PathMD™: Board Review Letter

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Case #1 Image for this case shows a positive fusion probe by FISH. Based on the image and associated information, what is the best diagnosis?

A. AML-M2
B. AML-M3
C. AML-M5
D. CML
E. Precursor B ALL

Answer: B. The image for this case illustrates a fusion probe by FISH for the t(15;17) PML:RARA which is the defining feature of acute promyelocytic leukemia (AML-M3). *Test taking strategy.* While this question presents a fancy fluorescence image, it has no row bearing on answer the question. This is often the case in test questions.

Case #2 The images for this case come from a 56-year-old Hispanic male who presents an otolaryngologist with a nasal mass. A surgical biopsy was performed, and representative images including immunohistochemical stains are shown. Based on the morphology and special stains, what is the best diagnosis?

A. Plasmacytoma
B. Blastic NK cell lymphoma
C. Extranodal NK/T-cell lymphoma, nasal type
D. Wegener's granulomatosis
E. Diffuse large B cell lymphoma

Answer: C. Extranodal NK/T-cell lymphoma, nasal type is an aggressive T-cell lymphoma is characterized by an angiocentric and angiodestructive process. There are often large areas of necrosis, and the malignant cells can usually be found around vessels. When the process is prominent and the malignant cells are difficult to find, Wegener's granulomatosis may sometimes be misdiagnosed. Most cases are EBV and CD56 positive. In addition, CD2 and cytoplasmic CD3 are positive. Other T-cell markers including surface CD3, CD4, CD5, CD8, and CD57 are usually negative. Occasional cases may be positive for CD7 or CD30. Most cases are positive for cytotoxic enzymes (granzyme-B, TIA-1, and perforin). In fact, the diagnoses should not be made in the absence of EBV or cytotoxic enzyme positivity. Those cases should be diagnosed as peripheral T-cell lymphoma, unspecified. (WHO, pages 204-207)

Case #3 The images of peripheral blood and a bone marrow biopsy come from a 25-year-old African-American female who presents with a WBC of 65, 000, which is composed of 90% neutrophils. The patient complains of B symptoms, but after extensive work of no infectious theology is found. Appropriate cytogenetic, FISH, and PCR studies were performed with no abnormalities. A bone marrow biopsy was performed and revealed no evidence of abnormal maturation in any of the hematopoietic lineages. The patient has a normal hemoglobin, in the monocytes are $<1x10^{9}$. Based on these findings, was most likely diagnosis?

A. Leukamoid reaction
B. Chronic myelogenous leukemia
C. Chronic neutrophilic leukemia
D. Atypical chronic myelogenous leukemia
E. Myelodysplastic syndrome, unclassifiable

Answer: C. This is a case of chronic neutrophilic leukemia in which all secondary causes were excluded. It is important to rule out a t(9;22) -- BCR:ABL translocation for CML. Most cases of chronic neutrophilic leukemia (90%) have no cytogenetic abnormality. Atypical chronic myelogenous leukemia would be considered in the differential diagnosis if dysplasia were present. Most cases of MDS present with peripheral cytopenias. Chronic neutrophilic leukemia is a diagnosis of exclusion. (WHO, pages 27-28)

Case #4 A 29-year-old African-American patient is found to have a peripheral eosinophilic count of 8000/microliter. The peripheral blood and bone marrow are shown for review. Conventional cytogenetics are normal, and appropriate FISH studies are normal. Flow cytometry was performed, and showed no monoclonal B-cell or aberrant T-cell population. Extensive allergy and infectious disease workup was negative. Based on these findings, what is the best diagnosis?

A. Chronic eosinophilic leukemia
B. Hypereosinophilic syndrome
C. Atypical chronic myelogenous leukemia
D. Chronic myelogenous leukemia
E. Cannot be determined with the given information

Answer: B. The best diagnosis for this case is hyper eosinophilic syndrome. The WHO classification combines chronic eosinophilic leukemia and hyper eosinophilic syndrome. The differentiating point between these two entities is proving clonality to diagnose chronic eosinophilic leukemia. This diagnostic category is exclusionary, in that allergic, infectious, and other neoplastic disorders (T-cell lymphoma, CML, MDS, etc.) must be excluded.

Follow-up question Based on the answer for case #4, what is the most important follow-up test?

A. Conventional cytogenetics
B. FISH for BCR:ABL
C. FISH for FIP1L1:PDGR-alpha
D. Flow cytometry for abnormal expression of myeloid antigens
E. None of the above

Answer: C. Cases of chronic eosinophilic leukemia/hyper eosinophilic syndrome should have FISH studies performed for the FIP1L1:PDGF-alpha fusion on chromosome 4. Identification of this fusion connotes excellent response to low dose Gleivec therapy.

Case #5 The blood smear shown in this case comes from a 62-year-old male with a white count of 55,000. Based on the findings, what is the most likely flow cytometry immunophenotype?

A. Positive: CD19, bright CD20, CD5 Negative: CD10
B. Positive: CD19, dim CD20, CD5 Negative: CD23
C. Positive: CD19, bright CD20, CD23 Negative: CD5
D. Positive: CD19, dim CD20, CD5 Negative: CD10
E. Positive: CD19, bright CD20, CD23 Negative: CD10

Answer: D. The most likely diagnosis would be CLL/SLL. It has a classic immunophenotype by flow cytometry of CD19, dim CD20, CD5, and CD23 positive with dim surface light chain expression. Mantle cell lymphoma, in contrast, is CD19, bright CD20, and CD5 positive. It is negative for CD23. CD10 is a

germinal center marker in found in cases of precursor B-ALL, Burkett lymphoma, follicular lymphoma, and diffuse large B cell lymphoma most commonly.

Case #6 The bone marrow biopsy in this case comes from a 63-year-old male is found to have a monoclonal IgM serum paraprotein. The patient had symptoms of hyperviscosity and received a plasma exchange. Flow cytometry the bone marrow aspirate showed positivity for CD19, CD20, CD22, CD79a, and CD38. The cells of interest were for negative for CD5, CD10, and CD23. Additional immunohistochemistry stains are shown in the images for this case. Conventional cytogenetics showed a translocation t(9;14)(p13;q32). Based on these findings was the most likely diagnosis?

A. CLL/SLL
B. Multiple myeloma
C. MALT lymphoma
D. Splenic marginal zone lymphoma
E. Lymphoplasmocytic lymphoma

Answer: E. This case represents lymphoplasmocytic lymphoma (LPL). LPL is classically associated with Waldenström macroglobulinemia and has an IgM paraproteinemia. LPL is a neoplasm of small-B lymphocytes, plasma cells, and plasmacytoid lymphocytes, and is usually negative for CD5 which helps to differentiate it from CLL/SLL. Other lymphomas including CLL, splenic marginal zone lymphoma, and MALT lymphoma may have an IgM paraprotein. Therefore, Waldenström macroglobulinemia is not exclusive to LPL, and these other lymphomas must be excluded when making the diagnosis of LPL. Translocation t(9;14)(p13;q32) has been characterized in significant number of LPL cases. (WHO, pages 132-135)

Question #1 In a normal 50 y/o adult, what is the expected bone marrow cellularity?

A. 10%
B. 25%
C. 50%
D. 75%
E. 100%

Answer: C. A 50 y/o adult can expect to have a bone marrow cellularity around 40-60%. A rough rule of thumb is expected cellularity = 100 – patients age. Infants ~100%; child, 60-80%; young adult, 50-70%; adult, 40-60%; elderly, 25-40%. (Foucar, K., *Practical Approach to Bone Marrow Examination;* 2005 CAP Meeting)

Question #2 Which of the following are individually specific markers used in flow cytometry analysis?

A. CD13
B. CD34
C. CD33
D. Both A and C are correct
E. All of the above are correct

Answer: D. CD13 and CD33 are myeloid markers, and CD34 is an immature marker. CD34 is not specific for lineage. *Test taking strategy.* This question is important to realize in what way and context the term specific is being used. It states the context is flow cytometry. Evaluating the answer, one could argue that

combined they are specific for a myeloblast. But the question is "individually" specific. CD34 alone is only a marker of immaturity.

Question #3 When examining a bone marrow core (trephine) biopsy, where should immature myeloid elements be localized?

A. Adjacent to boney trabeculae
B. Centrally, within the adipose tissue
C. Surrounding smaller caliber vessels
D. Both A and C are correct
E. All of the above are correct

Answer: D. Immature myeloid elements are found adjacent to bony trabeculae and smaller caliber vessels. As they mature they move more centrally within the hematopoetic compartment. {Foucar, K., *Practical Approach to Bone Marrow Examination;* 2005 CAP Meeting}

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)

