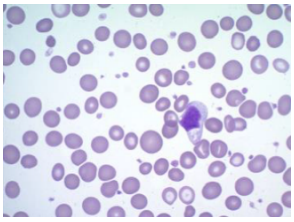
Myelodysplastic Syndrome Ruled Out For T-Cell Large Granular Leukemia

Case reviewed by Demetrios Braddock, MD PhD, Associate Professor of Pathology, Yale School of Medicine

Abstract:
An 80-year-old male patient with a history of a Myelodysplastic Syndrome (MDS) presented with anemia and pancytopenia. His oncologist obtained a peripheral blood specimen to send to Precipio for an Omnia™ comprehensive assessment. The case was assigned to Dr. Demetrios Braddock, Hematopathologist at Yale. Upon review of morphology, Dr. Braddock found scattered abnormal large lymphocytes with azurophilic cytoplasm as well as an abnormal population of T-cells with no expression of CD4 or CD8 by flow cytometry. These findings raised the concern for a T-cell Large Granular Lymphocytic Leukemia later confirmed by the detection of an abnormal T-cell rearrangement clone by molecular studies.
Dr. Braddock did not see signs of the previously reported myelodysplastic syndrome (MDS) but instead reached a final diagnosis of T-cell Large Granular Lymphocytic Leukemia (T-LGL).

Methods:
Morphologic assessment of the peripheral blood smears showed the presence of occasional, large lymphocytes with abundant, azurophilic cytoplasmic granules.



Occasional large granular lymphocyte

Flow cytometry detected an abnormal T-cell population that was positive for CD56 and CD57, with minimal expression of CD4 and CD8. Furthermore, this T-cell subpopulation expressed the T-cell gamma/delta receptor. Dr. Braddock requested molecular studies for T-cell gene rearrangement. The results showed that there was a clonal T-cell receptor gene rearrangement.

Results:
The detection of a clonal T-cell receptor gene rearrangement alone without morphologic and immunophenotypic correlation is not indicative of a malignancy as it can be found in healthy individuals. Additionally, the abnormal T-cell population detected by flow could have also been related to the patient's reported history of MDS.

This case benefited from the comprehensive testing approach of Omnia™; the expert review of the morphology correlating the findings in flow cytometry and molecular studies to rule out the presence of a myelodysplastic syndrome per the patient's history and confirm the diagnosis of a T-cell Large Granular Lymphocytic Leukemia.

Key Highlights:
- Due to clinical history, oncologist suspected MDS when patient presented with anemia and pancytopenia.
- Through Omnia™, Precipio's comprehensive assessment and testing algorithm, the pathologist correlated flow findings and abnormal lymphocytes with azurophilic cytoplasm identified by morphology to question the suspected initial diagnosis.
- Pathologist ordered T-cell gene rearrangement studies to confirm T-cell Large Granular Leukemia (TLGL)
- The results of these studies combined with morphology and flow led the pathologist to final diagnosis of a rare TLGL.

Clinical Implications:
About 25% of myelodysplastic syndromes have a high-risk of turning to acute myeloid leukemia in the absence of treatment[1,2]. T-cell Large Granular Lymphocytic Leukemia on the other hand follows an indolent clinical course in the majority of cases. The pathologist's ability to identify and correlate the laboratory results and rule out the initial suspicion of myelodysplastic syndrome avoided the need for unnecessary aggressive treatment for MDS and guided the oncologist to place the patient on the appropriate treatment plan.

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Final diagnosis provided by: Demetrios Braddock, MD, PhD
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1 Swerdlow, Steven H., et al. **WHO classification of tumours of haematopoietic and lymphoid tissues.** International Agency for Research on Cancer, 2017, pp 98.
2 Germing, Ulrich.,et al. **Myelodysplastic Syndromes: Diagnosis, Prognosis, and Treatment**. Dtsch Arztebl Int 2013; 110(46): 783-90; DOI: 10.3238/arztebl.2013.0783

