

Chronic Lymphocytic Leukemia: Review Questions

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QUESTIONS

Choose the single best answer for each question.

1. A 75-year-old woman is referred from her primary care physician with a leukocyte count of $34 \times 10^3/\text{mm}^3$ with 80% lymphocytes, hemoglobin concentration of 13 g/dL, hematocrit of 40%, and platelet count of $220 \times 10^3/\text{mm}^3$. A physical examination and computed tomography (CT) scan show no evidence of lymphadenopathy, splenomegaly, or hepatomegaly. She is asymptomatic. What is the most appropriate treatment for this patient at this time?

 - (A) Bone marrow transplantation
 - (B) Chlorambucil
 - (C) Chlorambucil and fludarabine in combination
 - (D) Hydroxyurea to eliminate the risk of leukostasis
 - (E) No treatment is indicated at this time
2. A 57-year-old man with a history of untreated stage I chronic lymphocytic leukemia (CLL) presents to the emergency department (ED) with a 1-week history of fatigue. He denies any trauma, melena, or hematemesis. His hematocrit is 14%, with a platelet count of $175 \times 10^3/\text{mm}^3$ and leukocyte count of $22 \times 10^3/\text{mm}^3$ with 68% lymphocytes. His chemistry profile is normal except for an elevated indirect bilirubin. A peripheral blood smear shows numerous spherocytes. His physical examination is unremarkable except for pallor. His most recent complete blood count (2 weeks earlier) revealed a hematocrit of 38%, a leukocyte count of $19 \times 10^3/\text{mm}^3$ with 70% lymphocytes, and a platelet count of $190 \times 10^3/\text{mm}^3$. What is this patient's most likely diagnosis?

 - (A) Autoimmune hemolytic anemia
 - (B) Progression to stage IV CLL with subsequent anemia from bone marrow replacement
 - (C) Pure erythrocyte aplasia
 - (D) Splenomegaly with splenic sequestration of erythrocytes
 - (E) Thrombotic thrombocytopenic purpura
3. A 65-year-old man has stage IV CLL, which was previously treated. Most recently, he was treated with alemtuzumab. One month after receiving alemtuzumab, he presents to the ED with a 1-week history of nonproductive cough, low-grade fevers, and progressive shortness of breath without prodromal symptoms. He lives in New Hampshire and has not traveled recently. He is tachypneic with an oxygen saturation of 85% on room air, hemodynamically stable, and has a temperature of 101.8°F. A chest radiograph shows a faint bilateral interstitial infiltrate. What is this patient's most likely diagnosis?

 - (A) Histoplasmosis
 - (B) Hypersensitivity pneumonitis from alemtuzumab
 - (C) *Pneumocystis carinii* pneumonia
 - (D) Pneumococcal pneumonia
 - (E) Pulmonary infiltration with CLL
4. A 56-year-old woman has stage I CLL characterized by cervical and axillary lymphadenopathy. She has never been treated. She presents to clinic complaining of a 2-week history of worsening fatigue but no other symptoms. On physical examination, a markedly enlarged right cervical lymph node is

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noted, while the remainder of her lymph nodes are unchanged from a previous examination. The oropharynx is slightly red, but the tonsils are normal and without exudate. Which of the following is the most appropriate diagnostic test?

- (A) Cervical lymph node biopsy
- (B) CT of the neck
- (C) Laryngoscopy
- (D) Monospot
- (E) Rapid test for streptococci

ANSWERS AND EXPLANATIONS

1. **(E) No treatment is indicated at this time.** This patient has stage 0 CLL, and no therapy is warranted. Early treatment of CLL has not been demonstrated to prolong survival compared with observation and delayed initiation of therapy.¹ Reasons to consider treatment include increasing symptoms (fatigue, night sweats, weight loss), a lymphocyte count that doubles in less than 6 months, significant anemia or thrombocytopenia, or symptomatic lymphadenopathy. When patients do need treatment, single-agent chlorambucil (an alkylating agent) or fludarabine (a nucleoside analog) both are appropriate, but there is a higher response rate with fludarabine. The combination of chlorambucil and fludarabine is relatively toxic, and the treatment arm of a trial that included this combination was closed early.² Patients with CLL rarely get symptomatic leukostasis, so hydroxyurea is almost never indicated. Bone marrow transplantation may cure a small percentage of patients with CLL, but this treatment is quite toxic and not appropriate as an initial therapy.
2. **(A) Autoimmune hemolytic anemia.** This case is most consistent with autoimmune hemolytic anemia, a known complication of CLL. The relatively rapid onset of symptoms and anemia, along with the presence of spherocytes on peripheral blood smear, are all consistent with autoimmune hemolysis. A direct Coombs test would establish the diagnosis. Prednisone is generally the initial therapy of choice. The anti-CD20 antibody, rituximab is an effective second-line therapy. Treatment of underlying CLL with chemotherapy is not necessary. Pure erythrocyte aplasia is a rare complication of CLL caused by the generation of autoantibodies against erythrocyte precursors. Unlike autoimmune hemolytic anemia, pure erythrocyte aplasia usually is indolent in onset. Idiopathic thrombocytopenic purpura is a complication of CLL but is unlikely in this case due to the minimal change in platelet count. Splenic sequestration is unlikely given the lack of a palpable spleen. Rapid progression of CLL is unlikely based upon the natural history of the

disease, the lack of progressive lymphadenopathy, and the lack of thrombocytopenia.

3. **(C) *P. carinii* pneumonia.** Alemtuzumab is an anti-CD52 monoclonal antibody that is approved for the treatment of relapsed CLL.³ Alemtuzumab also is a potent T-cell inhibitor and is associated with a very high risk of secondary infections including *P. carinii*, varicella zoster reactivation, and cytomegalovirus reactivation. Patients receiving alemtuzumab should be treated with prophylactic trimethoprim/sulfamethoxazole and acyclovir and should be monitored for cytomegalovirus reactivation. Patients with CLL are at increased risk for bacterial infections, such as sinusitis and pneumonia, as a result of disease-induced hypogammaglobulinemia and subtle defects in immune function. Despite this, pneumococcal pneumonia is less likely in this patient given the nonproductive cough and lack of a lobar infiltrate. Hypersensitivity pneumonitis can occur with any medication but does not occur this late after receiving alemtuzumab. Pulmonary infiltration from CLL is extremely rare. Histoplasmosis is unlikely given that this patient is from New Hampshire (an area of the country where histoplasmosis is not endemic) and has not traveled.
4. **(A) Cervical lymph node biopsy.** The rapidly growing lymph node and fatigue suggests Richter's transformation, the evolution of CLL to an aggressive lymphoma (most commonly diffuse large B-cell lymphoma). This phenomena occurs in up to 10% of patients with CLL.⁴ Lymph node biopsy would establish the diagnosis. The newly transformed lymphomas typically respond poorly to therapy, and most patients will die of their disease. The asymmetry of the lymphadenopathy and lack of pharyngitis makes strep throat and mononucleosis less likely. CT scans and laryngoscopy would be of little benefit.

REFERENCES

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