Incidental Absolute Leukocytosis

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Clinical History

An otherwise healthy 73-year-old Caucasian man presents for a routine physical. Review of systems is negative.

A CBC was obtained and reveals a leukocytosis with an absolute lymphocytosis. Peripheral blood smear review and flow cytometry were performed.
Peripheral Blood Smear
Peripheral Blood Smear
Peripheral Blood Smear Description

At low magnification, we note the presence of leukocytosis comprised of small to medium sized lymphocytes. At higher magnification, the lymphocytes have very round nuclei have condensed “soccer ball”- like chromatin, lack nucleoli, and have scanty cytoplasm. Smudge cells are noted.
Flow Cytometry
Question #1

Which of the following sentences is true concerning the data from the flow cytometry?

A. The results show polyclonal B-cell population as seen by the 4:1 kappa:lambda ratio.
B. The cell population of interest is dimly CD20+
C. The cell population of interest are the red blood cells
D. Roughly 84% of the cells are CD19 negative
Question #1 Answer and Rationale

Correct Answer: Choice B – the cell population of interest is dimly 20+

The purpose of this question is to reinforce how to interpret flow cytometry scatter plots and remember the antigens commonly expressed on the different leukocytes. In the CD19 vs CD5 plot, we notice that the proportion of CD19+ B-cells is markedly skewed (85%) with respect to normal (up to 20%). This suggests that there is probably a neoplastic proliferation of B-cells and, thus, choice B is correct.

Choice A is incorrect as the lower left flow cytometry graph shows a kappa:lambda ratio of 0.07:86.12 (= 0.00086). Choice C is incorrect as red blood cells are lysed before routine flow cytometry is performed. Finally for D, ~84% of cells are CD19+, so this statement is false.
Question #2

Smudge cells appear in which of the following disease processes?

A. Bordetella Pertussis
B. Hairy Cell Leukemia
C. Atrial Fibrillation
D. Ehlers-Danlos Syndrome Type III
Correct Answer: Choice A – Bordetella Pertussis

While smudge cells are most famously associated with chronic lymphocytic leukemia (CLL), they can also appear in other disease states in which there is a lymphocytosis, such as infectious mononucleosis, pertussis, and in other lymphomas/leukemias. Hairy cell leukemia characteristically shows hairy cell projections, so choice B is incorrect. For C, atrial fibrillation is not related to white cells. For D, Ehlers-Danlos syndrome Type III describes a problem producing collagen, with symptoms being hypermobility and pain. Collagen is an extracellular material. One of the elements associated with smudge cell formation, however, is vimentin content. Vimentin is a intermediate filament and is found inside the cell, and low amounts of it results in more smudge cells.
Question #3

Which of the following genetics confers a favorable prognosis in this malignant neoplasm?

A. Deletion 17p13.1  
B. Deletion 11q22.33  
C. Trisomy 12  
D. Deletion 13q14
Question #3 Answer and Rationale

Correct Answer: Choice D – deletion 13q14

To answer this question correctly, you must be able to correctly identify the characteristic immunophenotype of CLL in the flow cytometry scatter plots [CD5+, CD19+, dim CD20+, CD23+, dim surface lambda light chain+]. Choice D is correct, as those with a 13q14 deletion have a median survival of 133 months. CLL patients with a normal cytogenetic status have a median survival of 111 months. For A and B answer choices, 17p13.1 and 11q22.3 deletions have the worst prognosis, with a median survival of 32 months and 79 months, respectively. Trisomy 12 is considered an intermediate prognostic marker, making choice C incorrect.
CLL/SLL

- A chronic lymphoproliferative disorder, chronic lymphocytic leukemia (CLL) is characterized by an increased population of mature monoclonal B-cells lymphocytes; small lymphocytic lymphoma (SLL) and CLL are identical diseases, with SLL presenting with lymphadenopathy and CLL presenting in the peripheral blood.

- The molecular pathogenesis of CLL is complex, and many steps are still unknown.

- Most patients are male, over the age of 50, and often asymptomatic, but may present with fatigue, weight loss, anorexia, generalized lymphadenopathy, and hepatosplenomegaly.

- CLL/SLL is diagnosed using a combination of morphologic and immunophenotypic evaluation. The morphologic evaluation can be undertaken in peripheral blood and/or lymph node specimens. Immunophenotypically, CLL/SLL is positive for CD5 and CD23 and shows reduced intensity of CD20, surface light chain, and FMC-7 expression.

- CLL/SLL has a tendency to transform to more aggressive lymphoid neoplasms, such as diffuse large B-cell lymphoma (Richter’s syndrome, ~10% of patients).

- Patients are grouped by the Rai and Binet staging systems which are based on physical exam and CBC findings.

- Not all patients diagnosed with CLL require treatment at time of diagnosis, and which treatment chosen depends on the stage and cytogenetic classification. For localized SLL, involved-field radiation therapy is preferred over systemic chemotherapy or watchful waiting, while symptomatic or advanced stage SLL treatment is aimed towards symptom improvement and improving survival.

- As previously discussed, the survival varies substantially with a median overall survival of ~10 years.
Bibliography


