

Myeloma and Related Disorders: Review Questions

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QUESTIONS

Choose the single best answer for each question.

1. A 66-year-old man with cirrhosis comes to the primary care clinic because of back pain. He has had numerous falls because of his alcoholism. Radiographs show wedging of L4 and L5 vertebrae but no lytic lesions. Hematology and chemistry studies reveal a mild normochromic normocytic anemia. Bilirubin level is 1.2 mg/dL and aspartate aminotransferase, alanine aminotransferase, and alkaline phosphatase levels are normal. Albumin level is 2.8 g/dL and the globulin is 5.3 g/dL. A serum protein electrophoresis shows a polyclonal increase of gamma globulin. Which of the following is the most likely diagnosis for this patient?
 - (A) Myeloma
 - (B) Monoclonal gammopathy of unknown significance (MGUS)
 - (C) Either myeloma or MGUS
 - (D) Neither myeloma nor MGUS
2. A 57-year-old man is seen in the renal clinic for anemia, hematocrit of 34%, and proteinuria of 3 g/day. His creatinine level is 2.0 g/dL. Obtained as part of the work-up for renal failure, serum protein electrophoresis reveals a small monoclonal protein spike estimated as 0.2 g/dL. Urine protein electrophoresis is normal; the protein is all albumin with no monoclonal protein. Quantitative immunoglobulin results reveal: IgG, 1900 mg/dL (normal, 596–1744 mg/dL); IgA, 500 mg/dL (normal, 56–330 mg/dL); and IgM, 250 mg/dL (normal, 54–260 mg/dL). A bone marrow examination shows normocellular marrow with normal myeloid and erythroid maturation and approximately 5% plasma cells. No clumps of plasma cells are seen. Skeletal survey reveals no lytic lesions. Which of the following is the most likely diagnosis for this patient?
 - (A) Myeloma
 - (B) MGUS
 - (C) Either myeloma or MGUS
 - (D) Neither myeloma nor MGUS
3. A 50-year-old man presents to the emergency department for right hip pain. A radiograph reveals a lytic lesion of the right femur with impending fracture. He is sent to the operating room to have a pin placed in the femur. Biopsy of the lytic area shows sheets of plasma cells. History and physical examination are within normal limits except for the right hip. Laboratory studies include a hematocrit of 41%, a leukocyte count of $4.8 \times 10^3/\text{mm}^3$ with a normal differential, and a platelet count of $340 \times 10^3/\text{mm}^3$. Electrolytes, calcium and albumin levels, and results of renal and liver function studies are normal. A skeletal survey reveals no other lytic lesions. Bone marrow biopsy is normal. Serum protein electrophoresis reveals a monoclonal spike. Quantitative serum immunoglobulin levels are: IgG, 2400 mg/dL (normal, 596–1744 mg/dL); IgA, 500 mg/dL (normal, 56–330 mg/dL); and IgM, 250 mg/dL (normal, 54–260 mg/dL). Which of the following is the most likely diagnosis for this patient?
 - (A) Myeloma
 - (B) MGUS
 - (C) Either myeloma or MGUS
 - (D) Neither myeloma nor MGUS
4. A 50-year-old woman is evaluated for fatigue. Physical examination is unremarkable. She has a hematocrit of 31%, leukocyte count of $6.4 \times 10^3/\text{mm}^3$ with normal differential, platelet count of $210 \times 10^3/\text{mm}^3$, and 1.2% reticulocytes. Sodium, potassium, chloride, and bicarbonate levels are normal. Blood urea nitrogen is 50 mg/dL, and serum creatinine is 3.1 mg/dL. Albumin is 3.5 g/dL. Globulin is 2.6 g/dL. Calcium is 12.4 g/dL. Bilirubin and hepatic enzyme levels are normal. Serum protein electrophoresis is normal, but a urine protein electrophoresis shows a monoclonal spike identified as

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kappa chains. Quantitative serum IgG, IgA, and IgM results are normal. Skeletal survey shows lytic lesions in the right humerus, the right and left femur, and the skull. The bone marrow shows 60% plasma cells with many large clumps of plasma cells. The plasma cells are monoclonal and contain kappa light chains. Which of the following is the most likely diagnosis for this patient?

- (A) Myeloma
- (B) MGUS
- (C) Either myeloma or MGUS
- (D) Neither myeloma nor MGUS

ANSWERS AND EXPLANATIONS

1. **(D) Neither myeloma nor MGUS.** Despite the back pain and the abnormal radiograph, the key to the diagnosis in this case is that the increase in globulin is polyclonal. Polyclonal increases in globulin can occur in cirrhosis, the early stages of HIV infection, and in inflammatory disorders (eg, systemic lupus erythematosus). Both myeloma and MGUS, as indicated by the name, are associated with monoclonal elevations of either serum or urine gamma globulins (or light chains). While this case may seem to illustrate an obvious point, hematologists frequently are asked to see patients with polyclonal gammopathy to “evaluate for myeloma.”
2. **(B) MGUS.** In a patient with renal dysfunction and proteinuria, myeloma is part of the differential diagnosis. However, in myeloma, even though the majority of protein in the urine may be albumin (owing to tubular damage caused by light chains), one would expect to see some light chains. In this patient who has no light chains in the urine and only a small monoclonal serum protein spike, the chance of finding myeloma is very small and, in these clinical circumstances, one might have chosen not to do a marrow examination. The diagnosis of myeloma requires finding plasma cells occupying one half of a high power field. While this extent of marrow involvement can occur with only moderate elevations of serum immunoglobulins, IgG levels of greater than 3000 mg/dL or IgA levels greater than 2000 mg/dL often are seen at the time of diagnosis in patients with myeloma. Neither of these criteria is met in this case. Despite the presence of anemia, renal dysfunction, and a monoclonal protein, the working diagnosis is not myeloma but MGUS.
3. **(D) Neither myeloma nor MGUS.** Although the patient has a lytic lesion showing plasma cells and a monoclonal serum spike, there is no evidence of multiple lesions and the bone marrow is normal. As a result, this patient does not meet the criteria for myeloma. The lytic lesion with a pathologic fracture is incompatible with MGUS. The diagnosis for the case patient is solitary plasmacytoma of bone. Unfortunately, even when the work-up for myeloma is negative, approximately 70% of patients with “solitary plasmacytoma of bone” eventually prove to have multiple myeloma when followed over time. In contrast, the majority of patients with solitary soft tissue plasmacytoma (eg, involving the nasopharynx) do not progress to myeloma and may be cured by local radiation therapy.
4. **(A) Myeloma.** This patient has classic myeloma with lytic lesions, a monoclonal protein spike, and increased plasma cells in the bone marrow. Additionally, there is renal dysfunction. Of note, there is no serum monoclonal spike, only a urine monoclonal spike. Approximately 60% of patients with myeloma have a serum IgG lambda or kappa spike, 20% have an IgA lambda or kappa spike, and 20% have only a light chain spike. Myelomas associated with IgD or IgE or nonsecretory myelomas are very rare. Because free light chains have a low molecular weight, they generally are not seen in the serum, only the urine. For the case patient, the initial treatment would include a combination chemotherapy regimen (ie, vincristine, doxorubicin, dexamethasone) with the aim of producing at least a good partial response. The standard approach today is to follow chemotherapy with an autologous stem cell transplantation; however, this approach is not curative. Additionally, most patients with myeloma receive a bisphosphonate, such as pamidronate or zoledronic acid, to decrease the risk of fractures.

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HEMATOLOGY

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