

Proprietary IV-Cell Culture Media Enabled the Diagnosis of Acute Leukemia

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

Abstract:

A 75-year-old male was diagnosed with chronic lymphocytic leukemia 8 years ago and subsequently diagnosed with a gastrointestinal diffuse large B-cell lymphoma. The following year, he presented with a rapidly progressive pancytopenia and retroperitoneal lymphadenopathy. Suspecting CLL or DLBCL, a bone marrow biopsy was collected and sent to Precipio for diagnosis.

Methods:

Omnia™ comprehensive assessments took into account the patient's history to determine the best course of testing. Given the patient's history of CLL and DLBCL, a panel of tests primarily aimed at detecting lymphoid disorders was performed. The patient's cells were cultured using Precipio's proprietary IV-Cell cytogenetics media, enabling the culturing of all four hematopoietic cell lineages simultaneously. Due to its versatility, IV-Cell minimizes unsuccessful cultures and inefficient use of limited specimen.

Cytogenetic chromosomal analysis is a cornerstone in the diagnosis of acute leukemia. Performing accurate cytogenetic analysis or karyotyping using conventional cytogenetic culture media depends on the accuracy of the submitted clinical indication in order to determine the necessary stimulants for the correct cell lineage to be cultured and analyzed. However, the clinical indication is not always accurate and often times the final diagnosis is divergent from the initial indication. Precipio's IV-Cell media is designed to ensure timely and accurate karyotyping results for clinicians irrespective of the submitted indication.

Results:

Flow cytometry and morphologic analysis identified an increase in blasts (>30% of total cellularity), immature myeloid cells, raising the concern of an acute myeloid leukemia. With this new information, the cytogenetics team was able to focus the cell culturing on myeloid cells rather than lymphoid cells. While other labs would have cultured the cells with a media that selectively stimulates the B-lymphocytes only, Precipio's IV-Cell media allows all four lineages to be stimulated simultaneously, allowing the culture to be maneuvered given the new information from flow cytometry.

The resulting chromosome analysis of the patient showed an abnormal male karyotype with complex cytogenetic abnormalities including a deletion of 5q, loss of chromosome 7, 11, & 18, which are associated with myeloid malignancies. Such complex karyotypes are usually associated with acute myeloid leukemia with a poor prognosis. Thus karyotyping was able to detect abnormalities of the myeloid lineage cells despite the initial workup of the case being focused on detecting lymphoid disorders.

Additionally, FISH results showed an abnormal clone with MLL rearrangement involving cells analyzed with probes specific for recurrent abnormalities in Acute Myeloid Leukemia.

The final diagnosis was Acute Myeloid Leukemia with complex cytogenetic abnormalities including amplification of a variant MLL rearrangement (11;22).

Key Highlights:

- Precipio's Omnia™ assessment took into account patient's past history but was not limited by it
- Initial tests identified an increase in blasts, indicative of an acute leukemia, unrelated to the patient's history
- Proprietary IV-Cell cytogenetics media allowed the lab team to maneuver the culture at Dr. Braddock's instructions to be able to analyze the myeloid cells for chromosomal abnormalities as opposed to lymphoid cells initially suspected from patient's history
- Critical chromosomal abnormalities confirmatory of acute leukemia were identified which would have otherwise been missed because of the use of IV-Cell.

Clinical Implications:

Using conventional cytogenetic media, which would have limited the analysis to only one cell type. Another lab would have missed reporting on the abnormal myeloid cells' karyotype, given their culture would have been stimulated for B-cell growth only due to the submitted indication.

According to the 2016 College of American Pathologists guidelines, cytogenetic analysis is a critical component in the initial diagnosis of acute leukemia¹, as it provides prognostic indicators as well as classification of the leukemia. The use of Precipio Inc.'s proprietary IV-Cell media allowed for the abnormal cells to still be captured, gaining valuable information to facilitate the accurate karyotype results.

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¹ Arber DA, Borowitz MJ, Cessna M, et al. **Initial Diagnostic Workup of Acute Leukemia: Guideline From the College of American Pathologists and the American Society of Hematology.** Archives of Pathology & Laboratory Medicine. 2017;141(10):1342-1393. doi:10.5858/arpa.2016-0504-cp.