one of the most frequent numerical chromosomal abnormalities observed in myeloid neoplasms, including AML and myelodysplastic syndrome (MDS). Tetrasomy 8 is a rare cytogenetic abnormality reported in only a few cases, mainly AML of monocytic lineage. Herein, we describe a unique case of a patient with AMML with tetrasomy 8 and with morphologic and immunophenotypic features mimicking acute promyelocytic leukemia (APL).

Patient
The patient is a 63-year-old African American man who initially presented with loosening of left upper molar teeth with gingival swelling. He was diagnosed with an infection of the tooth and was placed on antibiotics. He showed no improvement in his symptoms and presented to another hospital with his tooth symptoms and dull, non-radiating chest pain. CBC was performed and showed marked leukocytosis (143.2), anemia (Hgb 9.5, Hct 28.5), and severe thrombocytopenia (14). The patient was transferred to the GW University Hospital for further management. A bone marrow aspirate and biopsy was performed. Aslo, aspirate sample was also sent for cytogenetic and molecular analysis.

Peripheral blood smear
Examination of the peripheral blood smear (Fig. A) revealed a marked increase in white cells, with approximately 40% small to medium size classical blast forms (Fig. B) with round nuclei, fine chromatin, small nucleoli, and a minimal amount of cytoplasm. Approximately, 40% of the white cells were slightly larger in size and exhibited a small to moderate amount of cytoplasm with a variable number of cytoplasmic granules (Fig. C). Approximately 10% of the white cells exhibited abundant cytoplasm and large primary-type cytoplasmic granules typical of promyelocytes (Fig. D). The remaining white cells consisted of lymphocytes, monocytes, and a small number of mature neutrophils. Platelets were markedly decreased in number and qualitatively unremarkable.

Bone Marrow
The bone marrow aspirate showed 30-40% blasts morphologically similar to those in the peripheral blood (Fig. E). The remaining approximately 50% of marrow elements consisted of immature precursors with fine chromatin, nucleoli, and moderate to abundant cytoplasm exhibiting a variable number of cytoplasmic granules (the granules varying from small to large in size), resembling promyelocytes of standard and microgranular types. Essentially no mature neutrophils were identified. Cytochemical stains performed on the aspirate showed alpha naphthyl butyrate esterase and Sudan Black positivity in approximately 10-20% and 20-30% of immature precursors, respectively (Fig. F, G).

Flow Cytometry and FISH studies
Flow cytometry showed a dominant population of classical blast-like cells (with dim CD45 expression and low side light scatter) representing approximately 80% of all flow events. The dominant population showed expression of CD33 and CD56, with subsets also showing expression of CD11b, CD13, and CD64; however, the blast were negative for HLA-DR, CD34 and CD117. FISH analysis of the bone marrow aspirate showed a subset of cells exhibiting tetrasomy 8. FISH analysis was negative for PML/RARA rearrangement and other common myeloid leukemia-associated abnormalities.

Discussion
The morphologic features of the leukemic cells were suggestive of APL and some of the immunophenotypic features, particularly absence of HLA-DR and CD34 expression, supported this subtype. A few of the features, however, were unusual for APL, including the low side light scatter by flow cytometry, the presence of CD11b expression, and absence of CD117 expression. Further studies on the bone marrow aspirate showed a subset of blasts positive for butyrate esterase and Sudan black.

References

Histology and Immunohistochemical stains

Discussion
Immunophenotypically, a subset of the blasts showed expression of CD11b, CD13, and CD64. FISH was positive for tetrasomy 8 and negative for PML/RARA rearrangement. The overall findings were ultimately consistent with AMML with tetrasomy 8, which carries a poor prognosis3. Tetrasomy 8 is a rare chromosomal abnormality which has been reported in AML with monocytic lineage2. In the present case, AMML with tetrasomy 8 morphologically and immunophenotypically mimicked APL. The treatment and prognosis of these subtypes of AML are significantly different. This case illustrates the importance of thorough bone marrow evaluation, careful assessment of immunophenotype, and FISH and/or cytogenetic analysis in determining the accurate diagnosis of AML subtypes.

Images

- Aspirate
- Bone Marrow
- Flow Cytometry and FISH studies
- Discussion

- Histology and Immunohistochemical stains

- Images of microscopic slides showing different stains and their respective magnifications.