PathMD™: Board Review Letter

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Case #1 An absolute leukocytosis was identified in a 71-year-old African-American male admitted to the hospital for an elective knee replacement. Based on the flow cytometry findings, what is the best diagnosis?

A. Reactive lymphocytosis
B. Monoclonal kappa CLL
C. Monoclonal lambda CLL
D. Biclonal CLL
E. Mantle Cell Lymphoma

Answer: D. Biclonal CLL. CLL has a characteristic immunophenotype with dim surface light chain expression, weak CD20 (usually), CD5, CD19, and CD23 positivity. By definition, <55% of the lymphocytes are prolymphocytes, and there is a lymphocytosis of at least 5,000/μL. FMC7 is negative. Rare well described cases have shown a biclonal leukemic cell population manifested by both separate kappa and lambda positive populations, as illustrated in this case. The key to evaluating this case is realizing that there is an abnormal population of lymphocytes coexpressing CD5 and CD23, which can only be accounted for by both the dim kappa and lambda positive populations. (Hsi, p. 798-803) In contrast, mantle cell lymphoma shows bright CD20 with coexpression of CD5 and bright light chain expression. CD23 is characteristically negative. FMC7 is usually positive. FMC7 detects a conformational epitope on the CD20 molecule. In CLL CD20 is weak and therefore the FMC7 expression is not seen. When the CD20 expression is brighter, as in mantle cell lymphoma, FMC7 positivity is more common.

Case #2 Several subcutaneous nodules were found in the axillary region of a 59-year-old male. Representative histologic images and special stains are shown. Based on these findings, which of the following is the best diagnosis?

A. Merkel cell carcinoma
B. Diffuse large B cell lymphoma, leg type
C. Subcutaneous panniculitic T-cell lymphoma
D. Granulocytic sarcoma
E. Poorly differentiated carcinoma

Answer: D. Chloroma/Granulocytic Sarcoma/Myeloid Sarcoma. Acute leukemia can sometimes present initially in the skin or other non-hematopoietic location. Often the most common error is to mistake this as lymphoma and not recognize it as leukemia. Lysozyme, CD34, myeloperoxidase, and CD 117 may be positive in acute leukemias. It is important to remember that these stains are not entirely specific, and must be interpreted in the overall context with a properly selected immunohistochemical panel.

Case #3 A splenectomy was performed in a three-year-old female. The spleen is approximately twice the normal size when adjusted for age. Based on the histologic findings shown for this case, which the following is the best diagnosis?

A. Autoimmune hemolytic anemia
B. Immune thrombocytopenia purpura
C. Sickle cell disease
D. Metabolic storage disease
E. Felty's syndrome

Answer: C. Sickle Cell Disease of the spleen. Sickle cell anemia results in sequestration of erythrocytes in the red pulp and chronic hypoxic organ damage. In childhood splenomegaly is present secondary to erythrocyte sequestration. 30% of infants and young children may have a sequestration crisis in the spleen. Splenectomy is sometimes performed in these patients because of recurrence risk of a sequestration crisis. As patients with sickle cell disease get older, they undergo an autosplenectomy from repeated infarcts. This process is characterized early on by the finding of Gamna-Gandy bodies, which are fibrotic nodules with iron and calcium deposition and possibly foreign body giant cells. (Neiman, pages 148-153)

Case #4 A submandibular mass has been noted for several months in a 40-year-old female patient. A FNA was performed with flow cytometry, which was negative for a monoclonal lymphoid population. A surgical excision of the lesion was performed and submitted in formalin. Representative histologic sections are shown along with immunohistochemistry. Based on the findings and clinical history, which of the following is the best diagnosis?

A. Follicular lymphoma
B. Reactive lymphoid hyperplasia
C. Castleman's disease
D. Kimura's disease
E. Marginal zone lymphoma

Answer: A. Low grade follicular lymphoma can be challenging to differentiate from a reactive lymph node. In this case the bcl-2 positivity is useful in differentiating a low grade follicular lymphoma from a reactive lymph node. Reactive germinal centers are negative for bcl-2 (bcl-2 is anti-apoptotic) while the surrounding cells in the mantle zone are positive. In follicular lymphoma the BCL2 gene is translocated to be next to the IgH gene, which results in upregulation of bcl-2 (hence the positivity). The important point to remember about bcl-2 expression is that it is not limited to follicular lymphoma, and is expressed in many other lymphomas. Bcl-2 staining is really only helpful diagnostically when differentiating between reactive and low grade follicular lymphoma.

Case #5 An isolated orbital mass present for several months was found in a 55-year-old female. A surgical excision was performed, and flow cytometry showed a CD20 positive, CD5 and CD10 negative, lambda restricted lymphoid cell population. Cytogenetic showed a t(14;18)(q32;q21) translocation. Representative histologic images for this case are shown along with selected immunohistochemistry. Which of the following is the best diagnosis?

A. Follicular lymphoma
B. Marginal zone lymphoma
C. CLL/SLL
D. Mantle cell lymphoma
E. Cannot be conclusively determined based on the given information

Answer: A. Follicular lymphoma (23% of cases) is second only to marginal zone lymphoma (52% of cases) in incidence as an etiology of ocular lymphomas. Ocular lymphomas represent approximately 8% of extranodal lymphomas. In this case, the differential diagnosis is between follicular and marginal zone lymphoma. The initial flow cytometry was consistent with a marginal zone lymphoma (no CD10 expression), but the cytogenetics makes one think of a follicular lymphoma. Actually, t(14;18)(q32;q21) can be seen in both follicular and marginal zone lymphomas. The follicular lymphoma translocation involves IgH/BCL2 while the marginal zone lymphoma translocation involves IgH/MALT1. Distinction between

these two translocations cannot be determined on routine cytogenetics. Interestingly, t(14;18) and t(3;14) are very common translocations in ocular marginal zone lymphomas. Therefore, given the information in the flow cytometry cytogenetics, the most likely diagnosis would be marginal zone lymphoma. However, the bcl-6 positivity in the image defines the lesion as follicular in origin and makes the correct diagnosis follicular lymphoma (CD10 would also establish the lesion as being follicular in origin). (Ferry, JA, pages 170-184)

Case #6 An osmotic fragility test was performed on the blood specimen from a 45-year-old patient who has a microcytic anemia (MCV = 73, RBC = 3.8 x 10^6/mL, Hb = 11.0 g/dL, & Hct. = 33.4%). Based on these laboratory values and the findings on the osmotic fragility test, what is the most likely diagnosis?

A. Hereditary spherocytosis
B. Iron deficiency anemia
C. Alpha thalassemia
D. Beta thalassemia
E. All of the above are diagnostic possibilities

Answer: A. The osmotic fragility test shows a shift to the left, which means the erythrocytes have a decreased ability to expand in a hypo-osmotic environment. Hereditary spherocytosis shows a shift to the left on the osmotic fragility diagram because the cells will lyse in a minimally hypo-osmotic environment (0.9% NaCl is approximately iso-osmotic). A shift to the right can be seen in conditions that have an increased surface to volume ratio such as thalassemias and iron deficiency anemia, which can tolerate a more hypo-osmotic environment. (Kjeldsberg, pages 100-102)

Question #1 Which of the following leukemias is least commonly associated with abnormalities involving chromosome 11q23?

A. AML secondary to topoisomerase II inhibitors
B. ALL
C. AML-M5a
D. AML-M5b
E. AML-M2

Answer: E. AML-M2 is most commonly associated with t(8;21), which is a better prognosis.. Answers A-D are all associated with abnormalities involving 11q23 (MLL gene), which is associated with a poor prognosis. (Kjeldsberg, pages 484-487)

Question #2 Examination of a lymph node shows extensive infiltration by macrophages with foamy cytoplasm. Staining with PAS, shows diastase resistant material. AFB stain is negative. Which of the following answers would be the best diagnosis:

A. MAI
B. Syphilis
C. Rosai-Dorfman
D. Toxoplasmosis
E. Whipple's disease

Answer: E. Whipple's disease is caused by bacillary organisms (Tropheryma whippelii), which fill the cytoplasm of histiocytes and stain with PAS, and are AFB negative. *Test taking strategy*. The following are important "catch" phrases for the other answers: MAI → AFB + histiocytes, Syphilis → Plasma cells, Roasi-Dorfman → Histiocytes with emperipolesis and perivascular plasma cells, and Toxoplasmosis → monocytoid B-cells.

Question #3 B-cell prolymphocytic leukemia is characterized by which of the following?

A. 1-10% prolymphocytes
B. 11-55% prolymphocytes
C. >55% prolymphocytes
D. > 75% prolymphocytes
E. None of the above

Answer: C. PLL is defined by >55% prolymphocytes. >10-55% is classified as CLL/PLL, and up to 10% is tolerated in CLL. (WHO, pages 127-130)

References:

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Notes for question set:[1]

[1] PathMD strives for the highest quality and accuracy. However, the *PathMD: Board Review Letter* is for review purposes and not meant for clinical decision making. It should not be used in place of review of primary reference texts and the current medical literature. If inaccuracies are identified, please notify us so that a correction may be published. (info@PathMD.com)

